View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by White Rose Research Online

This is a repository copy of *A systematic review of the clinical effectiveness and cost-effectiveness of pharmacological and psychological interventions for the management of obsessive–compulsive disorder in children/adolescents and adults*.

White Rose Research Online URL for this paper:
https://eprints.whiterose.ac.uk/132727/

Version: Published Version

Article:
Churchill, Rachel orcid.org/0000-0002-1751-0512, Skapinakis, Petros, Caldwell, Deborah et al. (1 more author) (2016) A systematic review of the clinical effectiveness and cost-effectiveness of pharmacological and psychological interventions for the management of obsessive–compulsive disorder in children/adolescents and adults. Health Technology Assessment. ISSN 2046-4924

https://doi.org/10.3310/hta20430

Reuse
Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown
If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

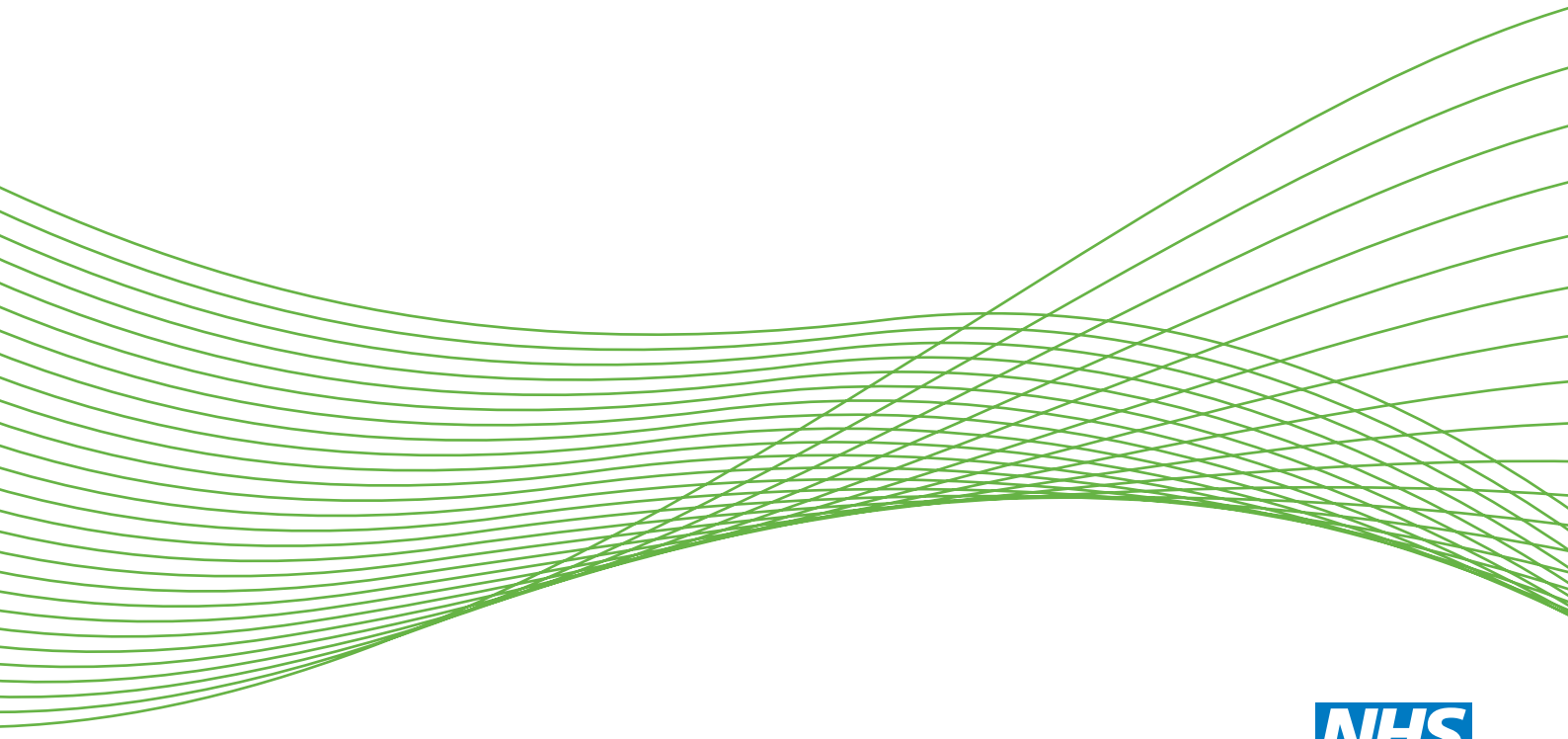
eprints@whiterose.ac.uk
https://eprints.whiterose.ac.uk/

HEALTH TECHNOLOGY ASSESSMENT

VOLUME 20 ISSUE 43 JUNE 2016
ISSN 1366-5278

A systematic review of the clinical effectiveness and cost-effectiveness of pharmacological and psychological interventions for the management of obsessive–compulsive disorder in children/adolescents and adults

Petros Skapinakis, Deborah Caldwell, William Hollingworth, Peter Bryden, Naomi Fineberg, Paul Salkovskis, Nicky Welton, Helen Baxter, David Kessler, Rachel Churchill and Glyn Lewis



NHS
National Institute for Health Research

DOI 10.3310/hta20430

A systematic review of the clinical effectiveness and cost-effectiveness of pharmacological and psychological interventions for the management of obsessive–compulsive disorder in children/adolescents and adults

Petros Skapinakis,[1]* Deborah Caldwell,[2] William Hollingworth,[2] Peter Bryden,[2] Naomi Fineberg,[3] Paul Salkovskis,[4] Nicky Welton,[2] Helen Baxter,[2] David Kessler,[2] Rachel Churchill[5] and Glyn Lewis[1]

[1]Division of Psychiatry, University College London, London, UK
[2]School of Social and Community Medicine, University of Bristol, Bristol, UK
[3]University of Hertfordshire and Hertfordshire Partnerships Mental Health Trust, Hatfield, UK
[4]Department of Psychology, University of Bath, Bath, UK
[5]Centre for Reviews and Dissemination, University of York, York, UK

*Corresponding author

Declared competing interests of authors: Professor Glyn Lewis is a board member of the National Institute for Health Research (NIHR) Efficacy and Mechanism Evaluation programme. Dr Naomi Fineberg reports grants and non-financial support from NIHR during the conduct of the study; grants, personal fees, non-financial support and other from Lundbeck (Copenhagen, Denmark); grants and personal fees from GlaxoSmithKline (London, UK); non-financial support from Novartis (Basel, Switzerland); other from Transcept Pharmaceuticals (Boston, MA, USA); grants, personal fees, non-financial support and other from Servier (Suresnes, France); grants, non-financial support and other from Cephalon (Frazer, PA, USA); grants and personal fees from AstraZeneca (London, UK); personal fees and non-financial support from the European College of Neuropsychopharmacology (Utrecht, the Netherlands); grants from the Medical Research Council (London, UK); grants from the Wellcome Foundation (London, UK); personal fees, non-financial support and other from Jazz Pharmaceuticals (Dublin, Ireland); personal fees and non-financial support from Bristol-Myers Squibb (New York, NY, USA); non-financial support and other from the Royal College of Psychiatrists (London, UK); non-financial support from Janssen (Beerse, Belgium); non-financial support from International College of Obsessive Compulsive Spectrum Disorders; non-financial support and other from British Association for Psychopharmacology, non-financial support from the Journal of Behavioural Addiction; and non-financial support from World Health Organization (Geneva, Switzerland) outside the submitted work, and is medical lead to a NHS service that provides treatment for treatment-refractory obsessive–compulsive and related

disorders, has been a Council member for the British Association for Psychopharmacology and sits on the Royal College of Psychiatrists Psychopharmacology Special Committee and the European College of Neuropsychopharmacology Education Committee and Research Network. Dr Deborah Caldwell reports grants from Medical Research Council Population Health Scientist fellowship (G0902118) during the conduct of the study.

Published June 2016
DOI: 10.3310/hta20430

This report should be referenced as follows:

Skapinakis P, Caldwell D, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, *et al*. A systematic review of the clinical effectiveness and cost-effectiveness of pharmacological and psychological interventions for the management of obsessive–compulsive disorder in children/adolescents and adults. *Health Technol Assess* 2016;**20**(43).

Health Technology Assessment is indexed and abstracted in *Index Medicus*/MEDLINE, *Excerpta Medica*/EMBASE, *Science Citation Index Expanded* (SciSearch®) and *Current Contents®*/ Clinical Medicine.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 5.027

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the ISI Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: nihredit@southampton.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the *Health Technology Assessment* journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

The HTA programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

For more information about the HTA programme please visit the website: http://www.nets.nihr.ac.uk/programmes/hta

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 10/104/41. The contractual start date was in November 2012. The draft report began editorial review in November 2014 and was accepted for publication in July 2015. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).

Health Technology Assessment Editor-in-Chief

Professor Hywel Williams Director, HTA Programme, UK and Foundation Professor and Co-Director of the Centre of Evidence-Based Dermatology, University of Nottingham, UK

NIHR Journals Library Editor-in-Chief

Professor Tom Walley Director, NIHR Evaluation, Trials and Studies and Director of the EME Programme, UK

NIHR Journals Library Editors

Professor Ken Stein Chair of HTA Editorial Board and Professor of Public Health, University of Exeter Medical School, UK

Professor Andree Le May Chair of NIHR Journals Library Editorial Group (EME, HS&DR, PGfAR, PHR journals)

Dr Martin Ashton-Key Consultant in Public Health Medicine/Consultant Advisor, NETSCC, UK

Professor Matthias Beck Chair in Public Sector Management and Subject Leader (Management Group), Queen's University Management School, Queen's University Belfast, UK

Professor Aileen Clarke Professor of Public Health and Health Services Research, Warwick Medical School, University of Warwick, UK

Dr Tessa Crilly Director, Crystal Blue Consulting Ltd, UK

Dr Peter Davidson Director of NETSCC, HTA, UK

Ms Tara Lamont Scientific Advisor, NETSCC, UK

Professor Elaine McColl Director, Newcastle Clinical Trials Unit, Institute of Health and Society, Newcastle University, UK

Professor William McGuire Professor of Child Health, Hull York Medical School, University of York, UK

Professor Geoffrey Meads Professor of Health Sciences Research, Health and Wellbeing Research and Development Group, University of Winchester, UK

Professor John Norrie Health Services Research Unit, University of Aberdeen, UK

Professor John Powell Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), UK

Professor James Raftery Professor of Health Technology Assessment, Wessex Institute, Faculty of Medicine, University of Southampton, UK

Dr Rob Riemsma Reviews Manager, Kleijnen Systematic Reviews Ltd, UK

Professor Helen Roberts Professor of Child Health Research, UCL Institute of Child Health, UK

Professor Jonathan Ross Professor of Sexual Health and HIV, University Hospital Birmingham, UK

Professor Helen Snooks Professor of Health Services Research, Institute of Life Science, College of Medicine, Swansea University, UK

Professor Jim Thornton Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

Please visit the website for a list of members of the NIHR Journals Library Board:
www.journalslibrary.nihr.ac.uk/about/editors

Editorial contact: nihredit@southampton.ac.uk

Abstract

A systematic review of the clinical effectiveness and cost-effectiveness of pharmacological and psychological interventions for the management of obsessive–compulsive disorder in children/adolescents and adults

Petros Skapinakis,[1]* Deborah Caldwell,[2] William Hollingworth,[2] Peter Bryden,[2] Naomi Fineberg,[3] Paul Salkovskis,[4] Nicky Welton,[2] Helen Baxter,[2] David Kessler,[2] Rachel Churchill[5] and Glyn Lewis[1]

[1]Division of Psychiatry, University College London, London, UK
[2]School of Social and Community Medicine, University of Bristol, Bristol, UK
[3]University of Hertfordshire and Hertfordshire Partnerships Mental Health Trust, Hatfield, UK
[4]Department of Psychology, University of Bath, Bath, UK
[5]Centre for Reviews and Dissemination, University of York, York, UK

*Corresponding author p.skapinakis@gmail.com

Background: Obsessive–compulsive disorder (OCD) is a relatively common and disabling condition.

Objectives: To determine the clinical effectiveness, acceptability and cost-effectiveness of pharmacological and psychological interventions for the treatment of OCD in children, adolescents and adults.

Data sources: We searched the Cochrane Collaboration Depression, Anxiety and Neurosis Trials Registers, which includes trials from routine searches of all the major databases. Searches were conducted from inception to 31 December 2014.

Review methods: We undertook a systematic review and network meta-analysis (NMA) of the clinical effectiveness and acceptability of available treatments. Outcomes for effectiveness included mean differences in the total scores of the Yale–Brown Obsessive–Compulsive Scale or its children's version and total dropouts for acceptability. For the cost-effectiveness analysis, we developed a probabilistic model informed by the results of the NMA. All analyses were performed using OpenBUGS version 3.2.3 (members of OpenBUGS Project Management Group; see www.openbugs.net).

Results: We included 86 randomised controlled trials (RCTs) in our systematic review. In the NMA we included 71 RCTs (54 in adults and 17 in children and adolescents) for effectiveness and 71 for acceptability (53 in adults and 18 in children and adolescents), comprising 7643 and 7942 randomised patients available for analysis, respectively. In general, the studies were of medium quality. The results of the NMA showed that in adults all selective serotonin reuptake inhibitors (SSRIs) and clomipramine had greater effects than drug placebo. There were no differences between SSRIs, and a trend for clomipramine to be more effective did not reach statistical significance. All active psychological therapies had greater effects than drug placebo. Behavioural therapy (BT) and cognitive therapy (CT) had greater effects than psychological placebo, but cognitive–behavioural therapy (CBT) did not. BT and CT, but not CBT, had greater effects than medications, but there are considerable uncertainty and methodological limitations that should be taken into account. In children and adolescents, CBT and BT had greater effects than drug placebo, but differences compared with psychological placebo did not reach statistical significance. SSRIs as a class showed a trend for superiority over drug placebo, but the difference did not reach statistical

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

significance. However, the superiority of some individual drugs (fluoxetine, sertraline) was marginally statistically significant. Regarding acceptability, all interventions except clomipramine had good tolerability. In adults, CT and BT had the highest probability of being most cost-effective at conventional National Institute for Health and Care Excellence thresholds. In children and adolescents, CBT or CBT combined with a SSRI were more likely to be cost-effective. The results are uncertain and sensitive to assumptions about treatment effect and the exclusion of trials at high risk of bias.

Limitations: The majority of psychological trials included patients who were taking medications. There were few studies in children and adolescents.

Conclusions: In adults, psychological interventions, clomipramine, SSRIs or combinations of these are all effective, whereas in children and adolescents, psychological interventions, either as monotherapy or combined with specific SSRIs, were more likely to be effective. Future RCTs should improve their design, in particular for psychotherapy or combined interventions.

Study registration: The study is registered as PROSPERO CRD42012002441.

Funding details: The National Institute for Health Research Health Technology Assessment programme.

Contents

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

List of tables

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

List of figures

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

List of abbreviations

BLOCS	Brown Longitudinal Obsessive–Compulsive Study
BT	behavioural therapy
CBT	cognitive–behavioural therapy
CCDAN	Cochrane Collaboration Depression, Anxiety and Neurosis
CCDANCTR	Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Registers
CEAC	cost-effectiveness acceptability curve
CG	clinical guideline
CI	confidence interval
CrI	credible interval
CT	cognitive therapy
CYBOCS	Children's Yale–Brown Obsessive–Compulsive Scale
DIC	deviance information criterion
DIS	diagnostic interview schedule
DSM	*Diagnostic and Statistical Manual of Mental Disorders*
ECA	Epidemiologic Catchment Area
EQ-5D	European Quality of Life-5 Dimensions
ERP	exposure and response prevention
FDA	Food and Drug Administration
GP	general practitioner
ICD-10	*International Classification of Diseases*, Tenth Edition
MD	mean difference
NEMESIS	NEtherlands MEntal health Survey and Incidence Study
NICE	National Institute for Health and Care Excellence
NMA	network meta-analysis
NMB	net monetary benefit
OCD	obsessive–compulsive disorder
OR	odds ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSR	psychiatric status rating
PSSRU	Personal Social Services Research Unit
QALY	quality-adjusted life-year
RCT	randomised controlled trial
SD	standard deviation
SF-6D	Short Form questionnaire-6 Dimensions
SSRI	selective serotonin reuptake inhibitor
WHO	World Health Organization
YBOCS	Yale–Brown Obsessive–Compulsive Scale

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Plain English summary

Obsessive–compulsive disorder (OCD) is a medical condition that affects 1–1.5% of the general population. It can begin in childhood. Several psychological therapies and drugs have been found to reduce symptoms and increase quality of life. Few studies, however, have directly compared these treatments. The current project assessed all treatment options for this condition. It aimed to establish if available treatments work equally well, taking into account their costs. Our review included 86 studies involving a total of over 8000 patients. In adults, we found that all treatments produced better results than an inactive pill. Specific psychological therapies were also more effective than non-specific therapy. Combinations of both drugs and therapy were also more effective than an inactive pill. Behavioural therapy and cognitive therapy showed a greater effect than drugs. However, there are many uncertainties regarding this difference. In children and adolescents, specific psychological therapies had greater effects than an inactive pill. The differences with non-specific psychological treatment or drugs were smaller. We may need to take into account the costs of treatments and the long-term results to make the best treatment options available. The findings of this review generally support the previously published guidelines on the management of OCD.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Scientific summary

Background

Obsessive–compulsive disorder (OCD) is the fourth most common mental disorder in the UK and ranks 10th in the World Health Organization's leading causes of disability worldwide. The course of the disorder is usually chronic and may lead to considerable disability without treatment. Despite its prevalence, the disorder is under-recognised and undertreated. The total costs of OCD have been estimated, in the USA, to be US$8.4B in 1990, which is 5.7% of the estimated US$147.8B cost of all mental illness and 18.0% of the costs of all anxiety disorders. Specific information on indirect and total costs of OCD and the cost-effectiveness of alternative treatments is limited in the UK and elsewhere.

Objectives

The main aim of this review was to determine the clinical effectiveness, acceptability and cost-effectiveness of pharmacological and psychological interventions for the treatment of OCD.

More specifically, the aims were the following:

1. to undertake a systematic review of the clinical effectiveness and acceptability of pharmacological and psychological interventions for the treatment of OCD in all age groups
2. to perform a network meta-analysis (NMA) of all randomised evidence (both direct and indirect), with the aim to rank all treatments in terms of efficacy and acceptability
3. to develop a probabilistic economic model of alternative treatments (pharmacological and psychological) for the management of OCD in order to evaluate the relative cost-effectiveness of these treatments.

Methods

Search methods and inclusion criteria

We searched the Cochrane Collaboration Depression, Anxiety and Neurosis Group Controlled Trials Registers from inception to 31 December 2014. Reports of trials for inclusion in the Group's registers are collated from routine searches of MEDLINE, EMBASE and PsycINFO, the Cochrane Central Register of Controlled Trials and review-specific searches of additional databases. A systematic review of economic evaluations of pharmacological and psychological interventions in OCD was also conducted using standard methods for evidence synthesis.

Only randomised controlled trials were eligible for inclusion. Studies that focused exclusively on treatment-refractory patients were not included. Active pharmacological interventions included any antidepressant medication with some serotonergic properties. Active psychological interventions included behavioural therapy (BT) (exposure and response prevention), cognitive–behavioural therapy (CBT) and cognitive therapy (CT). We used a standard methodology for data extraction.

Outcomes

For the clinical effectiveness analysis, we used the severity of OCD symptoms at the end of study or the change in symptoms from baseline as measured by the Yale–Brown Obsessive–Compulsive Scale in adults or the Children's Yale–Brown Obsessive–Compulsive Scale in children and adolescents. For the acceptability analysis, we used the total dropout rates. For the cost-effectiveness analysis, the model evaluated the cost-effectiveness of pharmacological interventions, psychological interventions and combinations of both from a NHS perspective.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Data synthesis

Pairwise analyses and NMAs were conducted in a Bayesian framework using OpenBUGS version 3.2.3 (members of OpenBUGS Project Management Group; see www.openbugs.net). Pairwise meta-analyses were conducted in a single model, assuming independent treatment effects and a shared heterogeneity parameter. In the NMA program code, we incorporated an additional class hierarchy, such that interventions with a similar mechanism of action were grouped together in a class in which pooled effects might be assumed to be 'similar'. Random-effects models were used, accounting for the correlation between trial-specific effects in multiarm studies. Vague priors were used for all parameters. We report the relative effectiveness of each treatment compared with every other treatment, as well as the probability that each treatment is the most effective on each outcome.

For the cost-effectiveness analysis, we developed a decision-analytics model to evaluate the cost-effectiveness [cost per quality-adjusted life-year (QALY) gained] of pharmacotherapies, psychological interventions and combinations of both from a NHS perspective over a 5-year time frame. All active interventions that were included in the NMA were compared in the model. We elected to evaluate selective serotonin reuptake inhibitors (SSRIs) at the class level in the cost-effectiveness analysis. In total, the cost-effectiveness of eight interventions in the adult model and five interventions in the children/adolescent model were compared. The model comprises a decision tree covering the initial response to treatment at 12 weeks and a Markov model to simulate the course, costs and outcomes (utilities) of OCD from 12 weeks to 5 years. The model draws on evidence from the NMA to inform the probability of response (full, partial and no response) and dropout during the initial 12 weeks. Initial pharmacological and psychological therapy costs are estimated based on data on mean daily dose and total number of therapist contact hours provided in the trials identified by the systematic review. Longer-term mortality, symptom course and NHS costs and utilities were estimated based on epidemiological and economic studies identified through reviews of the literature. The model uses probabilistic analysis to quantify the stochastic uncertainty around estimates of cost-effectiveness. The importance of parameter and structural uncertainty is also tested through a series of deterministic sensitivity analyses. The cost-effectiveness of each intervention is summarised using the net benefit statistic at thresholds of £20,000 and £30,000 per QALY gained. The probability that each intervention is the most cost-effective at a range of willingness-to-pay thresholds (£0–50,000 per QALY) is summarised using cost-effectiveness acceptability curves.

Results

Systematic review

A total of 1083 abstracts were screened and 86 studies reported in 85 papers were included in the review (64 in adults and 22 in children and adolescents), involving 8611 randomised patients (7306 adults and 1305 children and adolescents). In the total sample, 23 different interventions were tested in 194 arms. In adults, interventions with more studies were clomipramine ($n = 17$), fluvoxamine ($n = 16$) and BT ($n = 15$), whereas in children and adolescents CBT ($n = 9$), fluoxetine ($n = 4$), clomipramine ($n = 4$) and sertraline ($n = 4$) were the most frequently studied treatments. Regarding quality, the majority of the studies did not describe adequately the random sequence generation and the allocation sequence concealment. In the adult subset, $< 50\%$ of the trials reported results based on the intention-to-treat principle. Studies of clomipramine and studies of psychological interventions only were more likely to report completers' analysis. In addition, several studies with psychological arms have used waitlist controls and, therefore, these comparisons were unblinded from the patient's perspective.

Network meta-analysis

Clinical effectiveness in adults

A total of 54 studies were included in this analysis, involving 6652 randomised patients. All active interventions, apart from venlafaxine and hypericum, had a greater effect on symptom reduction than drug placebo. Regarding the pharmacological interventions, SSRIs as a class had greater effects than placebo [class effect mean difference (MD) –3.49, 95% credible interval (CrI) –5.12 to –1.81] with small differences between them. There was a trend for clomipramine to have a greater effect than SSRIs, but the 95% CrI included the null value. Regarding the psychological interventions, all active psychotherapies had greater effects than drug placebo; BT and CT had the largest effects and small differences were observed between them (class effect MD –1.12, 95% CrI –1.95 to 4.19 for the comparison between BT and CT). Regarding the comparison between psychological interventions and psychological placebo, both BT and CT had greater effects (MD –10.33, 95% CrI –13.38 to –7.29 and MD –9.21, 95% CrI –13.10 to –5.34, respectively) but the effect of CBT was not significantly different from psychological placebo (MD –1.22, 95% CrI –5.54 to 3.03). Regarding the comparison between psychological and pharmacological interventions, both BT and CT had greater effects than SSRIs as a class or clomipramine. The difference with CBT was smaller and the 95% CrI included the null value. Combinations of medications and psychotherapy showed large effects compared with drug placebo, with small differences between the effects of psychotherapy as monotherapy. In terms of ranking, BT and CT were the two best treatments, followed by combinations of drug and psychotherapy, CBT and clomipramine. Sensitivity analyses for incomplete outcome data showed that the effect of clomipramine and CT may have been overestimated, because most of the studies reported completers' analyses.

Clinical effectiveness in children and adolescents

Seventeen studies were included in the analysis, involving 991 randomised patients. CBT and BT had greater effects than drug placebo. Compared with psychological placebo, both therapies, and especially CBT, showed a non-significant trend for a greater effect. SSRIs as a class showed a non-significant trend for a greater effect compared with drug placebo. Individual SSRIs, however, reached marginal statistical significance. Compared with SSRIs as a class, both psychological therapies (BT and CBT) showed a non-significant trend for a greater effect. Similar results were found for clomipramine. It should be noted that a limitation of the CBT trials is that, in four of the seven included studies, the control group was the waitlist (unblinded comparison), and in such studies the effect of CBT was larger than in CBT trials that did not use the waitlist as the control. The combination of sertraline with CBT was associated with the largest effect compared with drug placebo, but compared with CBT as monotherapy, the combination had similar effects. These results should be interpreted with caution owing to the use of the waitlist control in CBT trials. Sensitivity analyses gave results with similar trends.

Acceptability

All active interventions except clomipramine showed good tolerability in adults compared with placebo. In children and adolescents, BT showed a non-significant trend towards worse tolerability, but this finding was based on two small trials. CBT in children and adolescents showed very good tolerability, and the combination of sertraline with CBT was ranked first in acceptability.

Cost-effectiveness analysis

The selection of the most cost-effective therapy for adults or children and adolescents with OCD is not clear-cut. In both populations, the most effective therapies were also among the more expensive therapies; there is a trade-off between the higher upfront costs of psychological therapies and the potential for them to improve outcomes and reduce long-term costs of care. In the primary economic evaluation in adults, psychological therapies, specifically CT and BT, had the highest probability of being most cost-effective at the conventional National Institute for Health and Care Excellence (NICE) thresholds (£20,000–30,000 per QALY) and above. CBT had a low probability of being cost-effective in adults at all cost-effectiveness thresholds. This was predominantly because of the substantially lower estimated effect size of CBT compared with CT and BT and the higher intensity and, therefore, cost of CBT evaluated in randomised

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

controlled trials. At lower willingness-to-pay thresholds (< £10,000 per QALY), pharmacotherapy had a relatively high probability of being cost-effective.

There is substantially less trial evidence in children and adolescents. Of the five interventions compared, SSRIs had the highest probability of being most cost-effective at lower willingness-to-pay thresholds (< £15,000 per QALY). At the conventional NICE thresholds (£20,000–30,000 per QALY) and above, CBT or CBT combined with a SSRI was more likely to be cost-effective.

Discussion

These results confirm previously published guidelines, based on direct evidence only, that a range of pharmacological and psychological interventions is effective in the short-term management of OCD. One of the advantages of the present analysis is that the use of a NMA allows the simultaneous comparison of multiple competing treatments in a single statistical model, even if treatments have not been directly compared. As there was no imbalance in the presence of potential effect modifiers, we can assume that there was no inconsistency between the direct and indirect sources of evidence.

The results of the NMA show that all active psychotherapies, in particular BT in adults and CBT in children and adolescents, had greater effects than drug placebo. CT in adults also showed a large effect compared with BT, but it is worth noting that this therapy had very few direct links with other interventions apart from BT, and the evidence is mainly based on completers' analyses. CBT in adults showed a small effect compared with the other two psychotherapies and its effect was not statistically significantly different from that of psychological placebo. In children and adolescents, CBT had a large effect, but a limitation is that most of the trials have used a waitlist control, and in these studies the effect of CBT was higher than in studies that used other control treatments.

Selective serotonin reuptake inhibitors had very good tolerability, but their effect in adults, although larger than that of drug placebo, was worse than that of psychotherapies. It should be pointed out that the majority of the psychotherapy trials included patients with stable medication use (mainly SSRIs) but who met diagnostic criteria for OCD and the severity of whose disease was above the cut-off point for inclusion in the study. It is likely that this may have influenced the results in favour of psychotherapies. In addition, there is evidence that longer-term treatment with medications may have beneficial effects over and above the effects reported in the short term. It should also be noted that several psychotherapy trials have used waitlists as their control and, therefore, the patients receiving the active intervention were not blinded to treatment. In children and adolescents, the effect of SSRIs as a class was non-significant, although individual drugs (sertraline and fluoxetine) were marginally more effective than drug placebo. The combination, however, of sertraline with CBT had the largest effect, which was comparable to the combination of drug placebo and CBT.

In adults, clomipramine showed a non-significant trend for superiority over SSRIs, but the exclusion of studies with completers' analysis attenuated this difference. However, clomipramine was associated with worse tolerability. Therefore, the results of the present analysis support the recommendation for the use of clomipramine as a second-line pharmacological treatment.

Combinations of medications with psychotherapies showed large effects that are comparable to psychotherapy monotherapies (although, as mentioned previously, most of the included patients in 'monotherapy' arms were also taking stable doses of SSRIs or clomipramine). Tolerability of the combinations was generally good and was excellent in children and adolescents.

The results of the economic evaluation reflect considerable uncertainty from many different sources. Results are sensitive to assumptions about the sustainability of treatment effects beyond the initial treatment period and exclusion of trials at high risk of bias.

Conclusions

The results of this review support a range of effective options, both pharmacological and psychological, for the management of OCD in all age groups. Regarding the relative effectiveness, our review highlighted the great uncertainty surrounding the published randomised evidence. Although specific psychological interventions were found to have larger effects than medications, there are important methodological limitations that need to be taken into account in future research before a final decision can be made. Regarding cost-effectiveness, current recommendations are not inconsistent with the evidence synthesised in this report, but, depending on the assumptions, economic implications between interventions may arise. Future randomised controlled trials should improve methods of investigating the relative effectiveness of pharmacological versus psychological interventions or combinations of them and take into account issues of blinding in psychotherapy trials.

Study registration

This study is registered as PROSPERO CRD42012002441.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Chapter 1 Background

Description of the health problem

Descriptions of obsessive–compulsive symptoms have been reported since the late medieval period, mainly in relation to religious or moral issues.[1] Several nineteenth- and early twentieth-century physicians showed great interest in these phenomena, including Carl Westphal in 1877 [who used the term 'Zwangsvorstellung' to describe obsessive–compulsive disorder (OCD)], Julius Donath in 1897 (who invented the term 'anancasmus' from the Greek word of the same root meaning 'to compel') and Pierre Janet in 1906 (who associated the symptom of obsessions with the 'psychasthenic' condition).[2] By 1906, the term 'Obsessional Insanity' had been included in the 'Nomenclature of Diseases' of the Royal College of Physicians in London, and Emil Kraepelin included in his textbooks the similar condition of 'Zwangsneurose'.[2] It is interesting that all the main symptoms of the current description of OCD have been described very accurately in the past, including the egodystonic nature of obsessions, the presence of both obsessions and compulsions in the majority of patients, the preservation of insight (the 'folie avec conscience' – insanity with insight – of the French psychopathologists), the accompanying anxiety, the common comorbidity with depression, the chronic and fluctuating course, and the tendency of patients to hide their symptoms and not seek help from doctors.

Diagnostic criteria: disease classification

The first two versions of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) of the American Psychiatric Association were heavily influenced by the psychodynamic concepts of mental illness and defined obsessive and compulsive phenomena accordingly. In the first edition (DSM-I), the term 'Obsessive Compulsive Reaction' was used; the term 'reaction' referred to the way in which a person reacts to unconscious intrapsychic conflicts using defence mechanisms.[3] This was classified under the broader category of 'Psychoneurotic Disorders'. In the second edition (DSM-II), the term 'Obsessive Compulsive Neurosis' was used.[4] Next editions of the manual abandoned the effort of classifying mental disorders in accordance with aetiology and adopted an atheoretical model based on descriptive phenomenology and empirical research. This was mainly done to increase the reliability of psychiatric diagnosis. The World Health Organization (WHO) followed along the same path and published clinical descriptions and specific diagnostic criteria for research.[5] From 1980 (DSM-III) to 2000, when the fourth edition of DSM was published (DSM-IV), there were few differences in the conceptualisation of OCD.[6] The disorder is classified under the broad category of 'Anxiety Disorders' and the two main characteristics are the presence of either obsessions or compulsions. Obsessions are defined as recurring and persistent thoughts, images or impulses that are intrusive and inappropriate and cause much distress and anxiety. Owing to their content, the patient tries to resist and control these thoughts or to suppress the resulting anxiety with compulsions. These are repetitive behaviours or mental acts that may aim to reduce the anxiety brought on by the obsession or that the person feels driven to perform in accordance with a rigid sequence or idiosyncratic rules. Quite often, these behaviours are not connected in a realistic way with what they aim to neutralise or prevent, or they are clearly excessive. In order for these symptoms to be considered clinically significant, they should have a considerable impact on the everyday functioning of the individual.

In the latest edition of the DSM (DSM-V),[7] there have been some slight changes to the definition of the disorder, some of the most important of which are the following:

(a) OCD has been separated from the broader category of 'Anxiety Disorders' and it is now described under the category of 'Obsessive–Compulsive and Related Disorders' which also includes body dysmorphic disorder, hoarding disorder, trichotillomania and excoriation disorder.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

(b) It is acknowledged that there is a spectrum of insight and that some patients may have absent insight or 'delusional' beliefs. Therefore, in DSM-V insight is coded as 'good/fair' (obsessions are recognised as excessive and abnormal ideas), 'poor' (obsessions take the form of overvalued ideas) or 'absent' (obsessions share some characteristics with delusions). An absent insight does not preclude the diagnosis of OCD. As Leckman *et al.*[8] point out, it is assumed that patients with currently absent insight have shown some insight in the past during the course of their disorder.
(c) Hoarding disorder is now a separate disorder and not a subtype of OCD.
(d) A form of OCD related to chronic tics is now included as a new subtype, as there is evidence that this subtype has a younger age at onset and different treatment response.[8]
(e) The definition of OCD according to the *International Classification of Diseases*, Tenth Edition (ICD-10), is very similar to that of the DSM, with slight and not essential differences.[8]
(f) The ICD-10 does not include separate definitions of obsessions and compulsions but the emphasis is placed on their shared characteristics.
(g) The DSM implies that obsessions and compulsions have a functional relationship (in the sense that compulsions are behaviours that aim to reduce the distress caused by the obsessions), whereas the ICD does not suggest such a connection.

Form and content of obsessions and compulsions

Previous studies of the phenomenology of OCD have described both the form and the content of obsessions and compulsions. Khanna *et al.*[9] described the following forms for obsessions (in order of frequency): fears, thoughts, doubts, urges, convictions and images; and, for compulsion: repeating, rituals, checking and avoiding.

The thematic content of obsessions and compulsions has been described in detail by Rasmussen and Eisen[10] and Foa *et al.*[11] Rasmussen and Eisen[10] have used data from their large cohort of 560 OCD patients (diagnosed in accordance with DSM-III or DSM-III-R criteria), whereas Foa *et al.*[11] reported data from 425 patients with OCD (in accordance with DSM-IV criteria). Although there are some differences between these two studies, it is generally accepted that common themes of obsessions are (all figures from Foa *et al.*[11]) worries about dirt/contamination (40%), aggressive obsessions (25%), content related to sexual or religious themes (12%), need for symmetry (10%), somatic/hypochondriac concerns (7%) and unacceptable urges (4%). In the Rasmussen and Eisen[10] cohort, pathological doubt (regarding responsibility for a terrible event) was the second most common content, reported in 40% of patients (this theme is related to aggressive ideas or harm-related content in the Foa *et al.*[11] study). Regarding compulsions, common themes include checking (28%), cleaning/washing (27%), repeating/counting (13%), mental rituals (11%), ordering/symmetry compulsions (6%) and hoarding-related compulsions (4%).

Given that there may be a functional relationship between obsessions and compulsions, some studies have investigated the structure of symptoms using the statistical techniques of factor or cluster analysis. Recently, Bloch *et al.*[12] carried out a meta-analysis of all studies that used factor-analytic methods to investigate the symptom structure of the most commonly used symptom scale, the Yale–Brown Obsessive–Compulsive Scale (YBOCS) ($n = 21$ studies involving 5124 participants). They concluded that four distinct factors explained 79% of the variance in the total sample: (1) a symmetry factor, which included symmetry obsessions and ordering, repeating and counting compulsions; (2) a factor associated with 'forbidden' thoughts, which included aggressive, sexual and religious obsessions; (3) a cleaning factor, including dirt/contamination obsessions and cleaning compulsions; and (4) a hoarding factor. The results were quite similar in both the children and adolescents and adults subsamples.

Although most patients have a main/primary theme for their obsession or compulsion, it is not uncommon to report other themes of milder intensity or frequency.[9] Mataix-Cols *et al.*[13] investigated the longitudinal stability of symptoms in 117 adult patients and concluded that symptoms were quite stable at 2 years' follow-up and that shifts between symptom dimensions were relatively rare.

Phenomenological differences between the two genders

The phenomenological differences between the two genders have been recently reviewed by de Mathis *et al.*[14] Men are younger at onset, and this is sometimes associated with the presence of chronic tics and a worse prognosis. Most phenomenological studies conclude that men are more likely to develop obsessions with a sexual/religious theme, whereas women more often develop dirt/contamination obsessions and cleaning compulsions.[15,16] Some studies also report that symmetry/ordering obsessions are more common in men,[15,17] whereas in women the presence of obsessions (either fears or impulses) with an aggressive content may be more common.[15,18]

Phenomenology in children and adolescents

Obsessive–compulsive disorder may start very early in childhood,[19] and it is interesting to investigate differences in the presentation of symptoms between children and adults. Geller *et al.*[20] compared symptom dimensions in a sample of 101 patients aged < 18 years, including a subsample of children ($n = 46$) and a subsample of adolescents ($n = 55$), and compared this with a reference adult patient sample previously reported in Rasmussen and Eisen.[21] Regarding obsessions, they reported significant differences between both the children and adolescents samples and the adults sample as regards the presence of aggressive/catastrophic obsessions (less common in the adult sample) and sexual/religious obsessions (which were more common in the adolescent sample). In addition, they reported that confessing/asking compulsions were more common in children. Similar studies have also confirmed that contamination obsessions and washing/cleaning compulsions are very common in children and adolescents.[22,23]

Measurement of disease severity

Several instruments have been developed to assess symptom severity in OCD. These include both clinician-administered interviews and self-report questionnaires (or parent report in the case of the paediatric population). Grabill *et al.*[24] included four clinician-administered instruments and 10 self-report questionnaires in their review of this issue.

Of the clinician-administered instruments, the YBOCS[25] is the most widely used instrument to assess symptom severity and is considered the gold standard in OCD literature, especially to assess change in symptoms after treatment.[26] This is a semistructured clinician-administered instrument assessing the severity and frequency of obsessions and compulsions. It yields three scores, an obsessions severity score, a compulsions severity score and a total score (ranging from 0 to 40 for the total). Good psychometric properties have been reported for both clinical and non-clinical samples of patients.[24] A cut-off score of 16 is often used in clinical trials for patients to be eligible for inclusion in a study. This score distinguishes patients with moderate-to-severe symptoms from patients with mild or subclinical symptoms and has demonstrated good sensitivity.[26] Other versions of the YBOCS include a self-report version[26] and a modified version (YBOCS-II)[27] to take into account more recent research on the phenomenology of OCD. An adaptation of the same scale for children and adolescents has been also developed, the Children's Yale–Brown Obsessive–Compulsive Scale (CYBOCS),[28] which has been used extensively in paediatric OCD trials. Studies of the factor structure of the YBOCS have generally confirmed the existence of two factors (severity of obsessions and severity of compulsions), although a third factor of resistance has been replicated in some studies.[24,29]

Aetiology

Obsessive–compulsive disorder is a complex neuropsychiatric disorder, and several genetic, biological and psychological factors may have an important role in the aetiology of the condition. Although aetiological research in the OCD field is very active, the clinical heterogeneity and complexity of the disorder have resulted in the limited translational capacity of basic research into clinical practice.[30]

Genetic factors

Family studies among relatives of both adults and children and adolescents with OCD have consistently shown that OCD is familial and that the risk of OCD is higher in first-degree relatives of patients. For example, in the Pauls *et al.* study,[31] the rate of OCD in relatives of patients was significantly higher than in

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

controls (10.3% vs. 1.9%). Similar results were reported by Nestadt *et al.*[32] (11.7% vs. 2.7%). Studies in children have reported an even higher familial association, with odds ratios (ORs) ranging from 12 to 30.[33–35]

Although family studies point to a possible genetic aetiology in OCD, twin studies are more suitable to distinguish between genetic and environmental factors. Adoption twin studies have not been conducted in the OCD field[36] and, therefore, most twin studies have compared the concordance rates in monozygotic versus dizygotic twin pairs. van Grootheest *et al.*[36] reviewed these studies and a meta-analysis of all available twin studies has been published more recently.[37] The conclusion of these studies is that approximately 40% of the variance in OCD can be explained by additive genetic factors, whereas 50% of the variance can be explained by non-shared environmental factors. Surprisingly, shared environmental factors (e.g. parental style or practices) were not associated with phenotypic variance.

Genetic linkage studies and the two published genome-wide association studies have been recently reviewed by Pauls *et al.*[33] The genetic linkage studies have identified two genomic regions (on chromosomes 9 and 15) that may be associated with an increased risk of OCD. Given that OCD is most probably a multigenic disorder, genetic linkage studies have limited power to identify multiple genes with a small-to-moderate effect. Genome-wide association studies may be more suitable, but the results of two such studies are inconclusive. It has been suggested that larger samples may be needed for the results to reach genome-wide significance.[33]

Taken together, findings from genetic research support the hypothesis that multiple genes, regulating parts of the serotonergic, dopaminergic and glutamatergic systems, may be related to an increased vulnerability to OCD, but non-shared environmental factors also play an important part in the development of the disorder.

Biological factors

There is a consensus, mainly due to functional imaging studies, that a dysregulation in the frontostriatal circuit is involved in the pathophysiology of OCD.[33] Studies have consistently shown an increased activation of the orbitofrontal and possibly the anterior cingulate cortex, and an hyperactivity of the head of the caudate nucleus. Increased activation of the caudate leads, through a positive feedback loop, to an increase in the excitatory glutamatergic output from the thalamus to the frontal cortex.[33] This results in exaggerated worries about danger, despite direct evidence from the senses that contradict this danger.[33,38] Recent experimental studies in animals using the technique of optogenetics have shown that repeated stimulation of the orbitofrontal cortex and the ventromedial striatum generates a progressive increase in compulsive behaviours in animals (e.g. increased grooming) that is reversed by the chronic, but not acute, administration of fluoxetine.[39]

Psychological factors

The psychological model of OCD postulates that patients interpret their unwanted intrusive thoughts (obsessions) in a maladaptive way. Salkovskis[40] suggested that faulty appraisals related to inflated responsibility are very important. Apart from inflated responsibility, other maladaptive appraisals include the overimportance of thoughts, the need to control those thoughts and the exaggerated estimate of the probability that an unwanted event will occur (thought–action fusion).[41] These appraisals lead to anxiety and the need to engage in neutralising behaviours (such as compulsions, avoidance and reassurance seeking) to prevent harm. Compulsions are positively reinforced because they reduce the anxiety caused by the faulty appraisals in the short term. However, in the long term they prevent habituation and fear extinction from happening and thereby help in the maintenance of obsessions. Therefore, compulsive behaviour is considered as a maladaptive response to obsessions. Based on these theories, both cognitive–behavioural therapy (CBT) and behavioural therapy (BT) [exposure and response prevention (ERP)] have been successfully used for the treatment of OCD.

Epidemiology

Prevalence in adults

The descriptive epidemiology of OCD has been recently reviewed by Fontenelle *et al.*[19] and Torres and Lima.[42] Before 1980, the prevailing view was that OCD is a relatively severe but rare psychiatric disorder. This view was mainly based on the frequently cited 1953 study by Rudin,[43] which estimated a prevalence of 0.05% in the general population.[10] However, even in this early period, which preceded modern diagnostic criteria, some studies showed a different situation for OCD prevalence. Among them, the careful psychiatric epidemiological study by Brunetti,[44] in the small community of Roussillon in south-east France, reported a higher prevalence of 1%, which is a figure very close to estimates in more recent studies. The view that OCD is a rare disease changed after the large American epidemiological study of the 1980s, the Epidemiologic Catchment Area (ECA) study.[45] This study used a fully structured diagnostic interview, designed to be used by lay interviewers, and included OCD in the assessment. The OCD data were analysed by Karno *et al.*[46] They reported a lifetime prevalence for OCD in adults of 2.5% and a 6-month prevalence of 1.5%, which was considerably higher than previous estimates. Prevalence of OCD was higher in women than in men (with a ratio of 1 : 4). The diagnostic interview schedule (DIS) that was used for the assessment has been criticised for its inability to assess reliably anxiety and phobic disorders.[47] Nelson and Rice[48] in a subsequent study examined the stability of the OCD diagnosis in the ECA data set using longitudinal data from the second wave, 12 months after the baseline measurement. They found that 80% of the participants who met lifetime criteria for OCD at baseline did not meet the same criteria at the second assessment. A clinical revalidation of OCD diagnosis in a subset of the ECA study showed a prevalence of clinically validated OCD of 0.3%, which was considerably lower than the DIS assessment.[47] Similarly, in a German study,[49] the lifetime prevalence in accordance with the DIS was 2%, whereas according to clinicians it was 1%. More recent epidemiological studies using the Composite International Diagnostic Interview have resulted in a much broader range of prevalence rates of OCD in adults, from 0.9% lifetime prevalence in the Netherlands[50] to 3% 1-month prevalence in Canada.[51] In this Canadian study, a clinical revalidation of the data resulted in a lower prevalence of 0.6%, whereas another 0.6% of patients met criteria for 'subclinical' OCD. According to the authors,[51] the differences between the results of the diagnostic interviews and clinicians' diagnoses are attributable to the following factors: (1) common or everyday worries are sometimes confused with obsessions in diagnostic interviews; and (2) it is likely that epidemiological interviews may overestimate the intensity or frequency of obsessions or compulsions.

Apart from DIS and the Composite International Diagnostic Interview, other studies have used the revised Clinical Interview Schedule and the Mini International Neuropsychiatric Interview. In one study,[52] the 1-month prevalence with the revised Clinical Interview Schedule was 1.1%. In Italy, Faravelli *et al.*[53] reported a lifetime prevalence of 2.4% using the Mini International Neuropsychiatric Interview. In Greece, Skapinakis *et al.*[54] reported a 1-month prevalence of 1.7% using the revised Clinical Interview Schedule.

There is great variability in the estimation of the prevalence of OCD in the general population and this is partly explained by the different samples and methodologies used. Taking into account the majority of the studies, a conservative estimate of the lifetime prevalence of OCD, using diagnostic interviews in the general population, is approximately 2%, and the 1- to 6-month prevalence is between 1% and 1.5%. These estimates would be reduced by approximately half if clinicians had been involved in the assessments.

Prevalence in children and adolescents

The prevalence of OCD in children and adolescents has been investigated in several studies either in the general population or in more selected samples (e.g. school-based surveys). Of the general population studies, three are particularly useful as a result of their large samples or their representativeness: (1) a British study[55] in a nationally representative sample of 10,000 children aged 5–15 years, which reported a low prevalence of current OCD at 0.2%; (2) a US study[56] in a sample of 4500 children aged 9, 11 and 13 years, which also reported a 3-month prevalence of 0.2%; and (3) a study from the Netherlands[57] in a nationally representative sample of 2916 adolescents aged 13–18 years, which reported a 6-month prevalence of 1%. It is worth noting that in both the Dutch study[57] and in another community study in the

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

USA,[58] the authors found that relying solely on parents' reports of symptoms may underestimate the true burden of OCD symptoms. This is especially relevant for studies of children < 12 years old, in which it is less likely that children will be directly asked to report their symptoms.

Incidence

The incidence of OCD has been studied less than the prevalence. A review by Fontenelle *et al.*[19] reported four studies in adults with an annual incidence ranging from 0.05% to 0.7%. The two most prominent studies are (1) a longitudinal study undertaken in the USA using a subset of the original ECA study[59] which specifically investigated the incidence of OCD; and (2) a longitudinal extension of the NEtherlands MEntal health Survey and Incidence Study (NEMESIS).[60] The former reported an incidence of 0.55 per 1000 person-years (approximately 0.05% per year), whereas the latter reported an incidence of 0.2% per year.

Regarding children and adolescent samples, a school-based study conducted in the USA among 488 adolescents aged 13–15 years[61] reported an annual incidence of OCD of 0.7% [95% confidence interval (CI) 0.12% to 1.34%].

Prevalence differences between men and women

Most studies conducted in the general population have shown a higher prevalence in women than men, with the female-to-male ratio ranging between 1.2 and 3.8 in several studies.[42,62] In one British study,[52] the ratio was 1.44. These findings show that the clinical observation that the number of women in clinical samples far outweighs the number of men is not the result of help-seeking bias.

Regarding children and adolescents, most studies in non-clinical samples seem to support a 1 : 1 ratio for prevalence in boys and girls,[55,61,63] although there are some studies reporting a higher prevalence for boys.[64,65] In clinical samples, there is an excess of boys, possibly owing to younger age at onset and more severe symptomatology.[62,63]

Socioeconomic status

Fontenelle and Hasler,[62] in their review of the analytical epidemiology of OCD, mention several studies that have shown a positive association between a higher socioeconomic status or education and OCD. However, other studies did not confirm this, or found a negative association (e.g. the study by Torres *et al.*[52]). It can be concluded from these studies that OCD, in contrast to other psychiatric disorders, displays no clear social gradient, although there is even a small possibility of a mild positive association. Regarding employment status, in most studies, individuals with OCD are more likely to be unemployed or economically inactive,[46,52,62] although this possibly reflects the generally negative association of the common mental disorders with employment status and is not specific to OCD. A similar observation can be made for marital or family status: individuals with OCD are more likely to be unmarried or to live alone, as is common for all other mental disorders.[62]

Comorbidity

Several studies with clinical samples have confirmed that OCD is often comorbid with other psychiatric disorders.[66–68] In most clinical studies, the most common comorbidity is mood disorders, a finding that is compatible with the view that patients with OCD will often seek help from a mental health specialist when they develop depression or some other psychiatric disorder. The reported prevalence of comorbid disorders differs from study to study depending on the methodology and the time frame used (e.g. 1 month, 1 year, lifetime). In a Dutch sample of 420 outpatients with OCD,[67] 24% had comorbid current depression/dysthymia and 13% had any anxiety disorder [most often social phobia (3.6%) and panic disorder (2.6%)]. These figures are much higher than the reported prevalence in the general population. One study reported that alcohol use disorders in patients with OCD were less common than in the general population.[67] Another study from the USA, which included 334 outpatients from the adult OCD clinic at the National Institute of Mental Health,[66] assessed the lifetime prevalence of comorbid disorders. Approximately 66% of patients had experienced major depression at some time in their lives, whereas one in four had experienced social phobia, panic disorder or dysthymia. It is worth noting that in this cohort, lifetime

alcohol dependence was high, at 25%. In women, the prevalence of eating disorders was increased (26% of the sample). Data from the Brown cohort[68] showed that a minority of patients (< 10%) had not experienced any other disorder in their life. As reported elsewhere, depression was the most common comorbid condition (67% lifetime prevalence and 15% current episode). Other common diagnoses in this cohort were social phobia (28% lifetime, 19% current), panic disorder (18% lifetime, 7% current) and alcohol dependence (23% lifetime, 4.5% current). Eating disorders were also common in this cohort (10% lifetime prevalence for the entire sample).

Studies conducted in the general population have confirmed that these patterns of comorbidity are not the result of help-seeking bias. In the British Psychiatric Morbidity Survey,[52] 37% of participants with OCD also met criteria for current depression. In addition, comorbidity with anxiety disorders, such as panic disorder (22%) and social phobia (17%), and with alcohol dependence (33% in men, 11% in women) was particularly high. In the replication study of the National Comorbidity Survey in the USA,[69] participants who met criteria for OCD had an increased lifetime prevalence for other mood and anxiety disorders (40% for depression, 44% for social phobia, 20% for panic disorder, 38% for alcohol dependence). These figures are very similar to those reported from the first large epidemiological survey of OCD in the US general population, the ECA study.[46]

The association of OCD with bipolar disorder has attracted research interest over the past decade. Several studies have reported that OCD patients have a lifetime history of bipolar disorder, mainly type 2 bipolar disorder (bipolar II), with prevalence rates that are much higher than in the general population (up to 15% in some samples[70]). Conversely, an OCD history is often reported in patients with bipolar disorder (up to 35% in a German study[71]). In a recent review of this issue,[72] it is pointed out that there are disagreements between studies regarding the extent of this comorbidity. For example, in a French study that included mainly type 1 bipolar disorder (bipolar I) patients,[73] history of OCD was quite low (at 3%), in contrast to histories of panic disorder and phobic disorders, which were higher (16% and 11%, respectively).

The relationship between obsessive–compulsive symptoms and psychotic disorders in general, or schizophrenia in particular, has been noted since the early twentieth century,[74,75] but only recently has this association been studied more systematically.[72] A recent meta-analysis of this topic identified 37 studies that aimed to estimate the prevalence of OCD in patients with schizophrenia and related disorders.[76] This analysis reported a mean OCD prevalence of 12.3% (95% CI 9.7% to 15.4%), which is much higher than that of the general population. Obsessive–compulsive symptoms were even more common. Eisen *et al.*,[77] in a study that used a very careful methodology, reported that the prevalence of OCD in 77 patients with psychotic disorders (schizophrenia, $n = 52$; schizoaffective disorder, $n = 25$) was 7.8% (6/77 patients). It is worth noting, however, that five of these six patients with OCD had schizoaffective disorder (5/25, 20%) and only one had schizophrenia (1/52 patients, 1.9%). Another interesting study from the Netherlands, among patients with first-episode psychosis or at ultra-high risk for developing psychosis,[75] reported that the prevalence of OCD was 1.5%, whereas that of obsessive–compulsive symptoms not meeting full diagnostic criteria for OCD was 9.3%. The authors note that these figures are very similar to those reported from general population samples. The prevalence of both the disorder and the symptoms was lower in those patients who met criteria for schizophrenia rather than schizophreniform or schizoaffective disorders. No significant differences were found between the time of onset of obsessive–compulsive symptoms prior to or after the onset of the first episode of psychosis. OCD did not precede the onset of psychosis in patients with both disorders. These findings are compatible with the view that obsessive–compulsive symptoms may be either prodromal symptoms of first-episode psychosis or a secondary side effect of antipsychotic medications.[75] Studies that have investigated the presence of psychotic symptoms among patients with OCD are few. In the Brown cohort,[78] 6% of OCD patients had a comorbid psychotic disorder (4% schizophrenia; 2% delusional disorder). In NEMESIS,[79] the presence of obsessive–compulsive symptoms at baseline predicted the onset of psychotic symptoms at follow-up and vice versa. From these studies, it is concluded that although there seems to be an association between symptoms of OCD and psychotic disorders, this association is bidirectional and complex.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Suicidality

In the past, OCD was considered a relatively rare condition,[19] with a low risk for suicide, at least compared with other mental disorders.[80,81] More recent studies, however, have changed this view. In Brazil, a large clinical study of outpatients with OCD ($n = 582$) found that 11% of the sample had attempted suicide at least once in their lifetime.[81] Studies in unselected samples of the general population have confirmed these findings. In the UK, a history of suicide attempt was reported by 26% of the participants who met criteria for OCD, compared with 14.5% of those with other common mental disorders, a statistically significant difference.[52] These studies were cross-sectional and assessed suicidality retrospectively. There are few longitudinal studies that have reported suicidal behaviour. In a prospective clinical study in Spain,[82] 218 outpatients with OCD were followed up for a mean duration of 4 years. Two patients (0.9%) committed suicide and 11 (5%) attempted suicide. Risk factors for suicidal behaviour were the presence of symmetry/ordering obsessions and the initial severity of depressive symptoms. In NEMESIS,[83] the cumulative incidence of suicide attempts in participants with OCD, after 3 years' follow-up, was 0.4%, a very low figure compared with other common mental disorders and the lowest among the anxiety disorders. Incidence of suicidal behaviour was also low in a meta-analysis that used data from patients who had participated in randomised controlled trials (RCTs) submitted to the US Food and Drug Administration (FDA).[84] In that analysis, the annual incidence of suicide attempts in OCD patients was approximately 1.47% (1468/100,000 per year) and the suicide rate was 0.11% (105/100,000 per year). It is worth noting that these figures were comparable with the other anxiety disorders covered in this analysis and significantly lower compared with the figures for depression (2.9% and 0.8%, respectively) that have been reported in a separate paper with the same methodology.[85]

In conclusion, the results of these studies show that suicide risk in OCD is higher than in the general population by a factor of 10 or more, but is comparable to risk in popuations with other anxiety disorders. It is lower than the risk associated with depression, but it should be pointed out that, because OCD is often comorbid with depression, the incidence in real clinical practice might be higher. In a secondary analysis of the NEMESIS sample, for example, the suicide risk (either attempt or ideation) was higher in participants who met criteria for both depression and anxiety disorders.[86]

The study of suicidal behaviour in child/adolescent OCD samples is not so extensive. A recent study of 54 patients aged 7–17 years from a tertiary centre in the USA[87] reported that 13% of the sample ($n = 7$) had clinically significant suicidal ideation during the past month. Significant associations were found with the presence of symmetry/ordering obsessions and obsessions of sexual or religious content, with increasing age and with the presence of depressive symptoms.

Natural history: prognosis

Historically, OCD was considered a disorder with a poor prognosis. This view was challenged by the seminal study of Pollitt.[88] Pollitt's study used a very strict methodology in a period in which there was no specific form of treatment other than leucotomy (with uncertain effects). To avoid any possible treatment effects of this procedure, Pollitt presents his results on the course of OCD separately for patients with or without leucotomy. According to this study, the longitudinal course of the illness was good: complete remission was observed in 24% of the patients after a mean duration of follow-up of 3.4 years (range 0.5–15 years), whereas 36% had a mild illness (i.e. 60% of the patients had a benign course). A study conducted in Sweden by Skoog and Skoog[89] included 144 patients with OCD who were examined by one of the authors between 1954 and 1956 by means of a semistructured clinical interview. The patients were re-examined by the same researcher after 40 years using the same methodology. Rates of complete remission (20%) were comparable to those in the Pollitt study,[88] whereas 28% of patients had mild symptoms at follow-up. Therefore, in this study almost half of the patients had a good course.

With the advent of new and effective treatments in the 1980s [BT/CBT, clomipramine and selective serotonin reuptake inhibitors (SSRIs)], it is interesting to review longitudinal studies of the prognosis of OCD in patients who received such treatments. Two such studies have been published recently. Bloch *et al.*[90] investigated the longitudinal course of illness (10–20 years) in 83 patients with OCD who

participated in clinical trials in their centre (Yale). The authors reported that 20% of the sample experienced complete remission, whereas another 30% experienced partial remission. Almost half of the patients still had symptoms that would make them eligible for inclusion in a new clinical trial (a score on the YBOCS of $\geq$ 16). It is worth noting that 70% of these patients were receiving medication at follow-up and approximately half had received BT or CBT at some point in their lives (after the baseline assessment). Similar results were reported in the study of the Brown cohort that included 213 patients with OCD.[91] Complete remission at 5 years' mean follow-up was observed in 17% of the sample, whereas partial remission was observed in 22% of patients. This study also assessed the rates of relapse after partial or complete remission, which were quite high (59%). In another study from Italy, which included 55 outpatients with OCD treated with SSRIs, the rates for complete and partial remission at 3 years' follow-up were 22% and 34%, respectively.[92]

The main conclusion that can be drawn from the above discussion is that remission rates in the modern era have not improved compared with those reported in earlier studies[88,89] despite the wide availability of effective treatments. It is difficult, however, to interpret this finding, as changes in diagnostic preferences or criteria may have resulted in non-comparable groups of patients being selected for inclusion in these studies.

Regarding the factors that are associated with a poor prognosis, several studies report that an early onset, more severe initial symptoms, a longer duration of illness and comorbidity with depression are all associated with a poor prognosis.[89,92–95] In the Brown cohort,[91] patients with primary hoarding obsessions/compulsions had a worse prognosis with very low remission rates, whereas patients with primary obsessions regarding an inflated sense of responsibility for harm had a better prognosis. In the Yale cohort,[90] an initial good response to SSRIs was a good prognostic factor. In other studies, the presence of schizotypal[92] or obsessive–compulsive personality disorder[91] was associated with a poor prognosis.

The long-term prognosis of OCD in children and adolescents has been reviewed by Stewart *et al.*,[96] who included 16 studies from various settings. Stewart *et al.*[96] report a mean remission of 40% after a mean duration of 5.7 years' follow-up. When including partial remission, this rate is increased to 59%. Focusing on the studies that have used non-clinical samples, the remission rate is even higher, at 74%. Some more recent studies from the USA[97,98] and the UK[99] have also been published. The results of more recent studies are similar to those seen in the Stewart *et al.* review,[96] despite the use of selected samples from tertiary centres. In the Yale cohort,[98] 58% of the patients had complete remission after a mean follow-up duration of 9 years. In the Maudsley cohort,[99] approximately 60% of the patients had at least a partial remission after 5 years' mean follow-up. From these findings it can be concluded that remission rates in children and adolescents may be higher than those in adults. Regarding factors associated with a poor prognosis, the following have been reported: duration of illness,[96,99] early onset[96] and presence of hoarding obsessions/compulsions.[98] A better prognosis has been reported in patients with chronic tics[98] and in patients who showed a good initial treatment response.[96]

Impact on quality of life and functioning

As a chronic disorder, OCD can have a severe impact on everyday functioning and quality of life. Two systematic reviews have recently investigated the published literature on this issue.[100,101] Most studies have used clinical samples and compared several dimensions of quality of life in OCD and other psychiatric disorders, chronic physical disorders and the general population. Fewer studies have used non-selected samples in the community,[101,102] but these have confirmed that OCD, even in individuals living in the community who have not made contact with services, can have a detrimental effect on quality of life compared with the healthy population. In a study in Asia, OCD was associated with a worse quality of life than in other common mental disorders.[103] Studies have reported that contact[104] or relationships with family members[103] may be more severely affected in patients with OCD than in patients with other mental disorders.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Most studies in clinical samples have compared quality of life in patients with OCD with that in patients with other mental disorders, chronic physical disorders or population norms. One of the most cited studies that compared the quality of life in patients with depression and anxiety disorders used data from patients who took part in several multicentre RCTs of sertraline.[105] According to this study, patients with OCD had a better overall quality of life compared with patients with depression and comparable to other anxiety disorders, with the exception of post-traumatic stress disorder. Olatunji *et al.*[106] carried out a meta-analysis of 33 studies that examined quality of life in patients with anxiety disorders. Six of these studies focused on OCD and their findings show that OCD is associated with a worse quality of life for patients than for the general population, but other anxiety disorders may have a more harmful effect (e.g. social phobia or post-traumatic stress disorder). In the clinical samples, the dimension of quality of life more severely affected in OCD is the one associated with social relationships.[101]

Some studies have investigated quality of life as a long-term outcome in RCTs of psychopharmacological or psychosocial interventions.[100] These studies have concluded that changes in quality of life can be quite delayed and certainly are not expected in the short term. In the psychopharmacology trials, these changes may become evident after 1 year of continuous treatment.[107] It should be pointed out that because OCD is often comorbid with other disorders, in particular depression, this may lead to further worsening of quality of life and, generally, is an important factor in determining levels of functional impairment.[100]

Studies conducted in child and adolescent samples are limited and assess functional impairment more often than quality of life. It should be noted that these are related but not identical concepts.[108]
Two recent studies have investigated quality of life in children and adolescents with OCD.[108,109] Both confirmed the negative effect of the disorder on the quality of life of patients compared with healthy children. An important factor that predicted a worse quality of life was the presence of comorbid internalising or externalising disorders.

Current service provision

Treatment options

Primary care

General practitioners (GPs) encounter patients with a range of OCD severity; milder presentations are not uncommon, although the major influence on people with mental disorders seeking help from their doctor is severity.[110] Many patients who see their GP with OCD symptoms are also suffering from comorbid depression or anxiety. Data from the 2000 British National Psychiatric Morbidity Survey have shown that less than 15% of patients with non-comorbid OCD were receiving any treatment for emotional problems, compared with 56% of patients with comorbid OCD and depression or other anxiety disorders.[52]

In recent years, it has been possible in the UK to refer patients with OCD to the Improving Access to Psychological Therapies service, and this has made both low-intensity and high-intensity CBT interventions more widely available. The National Institute for Health and Care Excellence (NICE) Clinical Guideline (CG) 31 states that low-intensity treatments, including ERP of up to 10 therapist hours per patient, are offered to those with milder degrees of functional impairment. This intervention includes brief self-help materials and may include group CBT. Those who do not respond to this or who find it difficult to engage are often treated with a SSRI. This also can have the benefit of treating coexisting symptoms of depression and anxiety. Although response may be seen fairly quickly for depressive symptoms, it is not uncommon for considerably longer response times to be seen for OCD symptoms, and SSRIs should be given at an adequate dose for at least 12 weeks and perhaps even longer before treatment can be said to be ineffective.[111] In more chronic and severe cases it may be necessary to go on to offer high-intensity individual CBT, including ERP, as well as a SSRI.

Secondary care

Those who do not experience a clinically significant improvement following these treatments are likely to be referred to secondary care for further assessment. Psychiatric services will often offer further CBT or BT and may switch medications from SSRIs to clomipramine.[112] If this is not successful, treatment with an antipsychotic in addition to the antidepressant may be considered.[111,113]

Tertiary care for treatment-refractory patients

In order to be considered treatment refractory, patients are required to score very highly on symptoms scales such as the YBOCS (≥ 30/40) and to have received at least two courses of CBT from an accredited therapist as well as two courses of a SSRI (or one course of a SSRI and one of clomipramine) at maximally tolerated doses as well as one attempt at pharmacological augmentation. Many patients referred to specialised services (usually judged to be at level 5 of the NICE stepped care pathway and, therefore, not eligible for highly specialised services) give a history of not receiving adequate treatment locally, despite high levels of distress and disability. There would appear to be problems in finding suitably trained and experienced clinicians for patients with severe OCD nationwide. OCD is a severe, chronic mental disorder and patients in remission have a high chance of relapse even after specialist care (around 60% over 5 years[91]). Full relapse is associated with major loss in health-related quality of life.[114] Ongoing co-ordinated clinical care from local mental health services is required for long periods to reduce the risks of relapse or to ensure early intervention to prevent full relapse occurring. The need for long-term responsive care in local NHS community services for individuals with OCD needs to be better recognised.

Patients eligible for highly specialised services

In recognition of the high levels of distress and serious functional impairment associated with severe and enduring OCD (and body dysmorphic disorder), patients with severe illness who have not responded to substantial evidence-based treatment with medication or CBT (at level 6 of the NICE stepped care pathway) may be referred for treatment from the highly specialised Obsessive–Compulsive Disorder and Body Dysmorphic Disorder Service commissioned by NHS England (see www.england.nhs.uk/). The aim of the service is to improve the mental health state of both adolescents and adults suffering with the most profound OCD/body dysmorphic disorder, who have failed all previous evidence-based pharmacological and psychological treatments (including home-based treatments). The service provides treatment across the lifespan (children, adolescents and adults), including intensive clinic-based, home-based and inpatient CBT, as well as specialist pharmacotherapy at the following centres:

(a) Hertfordshire Partnership NHS Foundation Trust, Queen Elizabeth II Hospital, Welwyn Garden City, UK (adults)
(b) South London and Maudsley Hospital Anxiety Disorders Residential Unit; Centre for Anxiety Disorders and Trauma (adults); Child and Adolescent OCD Service, London, UK
(c) South West London and St George's NHS Trust, Springfield Hospital (adults), London, UK
(d) The Priory Hospital Adolescent Inpatient Unit, London, UK.

A similar service is available in Scotland from the Advanced Interventions Service located at Ninewells Hospital, Dundee. This service additionally provides specialist neurosurgery for the most extreme cases of severe, refractory mental disorder including OCD (see www.advancedinterventions.org.uk/index.php/the-service).

Current guidelines

Table 1 presents the most recent published guidelines for the management of OCD. The most recent clinical practice guidelines for the pharmacological treatment of OCD have been published by the British Association for Psychopharmacology.[111] The Canadian Anxiety Disorders Association has also published guidelines for both pharmacological and psychological interventions for all anxiety disorders including a separate section for OCD.[115] The American Psychiatric Association had recently updated its previous detailed clinical practice guideline (see http://psychiatryonline.org).[116] The World Federation of Societies of Biological Psychiatry published its guidelines for all anxiety disorders, including OCD, in 2008.[117]

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 1 Recent published guidelines for OCD

Authors, year, country	Organisation	Title	Citation
Baldwin *et al.* 2014, UK[111]	British Association for Psychopharmacology	Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive–compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology	*J Psychopharmacol* 2014;**28**:403–39
Katzman *et al.* 2014, Canada[115]	Anxiety Disorders Association of Canada	Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive–compulsive disorders	*BMC Psychiatry* 2014;**14**(Suppl. 1):1
Koran *et al.* 2007, USA[116]	American Psychiatric Association	Practice guideline for the treatment of patients with obsessive–compulsive disorder	*Am J Psychiatry* 2007;**164**(Suppl. 7):5–53 (an updated supplement of this guideline up to March 2013 by the same authors is also available at: http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd-watch.pdf)
Bandelow *et al.* 2008, worldwide[117]	World Federation of Societies of Biological Psychiatry	World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive–compulsive and post-traumatic stress disorders – first revision	*World J Biol Psychiatry* 2008;**9**:248–312
NICE, 2005, UK[118]	NICE/Royal College of Psychiatrists/British Psychological Society	Obsessive–Compulsive Disorder: Core Interventions in the Treatment of Obsessive–Compulsive Disorder and Body Dysmorphic Disorder CG31	NICE. *Obsessive–Compulsive Disorder: Core Interventions in the Treatment of Obsessive–compulsive Disorder and Body Dysmorphic Disorder CG31*. London: NICE

In addition, NICE published a very comprehensive clinical practice guideline for OCD and body dysmorphic disorder in 2005 (NICE CG31).[118] NICE has recently placed the 2005 OCD guideline on a 'static' list of guidelines that will not be reviewed again within the next 5 years unless there is important new evidence of either efficacy or safety. NICE has also published a quick reference guide, which includes a detailed version of their stepped care model for treating OCD in all age groups (see www.nice.org.uk/nicemedia/live/10976/29945/29945.pdf).

Description of technology under assessment

Medications

Pharmacotherapy with the tricyclic antidepressant clomipramine or a SSRI (paroxetine, fluvoxamine, fluoxetine, citalopram, escitalopram and sertraline) has shown efficacy in OCD.[119] Meta-analyses of seven RCTs of clomipramine[120] and 17 randomised, double-blind placebo-controlled trials of various SSRIs[121] have been performed. The trials were generally short term (i.e. of 4–12 weeks' duration) and showed that all these compounds were superior to placebo. Patients were roughly twice as likely to respond to a SSRI as to placebo. Data on comparisons between different SSRIs and between SSRIs and clomipramine are limited but have shown no significant differences in efficacy. The SSRIs are recommended as the first-line pharmacological treatment for OCD, with clomipramine reserved for those who do not respond to or

tolerate SSRIs, owing to the more favourable adverse event profile.[111,116,118] SSRIs tend to take longer to be effective (between 4 and 12 weeks) when used for OCD than when used for other disorders, such as depression and anxiety. A positive dose–response relationship has been observed with several SSRIs (paroxetine, fluoxetine and escitalopram), and higher doses of SSRI are often required.[116,118,119] Approximately 40–70% of patients respond to a SSRI, but the long-term improvement in total symptom severity is relatively low, averaging 20–40%,[122,123] as is the remission rate, with full remission ranging from approximately 10%[123] to 40%.[124] A long duration of untreated illness,[94] coexisting tic[116] and hoarding symptoms[125] have all been associated with a poorer treatment response to clomipramine and the SSRIs.

The findings of acute treatment studies indicate that the proportion of responding patients increases steadily over time. Long-term (up to 12 months) double-blind RCTs demonstrate an advantage for continuing with medication in patients who have responded to acute treatment.[126,127] A randomised placebo-controlled trial with paroxetine as an active comparator found that a low dosage of escitalopram became efficacious only in the second half of a 24-week study.[124] Most (but not all) placebo-controlled relapse prevention studies in patients who have responded to previous acute treatment reveal a significant advantage for staying on active medication (escitalopram, fluoxetine at higher daily doses, paroxetine and sertraline), compared with switching to placebo, for up to 12 months,[128] but the optimal duration of continuation treatment is uncertain.[129] For these reasons, it is recommended that clinicians continue drug treatment for at least 12 months in patients who have responded to treatment.[111] As approximately 50% of patients with OCD relapse if they discontinue medication after up to 1 year of successful treatment, it is advisable to counsel patients about the risk of relapse prior to drug discontinuation and, if relapse occurs, medication is usually reinstated and continued indefinitely.[130]

Adverse events with medications

Selective serotonin reuptake inhibitors are generally safe and well tolerated, according to the placebo-referenced treatment trials that reported adverse event-related withdrawal rates of approximately 5–15%. As a group, however, SSRIs may cause unwanted nausea, insomnia, somnolence, dizziness and diarrhoea. Sexual side effects include reduced libido and delayed orgasm, and can affect up to 30% of individuals.[131] Fluoxetine has a long half-life and fewer discontinuation effects, which can be advantageous for patients who forget to take their tablets. It has also been extensively used in pregnancy and generally shown to be safe.[132] The recent demonstration of prolongation of the electrocardiogram QT-interval associated with higher dose levels of citalopram (and, to a lesser extent, escitalopram)[133] argues for a degree of caution in using higher doses of these compounds in OCD, especially if individuals are taking other medications that increase the QT interval. However, a recent large study found no elevated risks of ventricular arrhythmia or all-cause, cardiac or non-cardiac mortality associated with citalopram doses exceeding 40 mg per day.[133]

Clomipramine can also be associated with potentially dangerous side effects. Cardiotoxicity and cognitive impairment occur much more often with clomipramine than with SSRIs. In addition, there is an increased risk of convulsions in patients taking clomipramine (up to 2%). Overdose on clomipramine can prove fatal, and this needs to be borne in mind when prescribing for OCD, in view of the elevated suicide risk associated with the illness. Clomipramine is also associated with greater impairment of sexual performance (up to 80% of patients) compared with SSRIs, with weight gain and with troublesome anticholinergic effects.[134]

Suicide in children with obsessive–compulsive disorder receiving selective serotonin reuptakes inhibitors

Meta-analyses examining the effects of SSRIs in children aged 6–18 years have been performed, following warnings from the US FDA that SSRIs in the young may increase the risk of suicidal thoughts and behaviours. A pooled analysis of childhood OCD studies comparing ‘numbers needed to treat’ with those ‘needed to harm’ revealed no suicidal actions and a positive risk ratio for the use of sertraline in children and adolescents with OCD.[135]

© Queen’s Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

In the recent study by Bridge *et al.*,[136] 27 RCTs of SSRIs, of which six were in OCD, were identified. There were no completed suicides. The pooled absolute rates of either suicidal ideation or suicide attempt (treatment vs. placebo) in OCD (1% vs. 0.3%) compared favourably with the pooled absolute clinical response rates (treatment vs. placebo; 52% vs. 32%). The authors concluded that the benefits of SSRIs probably outweigh the risks in the OCD paediatric population, with the doctor–patient relationship playing an important part.

Psychotherapy

The general principles of the psychological model of OCD have been described (see *Aetiology*). Based on this model, a number of psychological treatments have been developed. A comprehensive historical review of these treatments is given by Abramowitz.[137] Two main treatments have been developed, a behaviourally oriented treatment (ERP) and a treatment based on the cognitive model of OCD.[40]

Exposure and response prevention was first described in a clinical setting by Meyer,[138] and the relative success of this method soon replaced other behaviourally oriented methods such as Wolpe's systematic desensitisation.[137] According to Abramowitz,[137] in ERP, first, the patient undergoes prolonged exposure to situations or stimuli that provoke obsessional fears and, second, the patient is advised to refrain from performing the compulsive behaviour (response prevention). Response prevention helps the patient learn that anxiety will eventually decrease on its own over time and also that obsessions are not really dangerous or do have catastrophic consequences.[137] The intensity of the treatment differs, but typical forms of therapy include at least 16 sessions over 8 weeks. Some of the sessions are supervised by the therapist and the patient also practises self-exposure between sessions.[137] Owing to the nature of the treatment, some patients may not tolerate the distress associated with the exposure or they may not be willing to refrain totally from the ritualistic behaviour. Despite the difficulties in applying this treatment, ERP has established its effectiveness both in research and practical settings.[118]

The cognitive model of obsessions is primarily based on the work of Salkovskis,[40] who suggested that, although disturbing, intrusive and unacceptable thoughts (normal obsessions) are experienced by all,[139] patients with abnormal obsessions appraise the intrusions in a pathological way. Salkovskis suggested that such appraisals 'appear to relate specifically to ideas of being responsible for damage or harm coming to oneself or to others'.[40] Compulsions are viewed as efforts by the individual to prevent any harmful consequences or to reduce the unwanted intrusions. Apart from Salkovskis' 'inflated responsibility', other faulty appraisals of intrusions have been described by the Obsessive Compulsive Cognitions Working Group,[140] such as the overimportance of thoughts, the excessive concern about the importance of controlling one's thoughts, the overestimation of threat and the intolerance of uncertainty. Based on the cognitive model, cognitive therapy (CT) that does not require the use of ERP techniques has been developed, although behavioural experiments are used to help patients modify their views about the risks associated with obsessions.[137] CBT for OCD combines both ERP techniques and cognitive restructuring.[137] There is now evidence that both therapies are effective in the management of OCD and have comparable efficacy to ERP with a slightly improved tolerability.[118]

Reasons for conducting this review

Two criteria have been taken into account in order to examine the need for a new review regarding the management of OCD:

(a) the need to update previous systematic reviews and/or meta-analyses, especially if new trials have been conducted since the publication of previous reviews, which could potentially change current recommendations
(b) the need to synthesise existing and updated evidence to answer the questions that matter most to clinicians and patients/carers using, if necessary, previously unavailable methodological techniques.

Although the number of new trials since previously published systematic reviews (e.g. NICE[118]) is relatively small, these were studies that reported direct comparisons between treatments that were not previously available. In addition, previous reviews have focused only on the available direct pairwise comparisons of active (either pharmacological or psychological) versus inactive interventions (drug placebo, waitlists, psychological placebo). Although these comparisons may be suitable for regulatory agencies or to establish efficacy, they may not be equally useful in directing real clinical practice or cost-effectiveness analyses. As a result, previous reviews could not rank the treatments depending on their efficacy or acceptability using all available evidence (both direct and indirect), and their results are inconclusive. Owing to these problems, it has been suggested that evidence for the superiority of a given treatment against another in OCD is absent and that clinicians' or patients' choices are based on preference, side-effect profile for drugs or comorbidity. The present review and economic evaluation aims to fill this gap in the knowledge, by applying appropriate statistical techniques of evidence synthesis that allow the ranking of treatments, taking into account both direct and indirect evidence, and will provide clinicians with a framework for decision-making for the optimum management of patients of all ages with OCD.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Chapter 2 Definition of the decision problem

This review addresses the research question: what is the clinical effectiveness, acceptability and cost-effectiveness of pharmacological and psychological (behavioural or cognitive–behavioural) interventions for the management of OCD?

Decision problem

Population

Children and adolescents, and adults with OCD.

Intervention and relevant comparators

Any antidepressant medication with some serotonergic properties used in the management of OCD (including amitriptyline, imipramine, clomipramine, all SSRIs, all serotonin–noradrenaline reuptake inhibitors, mirtazapine and hypericum), BT (therapy that includes some kind of exposure and/or response prevention), CT or CBT and any drug/psychotherapy combination of these interventions. Comparators included drug placebo, psychological placebo, waitlist and any other comparator from the list of interventions that would allow an indirect comparison with network meta-analysis (NMA).

Outcomes

The primary outcome for effectiveness was the reduction in symptoms of OCD as measured at the end of the study period by the YBOCS scale (or the CYBOCS). The secondary outcome was acceptability, as measured by the total number of dropouts in each intervention arm.

Subgroup analyses

Regarding the preplanned subgroup analyses, where sufficient data were available, metaregression/subgroup analyses were conducted to explore the impact of:

1. publication date
2. length of trial
3. inclusion of patients with comorbid depression
4. pharmaceutical sponsorship of drug trials.

Overall aims and assessment objectives

The main aim of this review was to determine the clinical effectiveness, acceptability and cost-effectiveness of pharmacological and psychological interventions for the treatment of OCD.

More specifically, the aims of this review were to:

1. undertake a systematic review of the clinical effectiveness and acceptability of pharmacological and psychological interventions (behavioural or cognitive–behavioural) for the treatment of OCD in children and adolescents, and in adults
2. use both direct and indirect evidence to simultaneously compare all multiple treatments (pharmacological and psychological) in a single analysis (multiple treatments meta-analysis) with the aim of ranking all treatments in terms of efficacy and acceptability
3. develop a probabilistic economic model of alternative treatments (pharmacological and psychological) for the management of OCD in order to evaluate the relative cost-effectiveness of these treatments.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Chapter 3 Systematic review methods: assessment of clinical effectiveness

Methods for reviewing clinical effectiveness

For this systematic review meta-analysis we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations[141] and the guidelines for conducting systematic reviews reported in the Cochrane Handbook.[142]

The protocol is registered with PROSPERO database number CRD42012002441 and can be accessed at www.crd.york.ac.uk/PROSPERO/display_record.asp?ID = CRD42012002441.

Identification of trials: search strategy

Search dates

We carried out searches between 1 December 2012 and 31 May 2014. A detailed description of the specific search strategy used is given in *Appendix 1*.

Search strategy

Electronic databases

We searched the twin Cochrane Collaboration Depression, Anxiety and Neurosis (CCDAN) Controlled Trials Registers (CCDANCTR). The CCDAN maintain two clinical trials registers at its editorial base in Bristol, UK: a references register (CCDANCTR-References) and a studies-based register (CCDANCTR-Studies). The CCDANCTR-References Register contains more than 27,000 reports of trials in depression, anxiety disorders (including OCD) and other neurotic disorders. Approximately 65% of these references have been tagged to individual, coded trials. The coded trials are held in the CCDANCTR-Studies Register and records are linked between the two registers through the use of unique study identification (ID) tags. Coding of trials is based on the EU-Psi coding manual (see http://psitri.stakes.fi/). Reports of trials for inclusion in the Group's registers are collated from routine (weekly), generic searches of MEDLINE, EMBASE and PsycINFO; quarterly searches of the Cochrane Central Register of Controlled Trials and review-specific searches of additional databases. Reports of trials are also sourced from international trials registers using WHO's trials portal, the International Clinical Trials Registry Platform (see http://apps.who.int/trialsearch/), drug companies, the hand-searching of key journals, conference proceedings and other (non-Cochrane) systematic reviews and meta-analyses. Details of CCDAN's generic search strategies can be found in the 'Specialized Register' section of the Cochrane Depression, Anxiety and Neurosis Group's website.

The CCDANCTR-Studies Register was initially searched (September–December 2012) using the following index terms:

Condition = obsess* or compulsi*

AND

Intervention = (Citalopram or (Clomipramin* or Clorimipramin* or Chlomipramin* or Chlorimipramin*) or Escitalopram or Fluoxetine or Fluvoxamine or Paroxetine or Sertraline or Venlafaxine or Duloxetine or Mirtazapine or SSRI* or Serotonin or cognitive* or behavi* or exposure or "response prevention").

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

The CCDANCTR-References Register was initially searched using a more sensitive set of free-text terms (to identify additional untagged/uncoded reports of trials):

((obsess* or compulsi* or OCD) AND (Citalopram or (Clomipramin* or Clorimipramin* or Chlomipramin* or Chlorimipramin*) or Escitalopram or Fluoxetine or Fluvoxamine or Paroxetine or Sertraline or Venlafaxine or Duloxetine or Mirtazapine or SSRI* or (Serotonin and (uptake or reuptake or re-uptake)) or SNRI* or CBT or cognitive* or behavioral or behavioural or exposure or ERP or "response prevention" or ((*therap* or train* or treatment*) and (behavi* or expos*)))).

As the number of studies retrieved in this initial search was not very large (643 studies), in order to increase the sensitivity of the search we decided to repeat the search using the condition only (obsess* or compulsi*) without any other terms.

Reference checking

The reference lists of all selected studies, as well as the references of previous systematic reviews, meta-analyses and evidence-based guidelines, were additionally inspected for potential studies or reports that had not been identified through our electronic search. We also searched papers that had cited previous meta-analyses or systematic reviews using Google Scholar (Google Inc., Mountain View, CA, USA) to identify potential new studies that had not been identified. No additional records were identified through this source.

Ongoing clinical trials

We also searched the controlled trials registers of the following organisations to identify ongoing studies that could potentially have published preliminary results or reports:

(a) ClinicalTrials.gov
(b) Controlled-Trials.com
(c) WHO's trials portal (International Clinical Trials Registry Platform).

We used the generic term (obsessive or compulsive) for these searches and we filtered the results by condition (OCD) and type of study (controlled intervention). We checked 145 records from https://clinicaltrials.gov, 19 from www.controlled-trials.com and 23 from WHO's portal for ongoing clinical trials.

Abstract appraisal

All abstracts identified through the search process were transferred into a Microsoft Excel® 2013 (Microsoft Corporation, Redmond, WA, USA) spreadsheet and were independently screened for potential inclusion by two reviewers (PS and HB). In cases of uncertainty (or disagreement), the full text was obtained. Abstracts excluded at this stage were not relevant to the present study either because they were observational studies or the interventions were not covered by the report (e.g. if they had investigated lithium, electroconvulsive therapy or repetitive transcranial magnetic stimulation vs. placebo). The full texts of all controlled trials studies that included at least one intervention covered by the report were obtained even if it was clear from the abstract that this should be excluded (e.g. because the comparator intervention was not covered or the patient population was treatment refractory). These studies were excluded at the full-text stage. Similarly, we obtained the full text of studies with special populations of OCD (e.g. hoarding patients) even if these would be excluded at the full-text stage.

Study selection: inclusion and exclusion criteria

Studies were included (or excluded) in accordance with the following criteria:

(a) *Study design*: RCT. Trials with a crossover design were not excluded and we tried to extract all available data up to the point of the crossover. Quasi-randomised trials (such as those allocating by using alternate days of week) were excluded. Owing to the aim of the review, we included trials irrespective of blinding (because otherwise a lot of psychotherapy trials might not be eligible for inclusion). Sensitivity analyses examined the possible effect of unblinded or single-blinded trials.

(b) *Patient population*.

- Age: all patients aged ≤ 74 years (if patients aged ≥ 75 years were included, mean age should be within the range).
- Diagnosis: a primary diagnosis of OCD in accordance with standardised diagnostic criteria (ICD, DSM, Feighner or research diagnostic criteria). Studies that specifically focused on treatment-resistant OCD were excluded. Treatment resistance should have been defined within the study using specific criteria. Most often, studies will have used a first, uncontrolled, treatment phase, in which all patients received the same intervention and the non-responders (usually showing $< 25\%$ reduction in the YBOCS scale) were eligible for the second randomised phase. Studies that had included patients that could be considered refractory to treatment outside the context of the particular study (e.g. because they might have tried medications or other interventions in the past unsuccessfully) were not excluded. It is worth noting that most psychotherapy trials have included patients who were symptomatic despite being stable on medications before entering the study.
- Comorbidities: these will be accepted if OCD was the primary disorder. However, studies that included patients with schizophrenia or bipolar disorder were excluded.
- Diagnostic criteria: the authors should have used established diagnostic criteria to diagnose OCD (either ICD, or any version of DSM, or Research Diagnostic Criteria or Feigner criteria). The method of assessment of these criteria (either through typical clinical examination or use of more formal diagnostic interviews) was not a reason for exclusion.

(c) *Experimental intervention*.

- For pharmacological interventions: any antidepressant medication with some serotonergic properties (including: amitriptyline, imipramine, clomipramine, all SSRIs, all serotonin-noradrenaline reuptake inhibitors, mirtazapine). Studies that have used hypericum were included, whereas other non-standard approaches were excluded (e.g. studies that have used folic acid, herbal medicines other than hypericum, vitamins or omega-3 supplements).
  Studies that had used a mainly noradrenergic medication as the experimental intervention of interest [e.g. reboxetine (Edronax®, Pfizer) or nortriptyline] were excluded.
- For psychological interventions: we included trials that have used as their main intervention (1) BT (therapy that included some kind of exposure and/or response prevention); (2) CBT; or (3) CT (therapy that included some kind of cognitive restructuring intervention). We excluded studies that used therapies based on psychodynamic principles (including interpersonal psychotherapy or other insight-oriented therapies exploring unconscious mental processes), Gestalt therapy, systemic therapy and family therapy. We also excluded studies that used behavioural-type therapies with no exposure component (e.g. behavioural activation, social skills training) and biofeedback as their experimental intervention.

(d) *Comparator intervention*.

- For pharmacological interventions: drug placebo or any other antidepressant with some serotonergic properties, or any other psychotherapy from those eligible (BT, CT, CBT), or other inactive type of therapy considered as 'control'.
- For psychological interventions: any type of psychological placebo (including attention placebo) or non-specific therapy (including supportive therapy), or waitlist/no treatment, or any other BT/CT/CBT type of therapy, or drug placebo, or any other antidepressant with some serotonergic properties.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

(e) *Focus of analysis*: Between-group comparison of treatments should be reported. Studies that report only additional secondary analyses (e.g. predictors of treatment outcome) were excluded. Studies that did not report continuous outcome were not included in the quantitative synthesis.

Study inclusion assessment

Inclusion/exclusion criteria were independently assessed by two reviewers (HB and PS) and validated by one reviewer (PS). The standardised data extraction form (see *Data extraction*) included a section on inclusion/exclusion criteria. This section was transferred to an Excel spreadsheet and we recorded all necessary information for the inclusion or exclusion of studies that had passed through abstract screening. For excluded studies, we noted the main reason for exclusion.

Data extraction

We used a standardised data extraction form to extract detailed information on included studies. This form also included a section on inclusion and exclusion criteria that was used for all studies that passed through the abstract screening. We originally developed this form in a Microsoft Word® 2013 (Microsoft Corporation, Redmond, WA, USA) document format, but to facilitate data extraction, we transferred the various sections of this form into several Excel spreadsheets. All information extracted was directly recorded onto these spreadsheets on a computer.

Initial data extraction was carried out independently by two reviewers (HB and PS). As the agreement between the reviewers was high, one reviewer independently extracted the remaining papers (HB) and a second reviewer (PS) validated the extraction. Potential discrepancies were discussed by the reviewers and, if necessary, by all other collaborators during the meetings.

Data extracted from papers included the following information:

(a) inclusion and exclusion criteria (study design, experimental intervention, control intervention, age range, primary diagnosis, diagnostic criteria, focus of analysis)
(b) details of participants (country, treatment setting, age, diagnostic classification, primary severity scale used, comorbidities)
(c) details of experimental and control interventions
(d) details of continuous outcome (primary scale used, end of treatment follow-up time)
(e) risk-of-bias assessment
(f) results [baseline, end of treatment continuous measures for YBOCS or other primary scale, change from baseline, mean difference (MD) between arms, completers analysis or use of methods for handling missing data such as last observation carried forward]
(g) dropouts (total dropouts per arm).

Risk-of-bias assessment: quality assessment strategy

To assess the methodological quality of included trials we used the criteria for quality assessment recommended by the *Cochrane Handbook for Systematic Reviews of Interventions*.[142] Two reviewers independently assessed and a second reviewer validated these criteria, which mainly focus on descriptions of sequence generation, allocation concealment, blinding, completeness of outcome data and selective outcome reporting, and other potential sources of bias (such as attrition rates). Studies were given a quality rating of 'low', 'unclear' or 'high' risk of bias in accordance with these criteria. If there was disagreement on quality assessment, the final rating was made by consensus with the involvement (if necessary) of another member of the review group. Studies with a high risk of bias were included in the main analysis, but we also examined in a sensitivity analysis the effect of excluding them.

Methods of network meta-analysis

Primary outcome

Pairwise analysis and NMA were conducted for the primary outcomes of reduction in OCD symptoms (as measured by the YBOCS in adults or the CYBOCS in children and adolescents) and for acceptability (as measured by total number of dropouts per study). A NMA is the simultaneous comparison of multiple competing treatments in a single statistical model.[143,144] In exploiting both direct and indirect evidence, a NMA produces estimates of the relative effects of each treatment compared with all others in the network, even if treatments have not been directly compared. It is then possible to calculate the probability of a treatment being better, or worse, for a specific outcome.

Derivation of primary outcome and handling of missing data

For the primary outcome, data are continuous and were reported as either (1) mean scores at baseline and at follow-up for treatment and control groups; or (2) mean change from baseline scores in each group. If both formats were reported, we chose the mean change from baseline score as our preferred summary, which captures correlations in measures within individuals.[145] If mean change from baseline was not reported, we used mean score at follow-up for each group, as this gives an unbiased estimate of treatment effect if randomisation is adequate.[145] If data were missing on either the total number of patients randomised or mean YBOCS/CYBOCS scores, the study was excluded from the quantitative analysis. Where possible, missing standard deviations (SDs) were derived from reported statistics following guidance in the *Cochrane Handbook for Systematic Reviews of Interventions*.[142] If derivation of missing SDs was not possible, they were estimated based on a prediction from a hierarchical model for SDs in those studies that did report them. Here, we assumed that any missing SD is exchangeable (i.e. broadly similar) with the reported SDs. (Further detail and code is available in *Appendix 8*.) For the secondary outcome, data are dichotomous and were extracted on intention-to-treat principles. Any participant dropout that occurred after the point of randomisation was included in our analysis.

Assessment of transitivity

The assumption of transitivity is the crucial starting point for a NMA.[146] Transitivity suggests that intervention A is similar when it appears in A versus B and A versus C studies.[147] It can be examined by comparing the distribution of potential effect modifiers across the different comparisons[148] because if there is an imbalance in the presence of effect modifiers across the A versus B and A versus C comparisons, the conclusions about B versus C may be in doubt.

Study-level characteristics that were considered potential effect modifiers were mean baseline symptom severity, gender, participant age, length of trial follow-up, proportion of participants with concurrent mental illness (depression) and year of trial publication. We examined the study characteristics tables (see *Tables 10* and *11*) and concluded that, with the exception of participant age, the assumption of transitivity was likely to hold across the trials and comparisons. We considered that the assumption may be breached on the basis of participant age, because it would appear that children and adolescents were more likely than adults to be randomised to a psychological therapy. Indeed, of pharmacological treatments, only sertraline and fluvoxamine are licensed for use in patients aged < 18 years in the UK, and NICE also mentions fluoxetine in cases with significant comorbid depression.[118] Therefore, we decided that, contrary to our protocol specification, we would analyse children and adolescents separately to adults.

Pairwise and network meta-analysis

Network diagrams were drawn using Stata version 13 (StataCorp LP, College Station, TX, USA) to ensure that treatments formed a connected network for both outcomes and populations considered.[149] Pharmacological placebo was considered as the reference treatment throughout all analyses.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

All analyses were conducted in a Bayesian framework and were undertaken using OpenBUGS version 3.2.3 (members of OpenBUGS Project Management Group; see www.openbugs.net). Pairwise meta-analyses were conducted in a single model assuming independent treatment effects and a shared heterogeneity parameter.[150] We used the NMA programme code given by Dias *et al.*[145] and modified to incorporate an additional class hierarchy,[151] such that interventions with a similar mechanism of action were grouped together in a class in which pooled effects might be assumed to be 'similar'. This approach allows both the relative effectiveness of the individual treatments and that of the classes to be estimated. On the basis of the systematic review and clinical expertise, it was assumed that only the SSRIs citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline could be considered a 'class' on this criterion. Psychological therapies were analysed as individual treatments. Non-specific psychological therapies ('psychological placebo') were distinguished from waitlist controls. In psychological therapies we did not distinguish between individual or group delivery format. In addition, we did not distinguish treatments based on drug dose or intensity of psychological treatment. (All OpenBUGS code is available in *Appendix 8*.)

Random-effects models were used, accounting for the correlation between trial-specific effects in multiarm studies.[145] Vague priors were used for all parameters, including the prior for within-class variability. Convergence was checked based on two chains using the Brooks–Gelman–Rubin diagnostic plots and visually using history plots available in OpenBUGS. In all cases, the first 50,000 iterations were discarded as 'burn-ins'. Reported estimates are based in the subsequent 100,000 iterations. We report the relative effectiveness of each treatment versus every other treatment and also the probability that each treatment is the most effective on each outcome.

Model fit and assessment of statistical inconsistency

Heterogeneity was assessed by examining the posterior median of the between-studies heterogeneity parameter from the random-effects model. Goodness of fit was measured by the posterior mean of the residual deviance. In a well-fitting model, the residual deviance should be close to the number of data points. Model comparison was based on the deviance information criterion (DIC).[152] A difference of 3 or more points was considered meaningful.[145] A key assumption of NMA is that of consistency between the direct and indirect evidence. To assess inconsistency, we compared the fit of a model assuming consistency with that of a model assuming independent treatment effects.[153] In addition, we also compared the results of the pairwise meta-analysis with the NMA. As a further proxy measure, where the NMA effect estimate did not fall within the 95% credible intervals (CrIs) from the pairwise analysis, we defined these as inconsistent.

Sensitivity analysis and meta-regression

Sensitivity analyses were conducted, excluding studies at high risk of bias on the following domains as defined by the Cochrane Collaboration's risk-of-bias assessment tool:[142]

1. allocation concealment
2. outcome assessor blinding
3. incomplete outcome data
4. studies with high levels of attrition (overall attrition > 25% or differential attrition > 15%).

Separate meta-regressions were also conducted assuming a common interaction term for the following study-level characteristics:

1. length of trial (including follow-up)
2. year of publication of trial
3. pharmaceutical sponsorship of drug trials.

Chapter 4 Results of the systematic review

Quantity of research available

Our initial search of CCDANCTR resulted in 1028 citations. An updated search in March 2014 yielded another 74 citations, bringing the total number of citations from this source to 1102. No additional trials that met the criteria of the review of having a projected end-of-study period before the end of the current project were identified from our search of the registers of ongoing clinical trials. After removing some duplicate entries, a total of 1083 abstracts were initially screened and 905 (84%) were excluded, as they were not relevant to the study aims.

A total of 178 full papers were retrieved as being potentially relevant to the study aims. Sixty-eight of these papers were excluded for one or more reasons (see *Studies excluded*).

Of the remaining 110 papers, 25 papers were assigned to the waiting status for one of the following reasons: (1) article written in Chinese ($n = 17$); (2) article written in Arabic ($n = 1$); (3) congress report with no further publication and no usable data reported ($n = 2$); (4) unable to locate articles in several languages ($n = 1$ in Japanese, $n = 1$ in Turkish and $n = 1$ in German); (5) inconsistent results reported in another publication (thesis) of the same data ($n = 1$, author has been contacted); and (6) unable to decide if paper reports duplicate data with previous publication ($n = 1$, authors have been contacted). A detailed list of the papers that have been assigned to the waiting status can be found in *Appendix 3*.

Eighty-five papers provided data for the analysis of at least one outcome. One paper[154] reported the results of two clomipramine trials and, therefore, the included papers included data on 86 trials. *Figure 1* presents the results of the search in the form of the PRISMA flow chart.

Studies excluded

Sixty-eight papers were excluded from the analysis. A detailed table of the excluded studies and the reasons for exclusion can be found in *Appendix 2*. *Table 2* shows the main reasons for exclusion.

General summary characteristics of the included studies

We included 86 unique studies reported in 85 publications. It can be seen from *Table 3* that 64 studies (74%) were conducted in adult patients, whereas 22 studies (26%) were conducted in child and adolescent samples. The majority of the studies (84%) had only two arms. Approximately half of the studies were conducted after the 2000s and 14% were conducted before the 1990s.

In total, 8611 patients were randomised (7306 adults and 1305 children and adolescents) into 194 arms including 23 different interventions or combinations of interventions. *Table 4* summarises data on the number of randomised patients in arms/studies.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

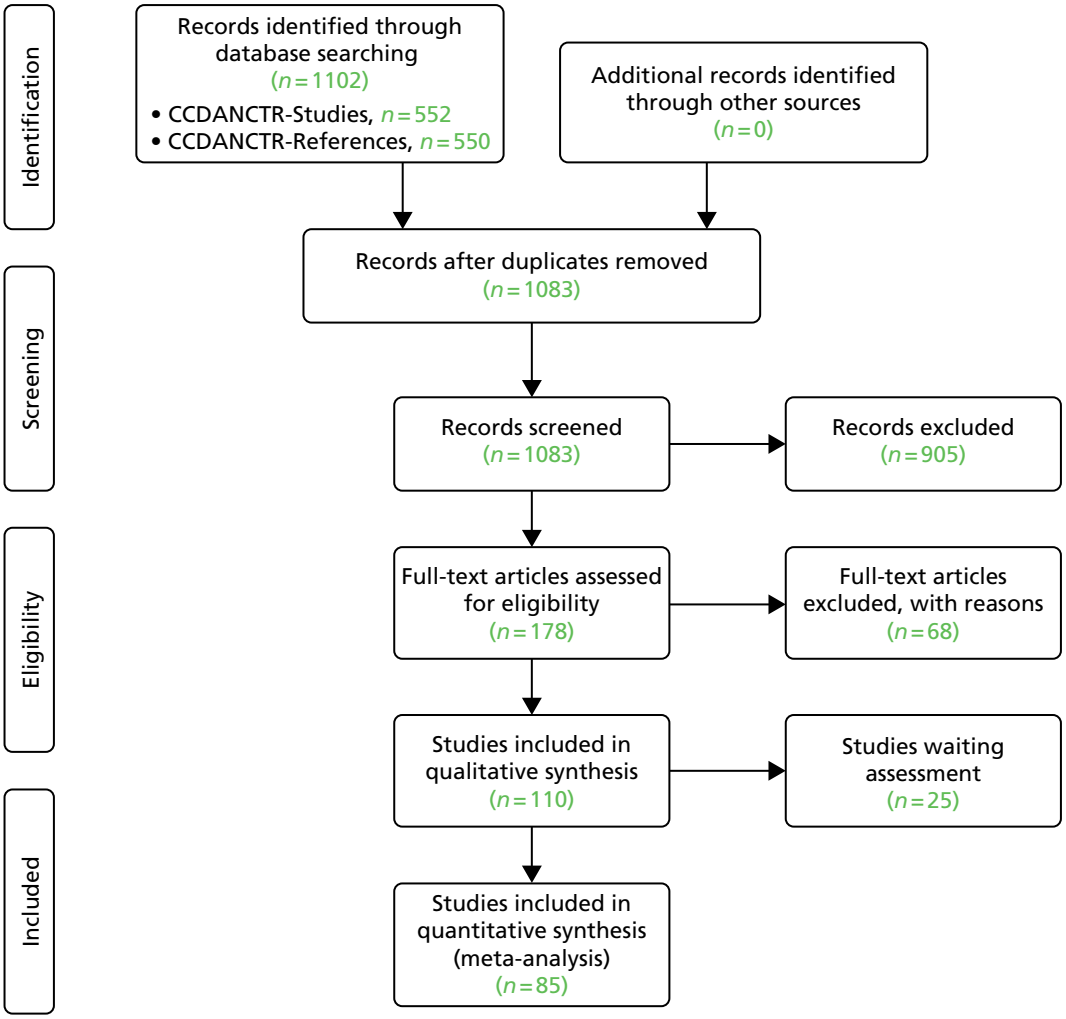


FIGURE 1 The PRISMA flow diagram.[141]

TABLE 2 Main reason for exclusion of studies

Main reason for exclusion	Number of papers
Duplicate publication	17
Control intervention not covered	11
Non-randomised design	10
Data not usable	9
Preliminary congress abstract report	8
Aim of the study not relevant (secondary analyses, relapse prevention studies)	5
Diagnosis not focused on OCD	4
Treatment-refractory patient population	2
Main intervention not covered	2
Total	68

TABLE 3 Number of included studies/arms/patients by age group and date of publication

Characteristics of studies	*n* (%)
Total studies included	86 (100)
Number of studies by age group	
Adults	64 (74)
Children/adolescents	22 (26)
Total number of arms	***194***
Adults	148 (76)
Children/adolescents	46 (24)
Number of studies by number of arms	
Two-arm studies: total	72 (84
Adults	51 (80)
Children/adolescents	21 (95)
Three-arm studies: total	6 (7)
Adults	6 (9)
Children/adolescents	0
Four-arm studies: total	8 (9)
Adults	7 (11)
Children/adolescents	1 (5)
Total patients randomised	***8611***
Adults	7306 (85)
Children/adolescents	1305 (15)
Number of studies by date of publication	
1980–90	12 (14)
1991–2000	32 (37)
2001–14	42 (49)

TABLE 4 Number of patients randomised per study/arm

Type of study	Number of arms	Number of patients	Minimum	Maximum	Mean	SD
Per arm	194 arms	8611	5	241	44	40
Per study/arm						
Two-arm studies	72 studies	5745	10	325	80	72
Three-arm studies	Six studies	789	21	406	131	158
Four-arm studies	Eight studies	2077	29	466	260	155

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Country of publication

Figure 2 presents summary data on the country of publication of included studies. The majority of the studies (52% in total; 48% in adults vs. 66% in children/adolescents) were conducted in North America (33 studies in the USA, eight in Canada and four in both for the total sample). Five studies (all in adults) were multinational, that is, defined as having recruited patients from three or more countries (one fluoxetine vs. placebo; one citalopram vs. placebo; one paroxetine vs. placebo and clomipramine; one escitalopram vs. placebo and paroxetine; and one fluvoxamine vs. clomipramine study). Countries with more than three studies were the Netherlands (five studies), and Australia, Brazil and UK (three studies each). A total of seven studies (six in adults and one in children/adolescents) were conducted in Asia (three in Japan, three in Iran and one in China). There were no studies from Africa.

Types of interventions

Fifty-six of the included arms (29%) involved a supposedly inactive intervention, either drug placebo (18.5%) or psychological placebo (4.5%), or a waitlist control (6%). *Table 5* shows the number of arms/number of patients per type of intervention in the total sample and *Figure 3* presents a relevant bar diagram.

It can be seen that in adults (*Table 6*), the most used active intervention was clomipramine (12%), followed by fluvoxamine (10%). Paroxetine, however, had the second largest sample of randomised patients after clomipramine. Overall, 48% of the arms in the adult set involved an active drug intervention, 22% involved an active psychological intervention and 4% involved a combination treatment. In children and adolescents (*Table 7*), the most used active intervention was CBT (18% of the arms), followed by sertraline (11.5%, either alone or in combination with CBT) and fluoxetine (9% of the arms). Approximately 30% of the arms in children and adolescent samples included a medication, 25% of the arms included a psychological intervention and 7% included a combination of both types of treatments.

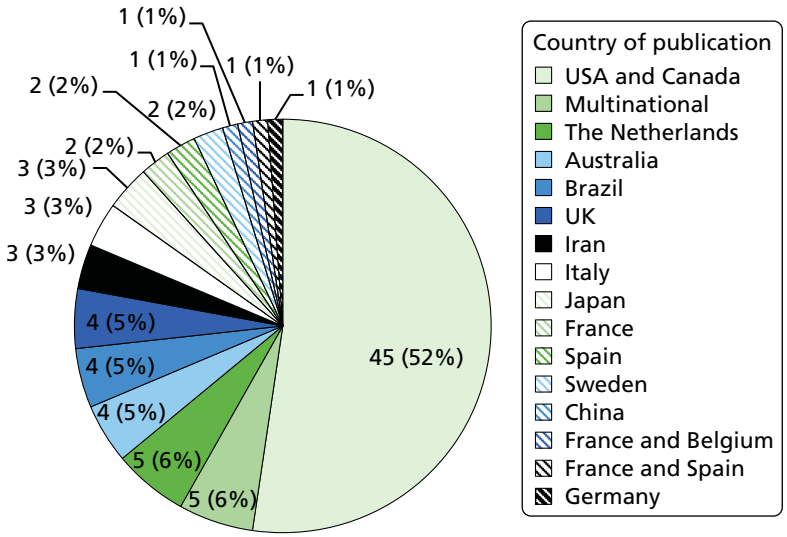


FIGURE 2 Country of publication [*n* (%) of included studies].

TABLE 5 Number of arms/number of patients per type of intervention: total sample

Intervention	Number of arms	Number of patients	% of arms	% of patients	Mean per arm	Minimum	Maximum
Placebo	36	2005	18.5	23.3	56	6	139
Clomipramine	21	1013	11	11.8	48	8	142
CBT	17	446	9	5.2	26	7	70
Fluvoxamine	17	641	9	7.5	38	5	127
BT	16	418	8	4.8	26	9	69
Fluoxetine	14	754	7	8.8	54	7	90
Waitlist	12	194	6	2.2	16	6	24
Paroxetine	11	1017	5.5	11.8	92	9	205
Sertraline	10	711	5	8.2	71	10	241
CT	9	252	5	2.9	28	10	49
Psychological placebo	8	251	4.5	2.9	31	9	75
Citalopram	5	325	2.5	3.8	65	11	102
Other drug	3	52	1.5	0.6	17	10	30
Fluvoxamine and BT	3	55	1.5	0.6	18	5	30
Escitalopram	2	232	1	2.7	116	116	116
Sertraline and CBT	2	42	1	0.5	21	14	28
Venlafaxine	2	101	1	1.2	50	26	75
Clomipramine and BT	1	33	0.5	0.4	33	33	33
Fluvoxamine and CBT	1	7	0.5	0.1	7	7	7
Placebo + BT	1	30	0.5	0.3	30	30	30
Placebo + CBT	1	16	0.5	0.2	16	16	16
Serotonergic medication	1	6	0.5	0.1	6	6	6
Serotonergic medication + CBT	1	10	0.5	0.1	10	10	10

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

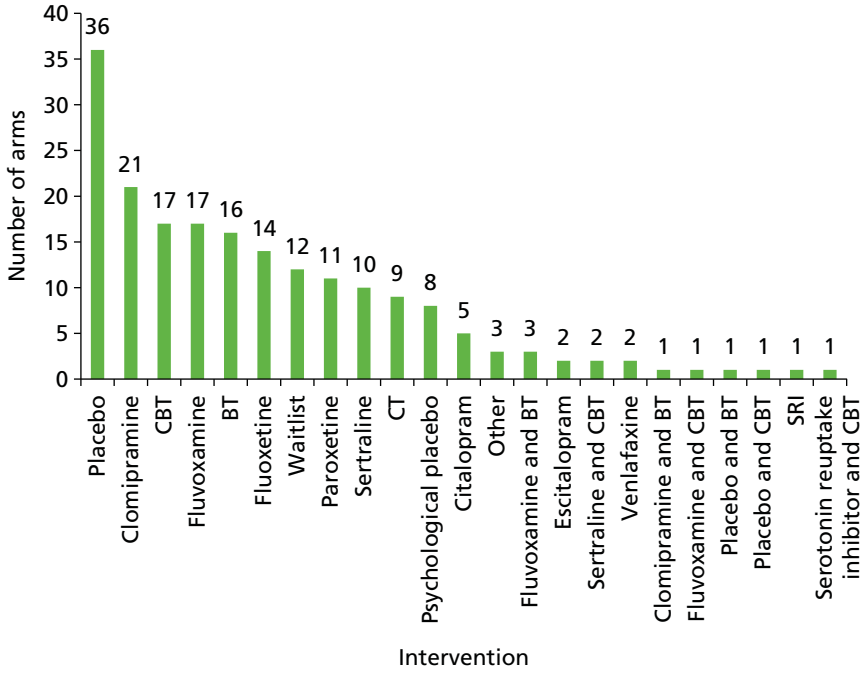


FIGURE 3 Number of arms per type of intervention: total sample. SRI, serotonin reuptake inhibitor.

TABLE 6 Number of arms/number of patients per type of intervention: adult subset

Intervention	Number of arms	Number of patients	% of arms	% of patients	Mean per arm	Minimum	Maximum
Placebo	26	1605	18	22.1	60	8	139
Clomipramine	17	955	12	13.2	53	8	142
Fluvoxamine	15	579	10	7.9	39	7	127
BT	14	395	9	5.4	28	9	69
Fluoxetine	10	640	6.7	8.6	64	23	90
Paroxetine	10	917	6.7	12.5	92	9	205
CBT	9	240	6	3.3	27	7	70
CT	9	252	6	3.4	28	10	49
Sertraline	7	571	4.7	7.8	82	10	241
Waitlist	7	111	4.7	1.5	16	6	24
Psychological placebo	6	209	4	2.8	35	9	75
Citalopram	4	311	2.8	4.2	78	11	102
Other drug	3	52	2	0.7	17	10	30
Escitalopram	2	232	1.3	3.2	116	116	116
Fluvoxamine and BT	2	50	1.3	0.7	25	20	30
Venlafaxine	2	101	1.3	1.4	50	26	75
Clomipramine + BT	1	33	0.7	0.5	33	33	33
Fluvoxamine + CBT	1	7	0.7	0.1	7	7	7
Placebo + BT	1	30	0.7	0.5	30	30	30
Serotonergic medication	1	6	0.7	0.1	6	6	6
Serotonergic medication + CBT	1	10	0.7	0.1	10	10	10

TABLE 7 Number of arms/number of patients per type of intervention: children and adolescents subset

Intervention	Number of arms	Number of patients	% of arms	% of patients	Mean per arm	Minimum	Maximum
Placebo	10	400	20.4	30.3	43	6	107
CBT	8	206	18	16	26	11	49
Waitlist	5	83	11.3	6.4	17	10	24
Fluoxetine	4	114	9.1	8.9	28	7	71
Clomipramine	4	58	7	3.8	16	8	31
Sertraline	3	42	7	3.3	21	14	28
BT	2	23	4.5	1.8	11	10	13
Fluvoxamine	2	62	4.5	4.8	31	5	57
Psychological placebo	2	42	4.5	3.3	21	20	22
Sertraline + CBT	2	140	4.5	10.9	47	20	92
Citalopram	1	14	2.3	1.1	14	14	14
Fluvoxamine + BT	1	5	2.3	0.4	5	5	5
Paroxetine	1	100	2.3	7.8	100	100	100
Placebo + CBT	1	16	2.3	1.2	16	16	16

Specific characteristics of individual studies

Tables 8 and *9* present specific characteristics of individual studies for the adult ($n = 64$ studies) and child and adolescent ($n = 22$ studies) subsets of data, respectively. The following data are presented for each individual study: study ID (including year of publication), total sample size (original number of randomised patients), number of arms, type of included interventions (grouped into three categories: medication arms only, psychological therapy arms only and arms with a combination of treatment interventions), specific intervention used in each arm, duration of the trial in weeks (primary end point), mean age of the total sample of randomised patients, percentage of female patients, primary scale used for the assessment of obsessive–compulsive symptoms, percentage of patients with depression comorbidity (grouped into six categories: none, < 25%, 25–50%, > 50%, unspecified and unclear), sponsorship of the study from drug companies (grouped into three categories: yes, no and unclear. This is not applicable for studies with psychological arms only. It should be noted that specific details of the interventions (mean dose, range of dose, number of psychotherapeutic sessions and mean duration of each session) are given for all studies in *Appendix 6*.

For the adult subset, the median number of randomised patients per study was 66 (range 16–466); 60% of the studies included drug arms only and 12% included combined arms; median duration of follow-up per study was 12 weeks (range 3–24 weeks); median percentage of female patients per study was 52.5% (range 0–94%); 85% of the studies used the YBOCS as their primary symptom scale, 54% of the studies excluded patients with major depression, and 60% of the studies that used at least one drug or combined arm were sponsored by the pharmaceutical industry. Of the 12 psychotherapy studies that used an inactive control condition, seven (58%) used a waitlist control (five CBT trials, one BT and one CT trial).

For the children and adolescents subset, the median number of randomised patients per study was 42 (range 9–207); 43% of the studies included drug arms only and 24% included combined arms; median duration per study was 12 weeks (range 5–43 weeks); median percentage of female patients per study was 42% (range 30–63%); 95% of the studies used the CYBOCS as their primary symptom scale; 24% of

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 8 Study-level characteristics: adult subset

Study ID	*n*	Number of arms	Intervention type	Arm 1	Arm 2	Arm 3	Arm 4	Duration, weeks	Mean age, years	Female, %	Scale used	Comorbid depression	Sponsorship
Albert *et al.*, 2002[155]	73	2	Drug	VEN	CLO			12	29.65	47.9	YBOCS	No	No
Ananth *et al.*, 1981[156]	20	2	Drug	CLO	AMI			4	36.9	65	Severity Questionnaire	Yes	Unclear
Anderson and Rees, 2007[157]	38	2	Therapy	CBT	Waitlist			10	33.18	•	YBOCS	Yes	NA
Andersson *et al.*, 2012[158]	101	2	Therapy	CBT	PsychPLA			10	34	66	YBOCS	Yes	NA
Belloch *et al.*, 2008[159]	33	2	Therapy	BT	CT			24	32	•	YBOCS	Yes	NA
Belotto-Silva *et al.*, 2012[160]	158	2	Combination	FLX	CBT			12	34.04	55	YBOCS	Yes	No
Bergeron *et al.*, 2002[161]	150	2	Drug	FLX	SER			24	36.53	54	YBOCS	No	Yes
Bisserbe *et al.*, 1997[162]	168	2	Drug	SER	CLO			16	39.77	63	YBOCS	No	Yes
CCSG1, 1991[154]	239	2	Drug	CLO	PLA			10	35.4	61	YBOCS	No	Yes
CCSG2, 1991[154]	281	2	Drug	CLO	PLA			10	35.6	51.5	YBOCS	No	Yes
Chouinard *et al.*, 1990[163]	87	2	Drug	SER	PLA			8	37.25	15	YBOCS	No	Yes
Cordioli *et al.*, 2003[164]	47	2	Therapy	CBT	Waitlist			12	36.5	51	YBOCS	Yes	NA
Cottraux *et al.*, 1993[165]	60	3	Combination	FLV	BT	BT + FLV		24	•	63	OCD symptom scales	Yes	No
Cottraux *et al.*, 2001[166]	65	2	Therapy	BT	CT			16	35.78	74	YBOCS	No	NA

Study ID	*n*	Number of arms	Intervention type	Arm 1	Arm 2	Arm 3	Arm 4	Duration, weeks	Mean age, years	Female, %	Scale used	Comorbid depression	Sponsorship
Denys *et al.*, 2003[167]	150	2	Drug	PAR	VEN			12	35	62	YBOCS	No	Yes
Emmelkamp and Beens, 1991[168]	30	2	Therapy	CT	BT			4	•	76	Maudsley OCI	Yes	NA
Emmelkamp *et al.*, 1988[169]	20	2	Therapy	CT	BT			8	29.9	•	Maudsley OCI	Yes	NA
Fals-Stewart *et al.*, 1993[170]	66	2	Therapy	BT	PsychPLA			12	30.5	55	YBOCS	No	NA
Foa *et al.*, 2005[171]	149	4	Combination	BT	CLO	BT + CLO	PLA	12	34.8	48	YBOCS	No	No
Freeman *et al.*, 1994[172]	66	2	Drug	FLV	CLO			10	33.01	47	YBOCS	No	Yes
Freeston *et al.*, 1997[173]	29	2	Therapy	CBT	Waitlist			16	35.8	45	YBOCS	Yes	NA
GlaxoSmithKline, 2005[174]	241	3	Drug	PLA	PAR	CLO		12	37.95	39	YBOCS	No	Yes
GlaxoSmithKline, 2005[175]	146	2	Drug	PAR	CLO			10	30.85	62	YBOCS	No	Yes
Goodman *et al.*, 1989[176]	46	2	Drug	PLA	FLV			6	37	55	YBOCS	Yes	No
Goodman *et al.*, 1996[177]	160	2	Drug	PLA	FLV			10	36.65	50	YBOCS	No	Yes
Greist *et al.*, 1995[126]	325	2	Drug	SER	PLA			12	38. 64	52	YBOCS	No	Yes
Greist *et al.*, 2002[178]	144	2	Therapy	BT	PsychPLA			10	39	42	YBOCS	Yes	NA
Hohagen *et al.*, 1998[179]	60	2	Combination	BT + PLA	BT + FLV			10	35.5	59	YBOCS	Yes	No

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 8 Study-level characteristics: adult subset (*continued*)

Study ID	*n*	Number of arms	Intervention type	Arm 1	Arm 2	Arm 3	Arm 4	Duration, weeks	Mean age, years	Female, %	Scale used	Comorbid depression	Sponsorship
Hollander *et al.*, 2003[180]	253	2	Drug	PLA	FLV			12	37.4	64	YBOCS	No	Yes
Hollander *et al.*, 2003[181]	348	4	Drug	PLA	PAR-20	PAR-40	PAR-60	12	41.36	26	YBOCS	No	Yes
Jaurrieta *et al.*, 2008[182]	38	2	Therapy	CBT	Waitlist			20	31.6	40.4	YBOCS	Yes	NA
Jenike *et al.*, 1990[183]	19	2	Drug	SER	PLA			10	39.7	21	YBOCS	No	Yes
Jenike *et al.*, 1990[184]	40	2	Drug	PLA	FLV			10	35.9	47	YBOCS	No	Yes
Jenike *et al.*, 1997[185]	44	2	Drug	PLA	FLX			10	34.86	48	YBOCS	No	No
Jones and Menzies, 1998[186]	23	2	Therapy	CT	Waitlist			8	38.52	90	Maudsley OCI	Unclear	NA
Kamijima *et al.*, 2004[187]	191	2	Drug	PLA	PAR			12	37.8	62	YBOCS	Yes	Unclear
Khodarahimi, 2009[188]	40	2	Therapy	Waitlist	BT			6	24.6	0	YBOCS	No	NA
Kobak *et al.*, 2005[189]	60	2	Drug	PLA	Hypericum			12	37.72	•	YBOCS	No	No
Koran *et al.*, 1996[190]	79	2	Drug	FLV	CLO			10	•	45	YBOCS	No	Yes
Kronig *et al.*, 1999[191]	167	2	Drug	SER	PLA			12	36.76	45	YBOCS	No	Yes
Lindsay *et al.*, 1997[192]	18	2	Therapy	BT	PsychPLA			3	32.8	66	YBOCS	Yes	NA
López-Ibor *et al.*, 1996[193]	55	2	Drug	FLX	CLO			8	34	62	YBOCS	No	Yes

Study ID	*n*	Number of arms	Intervention type	Arm 1	Arm 2	Arm 3	Arm 4	Duration, weeks	Mean age, years	Female, %	Scale used	Comorbid depression	Sponsorship
Mavissakalian *et al.*, 1985[194]	16	2	Drug	CLO	PLA			12	35.9	56	OCNS	Yes	Yes
McLean *et al.*, 2001[195]	93	2	Therapy	CT	BT			12	35	48	YBOCS	Yes	NA
Milanfranchi *et al.*, 1997[196]	26	2	Drug	CLO	FLV			9	27.35	42	YBOCS	No	Yes
Montgomery *et al.*, 1993[197]	217	4	Drug	PLA	FLX-20	FLX-40	FLX-60	8	37.16	47	YBOCS	Yes	Yes
Montgomery *et al.*, 2001[198]	401	4	Drug	PLA	CIT-20	CIT-40	CIT-60	12	37.82	54	YBOCS	Yes	Yes
Mundo *et al.*, 1997[199]	30	3	Drug	FLV	PAR	CIT		10	30.78	30	YBOCS	No	No
Mundo *et al.*, 2001[200]	227	2	Drug	CLO	FLV			10	35.2	45	YBOCS	No	Yes
Nakajima *et al.*, 1996[201]	94	2	Drug	FLV	PLA			8	34.38	46	YBOCS	Unclear	Unclear
Nakatani *et al.*, 2005[202]	31	3	Combination	PsychPLA	FLV	BT		12	33.66	68	YBOCS	No	No
O'Connor *et al.*, 1999[203]	29	4	Combination	SRI	Waitlist	CBT	CBT + SRI	20	35.94	37	YBOCS	Yes	No
O'Connor *et al.*, 2006[204]	21	2	Drug	PLA	FLV			20	35.76	57	YBOCS	No	No
Perse *et al.*, 1987[205]	20	2	Drug	PLA	FLV			8	•	•	Maudsley OCI	Yes	Yes
Shareh *et al.*, 2010[206]	21	3	Combination	FLV	CBT	FLV + CBT		10	26.84	53	YBOCS	No	No
Sousa *et al.*, 2006[207]	56	2	Combination	SER	CBT			12	38.5	77	YBOCS	No	No

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 8 Study-level characteristics: adult subset (*continued*)

Study ID	*n*	Number of arms	Intervention type	Arm 1	Arm 2	Arm 3	Arm 4	Duration, weeks	Mean age, years	Female, %	Scale used	Comorbid depression	Sponsorship
Stein *et al.*, 2007[124]	466	4	Drug	PLA	PAR	ESCIT-10	ESCIT-20	12	37.75	57	YBOCS	No	Yes
Thoren *et al.*, 1980[208]	16	2	Drug	CLO	PLA			5	38.9	94	OCD symptom scale	Yes	No
Tollefson *et al.*, 1994[127]	355	4	Drug	PLA	FLX-20	FLX-40	FLX-60	13	36.9	55.2	YBOCS	Yes	Yes
Van Oppen *et al.*, 1995[209]	71	2	Therapy	CT	BT			16	34.71	53	YBOCS	Yes	NA
Volavka *et al.*, 1985[210]	23	2	Drug	CLO	IMI			12	29.94	52	SRONS	No	Yes
Whittal *et al.*, 2005[211]	83	2	Therapy	CT	BT			12	34.89	62.5	YBOCS	Yes	NA
Whittal *et al.*, 2010[212]	73	2	Therapy	CT	PsychPLA			12	31.5	46.6	YBOCS	Yes	NA
Zohar and Judge, 1996[213]	406	3	Drug	PLA	PAR	CLO		12	37.94	52	YBOCS	No	Yes

AMI, amitriptyline; CCSG, Clomipramine Collaborative Study Group; CIT, citalopram; CLO, clomipramine; ESCIT, escitalopram; FLV, fluvoxamine; FLX, fluoxetine; IMI, imipramine; NA, not applicable; OCI, obsessive–compulsive inventory; OCNS, Obsessive–Compulsive Neurotic Scale; OCR, Obsessive–Compulsive Rating Scale; PAR, paroxetine; PLA, placebo; PsychPLA, psychological placebo; SER, sertraline; SRI, serotonin reuptake inhibitor; SRONS, Self-Rating Obsessional Neurotic Scale; VEN, venlafaxine.
Bullet points (•) indicate missing information (i.e. data not provided for this characteristic).

TABLE 9 Study-level characteristics: children and adolescents subset

Study ID	*n*	Number of arms	Arm 1	Arm 2	Arm 3	Arm 4	Duration, weeks	Mean age, years	Female, %	Scale used	Comorbid depression	Sponsorship
Alaghband-Rad and Hakimshooshtary, 2009[215]	29	2	FLX	CIT			6	•	41	CYBOCS	Unclear	Unclear
Asbahr *et al.*, 2005[216]	40	2	SER	CBT			12	13.05	35	CYBOCS	Yes	No
Barrett *et al.*, 2004[217]	48	2	CBT	Waitlist			14	11.25	48	CYBOCS	Yes	NA
Bolton and Perrin, 2008[218]	20	2	BT	Waitlist			7	13.2	30	CYBOCS	Yes	NA
Bolton *et al.*, 2011[219]	60	2	CBT	Waitlist			12	14.6	57	CYBOCS	No	NA
de Haan *et al.*, 1998[220]	23	2	CLO	BT			12	13.43	50	CYBOCS	No	No
DeVeaugh-Geiss *et al.*, 1992[221]	60	2	CLO	PLA			8	14.25	35	CYBOCS	No	Yes
Flament *et al.*, 1985[222]	19	2	CLO	PLA			5	14.5	26	OCR scale	Yes	No
Freeman *et al.*, 2008[223]	42	2	CBT	PsychPLA			14	7.11	57	CYBOCS	Yes	NA
Geller *et al.*, 2001[224]	103	2	FLX	PLA			13	11.4	52	CYBOCS	Yes	Yes
GlaxoSmithKline, 2001[225]	207	2	PAR	PLA			10	11.3	42	CYBOCS	Unclear	Yes
Liebowitz *et al.*, 2002[226]	43	2	FLX	PLA			8	12.65	42	CYBOCS	Yes	Yes
March *et al.*, 1990[227]	16	2	CLO	PLA			10	15	31	YBOCS	Yes	Yes
March *et al.*, 1998[228]	187	2	SER	PLA			12	12.6	•	CYBOCS	Yes	Yes
Neziroglu *et al.*, 2000[229]	10	2	FLV	FLV + BT			43	14.5	40	CYBOCS	Yes	Unclear
Piacentini *et al.*, 2011[230]	71	2	CBT	PsychPLA			14	12.2	63.4	CYBOCS	Yes	NA

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 9 Study-level characteristics: children and adolescents subset (*continued*)

Study ID	*n*	Number of arms	Arm 1	Arm 2	Arm 3	Arm 4	Duration, weeks	Mean age, years	Female, %	Scale used	Comorbid depression	Sponsorship
Riddle *et al.*, 1992[231]	13	2	FLX	PLA			8	12.7	61	CYBOCS	Yes	No
Riddle *et al.*, 2001[232]	120	2	FLV	PLA			10	13.03	47	CYBOCS	No	Yes
Storch *et al.*, 2011[233]	31	2	CBT	Waitlist			12	11.1	39	CYBOCS	Yes	NA
Storch *et al.*, 2013[234]	30	2	SER + CBT	CBT + PLA			18	12.13	40	CYBOCS	Yes	No
Williams *et al.*, 2010[235]	21	2	CBT	Waitlist			12	13.6	38	CYBOCS	Yes	NA
The Pediatric OCD Treatment Study, 2004[236]	112	4	SER	CBT	SER + CBT	PLA	12	11.77	50	CYBOCS	No	No

AMI, amitriptyline; CIT, citalopram; CLO, clomipramine; FLV, fluvoxamine; FLX, fluoxetine; NA, not applicable; PAR, paroxetine; PLA, placebo; PsychPLA, psychological placebo; SER, sertraline.
Bullet points (•) indicate missing information (i.e. data not provided for this characteristic).

the studies excluded patients with major depression; and 50% of the studies that used at least one drug or combined arm were sponsored by the pharmaceutical industry. Of the seven psychotherapy studies that used an inactive control condition, five (71%) used a waitlist control (four CBT trials and one BT trial).

Individual studies per included active intervention

For ease of reference, we also present separate tables with the included studies for each active intervention (*Tables 10* and *11* for adults and children and adolescent subsets, respectively). We present the following information: study ID (including year of publication); total sample size (original number of randomised patients); specific intervention used in each arm; duration of the trial in weeks (primary end point); and primary scale used for the assessment of obsessive–compulsive symptoms. It should be noted that some studies appear more than once because they compared an active drug with another active drug.

TABLE 10 Study-level characteristics per type of intervention: adult subset

Study ID	*n*	Arm 1	Arm 2	Arm 3	Arm 4	Duration (weeks)	Scale used
***Fluoxetine studies* (n = *6*)**							
Jenike *et al.*, 1997[185]	44	FLX	PLA			10	YBOCS
Montgomery *et al.*, 1993[197]	217	FLX-20	FLX-40	FLX-60	PLA	8	YBOCS
Tollefson *et al.*, 1994[127]	355	FLX-20	FLX-40	FLX-60	PLA	13	YBOCS
López-Ibor *et al.*, 1996[193]	55	FLX	CLO			8	YBOCS
Bergeron *et al.*, 2002[161]	150	FLX	SER			24	YBOCS
Belotto-Silva *et al.*, 2012[160]	158	FLX	CBT			12	YBOCS
Total	979						
***Fluvoxamine studies* (n = *16*)**							
Perse *et al.*, 1987[205]	20	FLV	PLA			8	Maudsley OCI
Goodman *et al.*, 1989[176]	46	FLV	PLA			6	YBOCS
Jenike *et al.*, 1990[184]	40	FLV	PLA			10	YBOCS
Goodman *et al.*, 1996[177]	160	FLV	PLA			10	YBOCS
Nakajima *et al.*, 1996[201]	94	FLV	PLA			8	YBOCS
Hollander *et al.*, 2003[181]	253	FLV	PLA			12	YBOCS
O'Connor *et al.*, 2006[204]	21	FLV	PLA			20	YBOCS
Freeman *et al.*, 1994[172]	66	FLV	CLO			10	YBOCS
Koran *et al.*, 1996[190]	79	FLV	CLO			10	YBOCS
Milanfranchi *et al.*, 1997[196]	26	FLV	CLO			9	YBOCS
Mundo *et al.*, 2001[200]	227	FLV	CLO			10	YBOCS
Mundo *et al.*, 1997[199]	30	FLV	PAR	CIT		10	YBOCS
Nakatani *et al.*, 2005[202]	31	FLV	BT	PsychPLA		12	YBOCS
Cottraux *et al.*, 1993[165]	60	FLV	FLV + BT	BT		24	OCD symptom scales
Hohagen *et al.*,1998[179]	60	FLV + BT	PLA + BT			10	YBOCS
Shareh *et al.*, 2010[206]	21	FLV	FLV + CBT	CBT		10	YBOCS
Total	1234						

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 10 Study-level characteristics per type of intervention: adult subset (*continued*)

Study ID	*n*	Arm 1	Arm 2	Arm 3	Arm 4	Duration (weeks)	Scale used
***Clomipramine studies* (n = *17*)**							
Thoren *et al.*, 1980[208]	16	CLO	PLA			5	OCD symptom scale
Mavissakalian *et al.*, 1985[194]	16	CLO	PLA			12	OCNS
CCSG1, 1991[154]	239	CLO	PLA			10	YBOCS
CCSG2, 1991[154]	281	CLO	PLA			10	YBOCS
Ananth *et al.*, 1981[156]	20	CLO	AMI			4	Severity questionnaire
Volavka *et al.*, 1985[210]	23	CLO	IMI			12	SRONS
Freeman *et al.*, 1994[172]	66	CLO	FLV			10	YBOCS
Koran *et al.*, 1996[190]	79	CLO	FLV			10	YBOCS
Milanfranchi *et al.*, 1997[196]	26	CLO	FLV			9	YBOCS
Mundo *et al.*, 2001[200]	227	CLO	FLV			10	YBOCS
López-Ibor *et al.*, 1996[193]	55	CLO	FLX			8	YBOCS
GlaxoSmithKline, 2005[175]	146	CLO	PAR			10	YBOCS
GlaxoSmithKline, 2005[174]	241	CLO	PAR	PLA		12	YBOCS
Zohar and Judge, 1996[213]	406	CLO	PAR	PLA		12	YBOCS
Bisserbe *et al.*, 1997[162]	168	CLO	SER			16	YBOCS
Albert *et al.*, 2002[155]	73	CLO	VEN			12	YBOCS
Foa *et al.*, 2005[171]	149	CLO	CLO + BT	BT	PLA	12	YBOCS
Total	2231						
***Paroxetine studies* (n = *8*)**							
Hollander *et al.*, 2003[180]	348	PAR-20	PAR-40	PAR-60	PLA	12	YBOCS
Kamijima *et al.*, 2004[187]	191	PAR	PLA			12	YBOCS
GlaxoSmithKline, 2005[175]	146	PAR	CLO			10	YBOCS
GlaxoSmithKline, 2005[174]	241	PAR	CLO	PLA		12	YBOCS
Zohar and Judge, 1996[213]	406	PAR	CLO	PLA		12	YBOCS
Mundo *et al.*, 1997[199]	30	PAR	CIT	FLV		10	YBOCS
Stein *et al.*, 2007[124]	466	PAR	ESCIT-10	ESCIT-20	PLA	12	YBOCS
Denys *et al.*, 2003[167]	150	PAR	VEN			12	YBOCS
Total	1978						

TABLE 10 Study-level characteristics per type of intervention: adult subset (*continued*)

Study ID	*n*	Arm 1	Arm 2	Arm 3	Arm 4	Duration (weeks)	Scale used
***Sertraline studies* (n = *7*)**							
Chouinard *et al.*, 1990[163]	87	SER	PLA			8	YBOCS
Jenike *et al.*, 1990[183]	19	SER	PLA			10	YBOCS
Greist *et al.*, 1995[126]	325	SER	PLA			12	YBOCS
Kronig *et al.*, 1999[191]	167	SER	PLA			12	YBOCS
Bisserbe *et al.*, 1997[162]	168	SER	CLO			16	YBOCS
Bergeron *et al.*, 2002[161]	150	SER	FLX			24	YBOCS
Sousa *et al.*, 2006[207]	56	SER	CBT			12	YBOCS
Total	972						
***Citalopram studies* (n = *2*)**							
Montgomery *et al.*, 2001[198]	401	CIT-20	CIT-40	CIT-60	PLA	12	YBOCS
Mundo *et al.*, 1997[199]	30	CIT	FLV	PAR		10	YBOCS
Total	431						
***Escitalopram studies* (n = *1*)**							
Stein *et al.*, 2007[124]	466	PLA	PAR	ESCIT-10	ESCIT-20	12	YBOCS
***Other medications* (n = *3*)**							
Ananth *et al.*, 1981[156]	20	AMI	CLO			4	Severity questionnaire
Volavka *et al.*, 1985[210]	23	IMI	CLO			12	SRONS
Kobak *et al.*, 2005[189]	60	Hypericum	PLA			12	YBOCS
Total	103						
***Venlafaxine studies* (n = *2*)**							
Albert *et al.*, 2002[155]	73	VEN	CLO			12	YBOCS
Denys *et al.*, 2003[167]	150	VEN	PAR			12	YBOCS
Total	223						
***BT studies* (n = *15*)**							
Fals-Stewart *et al.*, 1993[170]	66	BT	PsychPLA			12	YBOCS
Lindsay *et al.*, 1997[192]	18	BT	PsychPLA			3	YBOCS
Greist *et al.*, 2002[178]	144	BT	PsychPLA			10	YBOCS
Khodarahimi, 2009[188]	40	BT	Waitlist			6	YBOCS
Foa *et al.*, 2005[171]	149	BT	BT + CLO	CLO	PLA	12	YBOCS
Cottraux *et al.*, 1993[165]	60	BT	BT + FLV	FLV		24	OCD symptom scales
Nakatani *et al.*, 2005[202]	31	BT	FLV	PsychPLA		12	YBOCS

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 10 Study-level characteristics per type of intervention: adult subset (*continued*)

Study ID	*n*	Arm 1	Arm 2	Arm 3	Arm 4	Duration (weeks)	Scale used
Hohagen *et al.*, 1998[179]	60	BT + FLV	BT + PLA			10	YBOCS
Emmelkamp and Beens, 1991[168]	30	BT	CT			4	Maudsley OCI
Van Oppen *et al.*, 1995[209]	71	BT	CT			16	YBOCS
Emmelkamp *et al.*, 1988[169]	20	BT	CT			8	Maudsley OCI
Cottraux *et al.*, 2001[166]	65	BT	CT			16	YBOCS
McLean *et al.*, 2001[195]	93	BT	CT			12	YBOCS
Whittal *et al.*, 2005[211]	83	BT	CT			12	YBOCS
Belloch *et al.*, 2008[159]	33	BT	CT			24	YBOCS
Total	963						
***CBT studies* (n = 9)**							
Andersson *et al.*, 2012[158]	101	CBT	PsychPLA			10	YBOCS
Freeston *et al.*, 1997[173]	29	CBT	Waitlist			16	YBOCS
Cordioli *et al.*, 2003[164]	47	CBT	Waitlist			12	YBOCS
Anderson and Rees, 2007[157]	38	CBT	Waitlist			10	YBOCS
Jaurrieta *et al.*, 2008[182]	38	CBT	Waitlist			20	YBOCS
Belotto-Silva *et al.*, 2012[160]	158	CBT	FLX			12	YBOCS
Shareh *et al.*, 2010[206]	21	CBT	CBT + FLV	FLV		10	YBOCS
Sousa *et al.*, 2006[207]	56	CBT	SER			12	YBOCS
O'Connor *et al.*, 1999[203]	29	CBT	CBT + SRI	SRI	Waitlist	20	YBOCS
Total	517						
***CT studies* (n = 9)**							
Whittal *et al.*, 2010[212]	73	CT	PsychPLA			12	YBOCS
Jones and Menzies, 1998[186]	23	CT	Waitlist			8	Maudsley OCI
Emmelkamp *et al.*, 1988[169]	20	CT	BT			8	Maudsley OCI
Emmelkamp and Beens, 1991[168]	30	CT	BT			4	Maudsley OCI
Van Oppen *et al.*, 1995[209]	71	CT	BT			16	YBOCS
Cottraux *et al.*, 2001[166]	65	CT	BT			16	YBOCS
McLean *et al.*, 2001[195]	93	CT	BT			12	YBOCS
Whittal *et al.*, 2005[211]	83	CT	BT			12	YBOCS
Belloch *et al.*, 2008[159]	33	CT	BT			24	YBOCS
Total	491						

AMI, amitriptyline; CCSG, Clomipramine Collaborative Study Group; CIT, citalopram; CLO, clomipramine; ESCIT, escitalopram; FLV, fluvoxamine; FLX, fluoxetine; IMI, imipramine; OCI, obsessive–compulsive inventory; PAR, paroxetine; PLA, placebo; PsychPLA, psychological placebo; SER, sertraline; SRONS, Self-Rating Obsessional Neurotic Scale; VEN, venlafaxine.

TABLE 11 Study-level characteristics per type of intervention: children and adolescents subset

Study ID	*n*	Arm 1	Arm 2	Arm 3	Arm 4	Duration (weeks)	Scale used
***Fluoxetine studies* (n = 4)**							
Riddle *et al.*, 1992[231]	13	FLX	PLA			8	CYBOCS
Geller *et al.*, 2001[224]	103	FLX	PLA			13	CYBOCS
Liebowitz *et al.*, 2002[226]	43	FLX	PLA			8	CYBOCS
Alaghband-Rad and Hakimshooshtary, 2009[215]	29	FLX	CIT			6	CYBOCS
Total	188						
***Fluvoxamine studies* (n = 2)**							
Riddle *et al.*, 2001[232]	120	FLV	PLA			10	CYBOCS
Neziroglu *et al.*, 2000[229]	10	FLV	FLV + BT			43	CYBOCS
Total	130						
***Clomipramine studies* (n = 4)**							
Flament *et al.*, 1985[222]	19	CLO	PLA			5	OCR scale
March *et al.*, 1990[227]	16	CLO	PLA			10	YBOCS
DeVeaugh-Geiss *et al.*, 1992[221]	60	CLO	PLA			8	CYBOCS
de Haan *et al.*, 1998[220]	23	CLO	BT			12	CYBOCS
Total	99						
***Paroxetine studies* (n = 1)**							
GlaxoSmithKline, 2001[225]	207	PAR	PLA			10	CYBOCS
***Sertraline studies* (n = 4)**							
March *et al.*, 1998[228]	187	SER	PLA			12	CYBOCS
The Pediatric OCD Treatment Study, 2004[236]	112	SER	SER + CBT	CBT	PLA	12	CYBOCS
Asbahr *et al.*, 2005[216]	40	SER	CBT			12	CYBOCS
Storch *et al.*, 2013[234]	30	SER + CBT	PLA + CBT			18	CYBOCS
Total	369						
***Citalopram studies* (n = 1)**							
Alaghband-Rad and Hakimshooshtary, 2009[215]	29	CIT	FLX			6	CYBOCS
***BT studies* (n = 3)**							
Bolton and Perrin, 2008[218]	20	BT	Waitlist			7	CYBOCS
de Haan *et al.*, 1998[220]	23	BT	CLO			12	CYBOCS
Neziroglu *et al.*, 2000[229]	10	BT + FLV	FLV			43	CYBOCS
Total	53						

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 11 Study-level characteristics per type of intervention: children and adolescents subset (*continued*)

Study ID	*n*	Arm 1	Arm 2	Arm 3	Arm 4	Duration (weeks)	Scale used
***CBT studies* (n = 9)**							
Freeman *et al.*, 2008[223]	42	CBT	PsychPLA			14	CYBOCS
Piacentini *et al.*, 2011[230]	71	CBT	PsychPLA			14	CYBOCS
Barrett *et al.*, 2004[217]	48	CBT	Waitlist			14	CYBOCS
Williams *et al.*, 2010[235]	21	CBT	Waitlist			12	CYBOCS
Bolton *et al.*, 2011[219]	60	CBT	Waitlist			12	CYBOCS
Storch *et al.*, 2011[233]	31	CBT	Waitlist			12	CYBOCS
The Pediatric OCD Treatment Study, 2004[236]	112	CBT	SER			12	CYBOCS
Asbahr *et al.*, 2005[216]	40	CBT	SER			12	CYBOCS
Storch *et al.*, 2013[234]	30	CBT + PLA	CBT + SER			18	CYBOCS
Total	455						

AMI, amitriptyline; CIT, citalopram; CLO, clomipramine; FLV, fluvoxamine; FLX, fluoxetine; OCR, Obsessive–Compulsive Rating Scale; PAR, paroxetine; PLA, placebo; PsychPLA, psychological placebo; SER, sertraline.

Quality of included trials (risk-of-bias assessment)

The methodological quality of included trials is summarised in *Table 12* and *Figure 4* for the adult subset and *Table 13* and *Figure 5* for the children and adolescents subset. We used the criteria for quality assessment recommended by the *Cochrane Handbook for Systematic Reviews of Interventions*.[142] We have included the following criteria: random sequence generation; allocation sequence concealment; blinding of participants; blinding of those delivering the intervention; blinding of the outcome assessor; completeness of outcome data; and selective outcome reporting and other potential sources of bias. Studies were given a quality rating of 'low', 'unclear' or 'high' risk of bias in accordance with these criteria. For the last criterion of 'any other potential source of bias', we categorised studies as high risk if the overall attrition rate was > 25% or if there was evidence of differential attrition between arms of > 15%. The tables present the summary results for each criterion, and a more detailed table in *Appendix 7* includes a description of the reason behind the specific categorisation. Studies with a high risk of bias were included in the main analysis but we also examined, in a sensitivity analysis, the effect of excluding them.

Figures 4 and *5* show that the majority of the studies in the adult subset have not described adequately the random sequence generation or the way in which they have concealed the allocation sequence. Similar findings are reported for the children and adolescents subset.

We have also extracted data on the type of analysis (whether or not the authors have performed an intention-to-treat analysis) and the method of handling missing data. *Tables 14* and *15* present this information for adults and for children and adolescents, respectively. It can be seen that the majority (81%) of the children and adolescents studies have used intention-to-treat analysis, compared with 43% of the adult studies. The last observation carried forward was the most common method for imputing missing observations.

In the adult subset, 54% of the trials either did not report intention-to-treat results or did not describe the way in which missing data were handled. Tabulation per type of intervention showed that in studies with medication arms only, the percentage was 41% (16 out of 39), compared with 77% (14 out of 18) of trials with psychological interventions only and 62% (5/8) of trials with combined arms. The majority of the studies with medication arms only involved clomipramine (10/16 studies that did not report such data), whereas those studies of psychological interventions involved either CT or compared CT and BT (9/14 studies that did not report such data).

TABLE 12 Methodological quality summary: reviewers' judgements about each methodological criterion: adult subset

Study ID	Sequence generation	Allocation sequence concealment	Blinding of participants	Blinding of those delivering the intervention	Blinding of the outcome assessor	Incomplete outcome data	Selective outcome reporting	Any other potential threats to validity
Albert *et al.*, 2002[155]	Unclear	Unclear	High	High	Low	High	High	High
Ananth *et al.*, 1981[156]	Unclear	Unclear	Low	Low	Unclear	High	Low	Low
Anderson and Rees, 2007[157]	Unclear	Unclear	High	High	Unclear	Low	High	Low
Andersson *et al.*, 2012[158]	Low	Unclear	High	High	Low	Low	Low	Low
Belloch *et al.*, 2008[159]	Unclear	Unclear	High	High	Low	High	Low	Low
Belotto-Silva *et al.*, 2012[160]	Low	Low	High	High	Low	Low	Low	Low
Bergeron *et al.*, 2002[161]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	High
Bisserbe *et al.*, 1997[162]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High	High
CCSG1, 1991[154]	Unclear	Unclear	Low	Low	Unclear	Unclear	High	High
CCSG2, 1991[154]	Unclear	Unclear	Low	Low	Unclear	Unclear	High	High
Chouinard *et al.*, 1990[163]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High	Low
Cordioli *et al.*, 2003[164]	Low	Low	High	High	Low	Low	Low	Low
Cottraux *et al.*, 1993[165]	Unclear	Unclear	Unclear	Unclear	Unclear	High	Low	High
Cottraux *et al.*, 2001[166]	Unclear	Unclear	High	High	Low	High	High	Low
Denys *et al.*, 2003[167]	Unclear	Unclear	Low	Low	Low	Low	Low	Low
Emmelkamp and Beens, 1991[168]	Unclear	Unclear	High	High	Low	High	Low	High
Emmelkamp *et al.*, 1988[169]	Unclear	Unclear	High	High	Low	High	Low	Low
Fals-Stewart *et al.*, 1993[170]	Unclear	Unclear	High	High	Unclear	High	High	Low
Foa *et al.*, 2005[171]	Low	Unclear	Unclear	Low	Low	Low	Low	High
Freeman *et al.*, 1994[172]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High	High
Freeston *et al.*, 1997[173]	Unclear	Unclear	High	High	High	Low	Low	Low
GlaxoSmithKline, 2005[174]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	High

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 12 Methodological quality summary: reviewers' judgements about each methodological criterion: adult subset (*continued*)

Study ID	Sequence generation	Allocation sequence concealment	Blinding of participants	Blinding of those delivering the intervention	Blinding of the outcome assessor	Incomplete outcome data	Selective outcome reporting	Any other potential threats to validity
GlaxoSmithKline, 2005[175]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High
Goodman *et al.*, 1989[176]	Unclear	Unclear	Low	Low	Low	Low	Low	High
Goodman *et al.*, 1996[177]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High	Low
Greist *et al.*, 1995[126]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High
Greist *et al.*, 2002[178]	Unclear	Unclear	High	High	High	Low	Low	Low
Hohagen *et al.*, 1998[179]	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Low	High
Hollander *et al.*, 2003[180]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High	Low
Hollander *et al.*, 2003[181]	Low	Low	Low	Low	Unclear	Low	High	Low
Jaurrieta *et al.*, 2008[182]	Low	Low	High	High	Unclear	Low	High	Low
Jenike *et al.*, 1990[183]	Unclear	Unclear	Low	Low	Unclear	Low	Low	Low
Jenike *et al.*, 1990[184]	Unclear	Unclear	Low	Low	Low	High	High	Low
Jenike *et al.*, 1997[185]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Jones and Menzies, 1998[186]	Unclear	Unclear	High	High	High	Unclear	Low	Low
Kamijima *et al.*, 2004[187]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High	Low
Khodarahimi, 2009[188]	Low	Unclear	High	High	Unclear	High	Low	Low
Kobak *et al.*, 2005[189]	Unclear	Unclear	Low	Low	Unclear	Low	Low	Low
Koran *et al.*, 1996[190]	Low	Unclear	Low	Low	Unclear	Low	Low	High
Kronig *et al.*, 1999[191]	Low	Unclear	Unclear	Unclear	Unclear	Low	High	High
Lindsay *et al.*, 1997[192]	Unclear	Unclear	High	High	Unclear	Unclear	Unclear	Low
López-Ibor *et al.*, 1996[193]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Mavissakalian *et al.*, 1985[194]	Unclear	Unclear	Unclear	Unclear	Unclear	High	High	Low
McLean *et al.*, 2001[195]	Low	Unclear	High	High	Unclear	High	Low	Low

Study ID	Sequence generation	Allocation sequence concealment	Blinding of participants	Blinding of those delivering the intervention	Blinding of the outcome assessor	Incomplete outcome data	Selective outcome reporting	Any other potential threats to validity
Milanfranchi *et al.*, 1997[196]	Unclear	Unclear	Low	Low	Unclear	High	Low	Low
Montgomery *et al.*, 1993[197]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Montgomery *et al.*, 2001[198]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Mundo *et al.*, 1997[199]	Unclear	Unclear	High	High	Low	Low	Low	Low
Mundo *et al.*, 2001[200]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High	Low
Nakajima *et al.*, 1996[201]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Nakatani *et al.*, 2005[202]	Unclear	Low	High	Unclear	Low	High	Low	Low
O'Connor *et al.*, 1999[203]	High	Unclear	High	High	Low	High	High	Low
O'Connor *et al.*, 2006[204]	Unclear	Low	Low	Low	Low	High	Low	Low
Perse *et al.*, 1987[205]	Unclear	Unclear	Unclear	Unclear	Low	High	High	Low
Shareh *et al.*, 2010[206]	Unclear	Unclear	High	High	Unclear	High	Low	High
Sousa *et al.*, 2006[207]	Low	Unclear	High	High	Low	Low	High	Low
Stein *et al.*, 2007[124]	Low	Low	Low	Low	Low	Low	Low	Low
Thoren *et al.*, 1980[208]	Unclear	Unclear	Low	Low	Unclear	High	High	Low
Tollefson *et al.*, 1994[127]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High	High
Van Oppen *et al.*, 1995[209]	Unclear	Unclear	High	High	Unclear	High	High	Low
Volavka *et al.*, 1985[210]	Low	Low	Low	Low	Unclear	High	Low	Low
Whittal *et al.*, 2005[211]	Unclear	Unclear	High	High	Low	High	Low	Low
Whittal *et al.*, 2010[212]	Unclear	Unclear	High	High	Unclear	High	Low	Low
Zohar and Judge, 1996[213]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	High

CCSG, Clomipramine Collaborative Study Group; high, high risk of bias; low, low risk of bias; unclear, unclear risk of bias.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

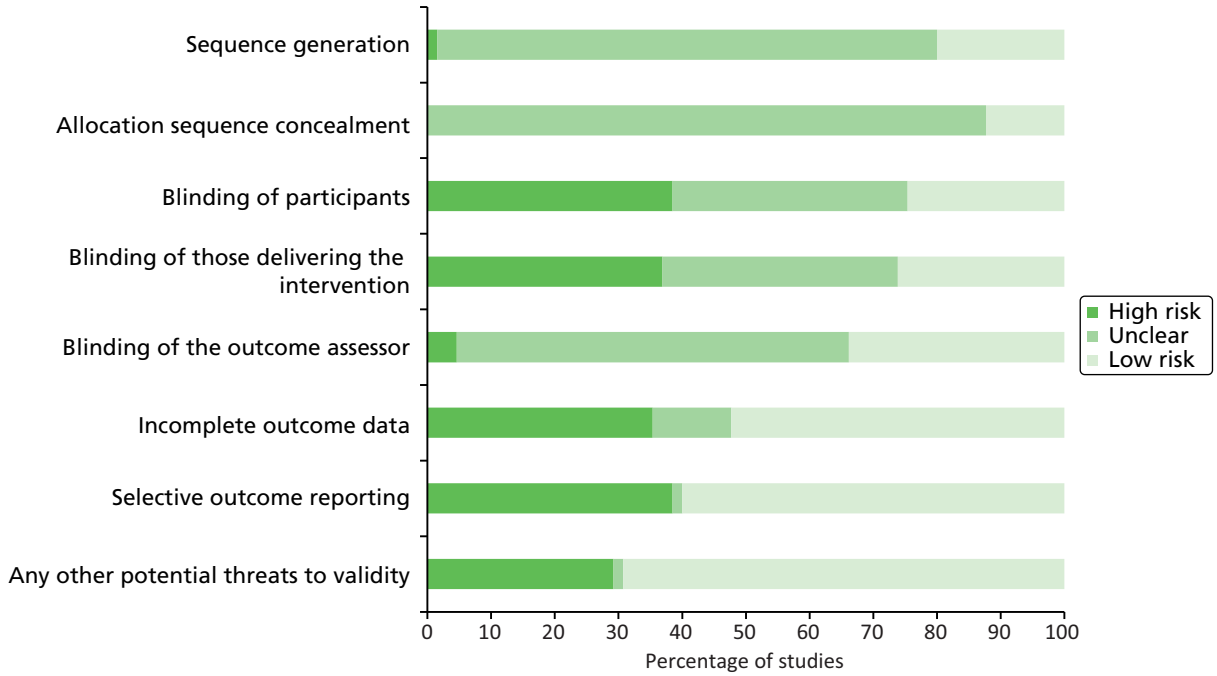


FIGURE 4 Methodological quality graph for the adult subset ($n = 64$): reviewers' judgements about each criterion as percentages across all included studies.

TABLE 13 Methodological quality summary: reviewers' judgements about each methodological criterion: children and adolescents subset

Study ID	Sequence generation	Allocation sequence concealment	Blinding of participants	Blinding of those delivering the intervention	Blinding of the outcome assessor	Incomplete outcome data	Selective outcome reporting	Any other potential threats to validity
Alaghband-Rad and Hakimshooshtary, 2009[215]	Unclear	Unclear	Unclear	Unclear	Unclear	High	High	High
Asbahr *et al.*, 2005[216]	Unclear	Unclear	High	High	Low	Low	High	Low
Barrett *et al.*, 2004[217]	Low	Unclear	High	High	Unclear	Unclear	High	Low
Bolton and Perrin, 2008[218]	Low	Low	High	High	High	Low	Low	Low
Bolton *et al.*, 2011[219]	Low	Low	High	High	Low	Low	Low	Low
de Haan *et al.*, 1998[220]	Unclear	Unclear	High	High	Unclear	Low	Low	Low
DeVeaugh-Geiss *et al.*, 1992[221]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High	Low
Flament *et al.*, 1985[222]	Unclear	Unclear	Low	Low	Low	Unclear	High	Low
Freeman *et al.*, 2008[223]	Unclear	Unclear	High	High	Low	Low	Low	High
Geller *et al.*, 2001[224]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	High
GlaxoSmithKline, 2001[225]	Low	Unclear	Low	Low	Unclear	High	Low	High
Liebowitz *et al.*, 2002[226]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low
March *et al.*, 1990[227]	Unclear	Unclear	Low	Low	Unclear	Low	Low	Low
March *et al.*, 1998[228]	Low	Unclear	Low	Low	Unclear	Low	High	Low
Neziroglu *et al.*, 2000[229]	Unclear	Unclear	High	High	Unclear	Low	Low	Low
Piacentini *et al.*, 2011[230]	Unclear	Unclear	High	High	Low	Low	Low	Low
Riddle *et al.*, 1992[231]	Unclear	Low	Low	Low	Unclear	Low	Low	Low
Riddle *et al.*, 2001[232]	Unclear	Unclear	Low	Low	Low	Low	Low	High
Storch *et al.*, 2011[233]	Low	Unclear	High	High	Low	Low	Low	Low
Storch *et al.*, 2013[234]	Low	Unclear	Unclear	Unclear	Low	Low	Low	High
Williams *et al.*, 2010[235]	Low	Low	High	High	Low	Low	High	Low
The Pediatric OCD Treatment Study, 2004[236]	Low	Low	Unclear	Unclear	Low	Low	Low	Low

High, high risk of bias; low, low risk of bias; unclear, unclear risk of bias.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

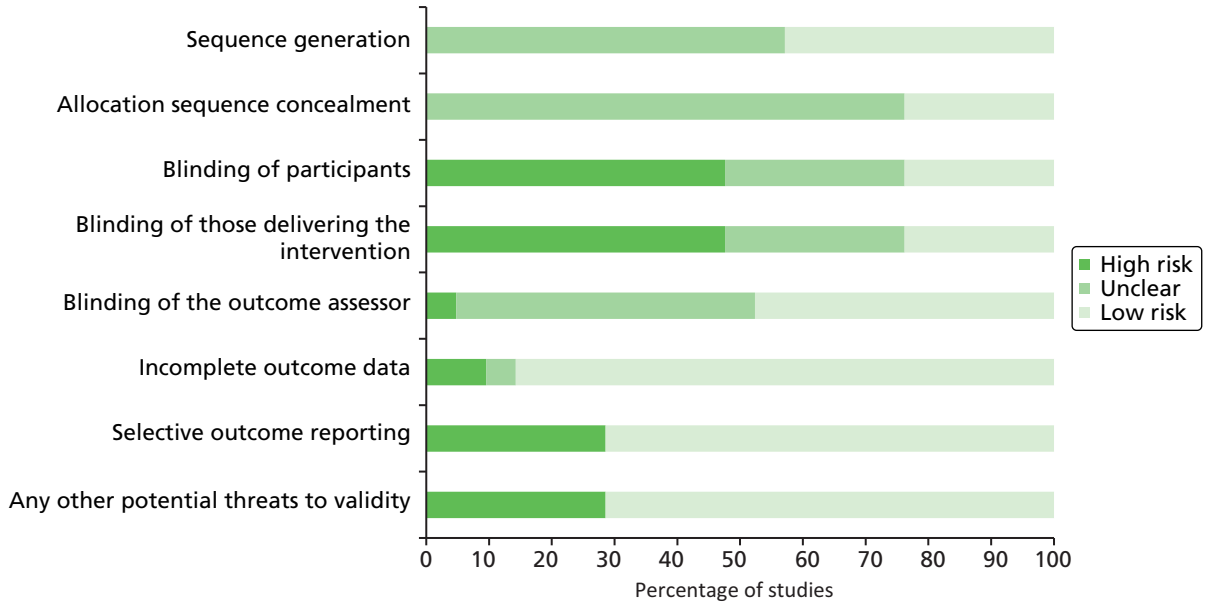


FIGURE 5 Methodological quality graph for the children and adolescents subset ($n = 22$): reviewers' judgements about each criterion as percentages across all included studies.

TABLE 14 Type of analysis and handling of missing data: adult subset

Intention-to-treat analysis	Number of studies	% of studies
Yes	28	44
No	26	41
Unclear	8	12
Not applicable	2	3
Total	64	100
Imputation method		
Last observation carried forward	25	39
Linear mixed-effects models	1	2
Unclear	10	16
No	26	40
Not applicable	2	3
Total	64	100

TABLE 15 Type of analysis and handling of missing data: children and adolescents subset

Intention-to-treat analysis	Number of studies	% of studies
Yes	17	77
No	3	14
Unclear	2	9
Total	22	100
Imputation method		
Last observation carried forward	14	65
Mixed-effects models	1	4
Other	1	4
Unclear	2	9
No	3	14
Not applicable	1	4
Total	22	100

Chapter 5 Network meta-analysis results (adults)

Clinical effectiveness: symptom reduction in the Yale–Brown Obsessive–Compulsive Scale

Description of the data set

Table 16 presents the raw data used for the YBOCS analysis in the adult subset of the data (a complete copy of the full data extraction is available in *Appendix 4*). Of the 64 studies eligible for inclusion in the NMA, 9 were excluded because they had not used the YBOCS scale.[156,165,168,169,186,194,205,208,210] This decision was made in light of the well-documented methodological and interpretational difficulties associated with the standardised MD.[142] The excluded studies are summarised here for completeness: these studies involved a total of 288 randomised patients (4% of the total randomised patients in the adult subset) and four clomipramine arms, three BT arms, three CT arms, two fluvoxamine arms, one amitriptyline arm, one imipramine arm and three placebo arms. One additional study was excluded because it was not part of the connected network.[179] Therefore, 54 studies were included in this analysis (see *Table 16*).

Table 17 presents summary data per type of intervention for the studies included in the NMA (number of arms and number of randomised patients per intervention).

Network meta-analysis: results

Network geometry

Figure 6 shows the network geometry of the YBOCS outcome in the adult subset, and *Table 18* presents summary data per type of intervention (number of patients randomised, total number of links with other treatments, number of unique treatments compared). Overall, of the 136 pairwise comparisons that can be made among the 17 treatment conditions, only 37 (27%) were studied directly by head-to-head comparison in 54 studies involving 6652 randomised patients. It should be noted, however, that 24 of these 37 direct comparisons are made in single trials. Each circle (node) represents an intervention and is proportional to the number of participants randomised to each treatment (i.e. the larger the node, the greater the number of participants randomised to each intervention). Placebo ($n = 1515$), paroxetine ($n = 902$), clomipramine ($n = 831$), fluoxetine ($n = 633$), sertraline ($n = 565$), fluvoxamine ($n = 521$), citalopram ($n = 311$), BT ($n = 287$), CBT ($n = 231$), escitalopram ($n = 226$), psychological placebo ($n = 196$), CT ($n = 172$), venlafaxine ($n = 98$) and waitlist ($n = 97$) had a sample approximately ≥ 100 (*Table 18*). Lines represent the available direct evidence and are proportional to the number of trials making a randomised comparison of each pair of treatments. *Figure 6* includes 79 randomised pairwise comparisons and the most common comparisons are those between placebo versus paroxetine ($n = 7$), placebo versus fluvoxamine ($n = 6$), placebo versus fluoxetine, placebo versus clomipramine, CBT versus waitlist and BT versus psychological placebo ($n = 5$ each), placebo versus sertraline and fluvoxamine versus clomipramine ($n = 4$ each). Nodes with the most connections (links) in the network (see *Table 24*) are drug placebo ($n = 35$ links with 10 different interventions), clomipramine ($n = 17$ links with eight different interventions), fluvoxamine ($n = 16$ links with seven different interventions), paroxetine ($n = 15$ links with six different interventions), BT ($n = 14$ links with seven different interventions), CBT ($n = 9$ links with six different interventions), fluoxetine ($n = 8$ links with four different interventions), sertraline ($n = 7$ links with four different interventions), psychological placebo ($n = 6$ links with four different interventions), waitlist ($n = 6$ links with two different interventions), citalopram ($n = 5$ links with two different interventions) and CT ($n = 5$ links with two different interventions).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 16 Raw data used for the YBOCS analysis (adult subset) sorted by study ID and number of arms

Study ID	t[i,1]	y[i,1]	n[i,1]	sd[i,1]	t[i,2]	y[i,2]	n[i,2]	sd[i,2]	t[i,3]	y[i,3]	n[i,3]	sd[i,3]	t[i,4]	y[i,4]	n[i,4]	sd[i,4]	Arms
Albert *et al.*, 2002[155]	8	18.36	25	7.11	9	17.3	40	6.15	NA	NA	NA	NA	NA	NA	NA	NA	2
Anderson and Rees, 2007[157]	2	23.5	14	6.4	11	16.7	17	6.8	NA	NA	NA	NA	NA	NA	NA	NA	2
Andersson *et al.*, 2012[158]	11	12.94	49	6.26	17	18.88	51	4.18	NA	NA	NA	NA	NA	NA	NA	NA	2
Belloch *et al.*, 2008[159]	10	8.31	13	8.75	12	6.8	16	3.55	NA	NA	NA	NA	NA	NA	NA	NA	2
Belotto-Silva *et al.*, 2012[160]	3	20.29	88	8.05	11	19.97	70	8.48	NA	NA	NA	NA	NA	NA	NA	NA	2
Bergeron *et al.*, 2002[161]	3	–9.7	72	7.7	6	–9.6	76	7.9	NA	NA	NA	NA	NA	NA	NA	NA	2
Bisserbe *et al.*, 1997[162]	6	–14.3	86	NA	9	–11.71	81	NA	NA	NA	NA	NA	NA	NA	NA	NA	2
CCSG1 1991[154]	1	25.11	108	6.34	9	16.23	102	7.37	NA	NA	NA	NA	NA	NA	NA	NA	2
CCSG2 1991[154]	1	25.59	119	5.78	9	14.7	120	7.45	NA	NA	NA	NA	NA	NA	NA	NA	2
Chouinard *et al.*, 1990[163]	1	–1.48	44	NA	6	–3.79	43	NA	NA	NA	NA	NA	NA	NA	NA	NA	2
Cordioli *et al.*, 2003[164]	2	23.2	24	5.5	11	15.1	23	7.8	NA	NA	NA	NA	NA	NA	NA	NA	2
Cottraux *et al.*, 2001[166]	10	–12.1	30	7.8	12	–12.5	30	8.2	NA	NA	NA	NA	NA	NA	NA	NA	2
Denys *et al.*, 2003[167]	5	–7.8	72	5.4	8	–7.2	73	7.5	NA	NA	NA	NA	NA	NA	NA	NA	2
Fals-Stewart *et al.*, 1993[170]	10	–8.1	31	NA	17	–1.8	32	NA	NA	NA	NA	NA	NA	NA	NA	NA	2
Foa *et al.*, 2005[171]	1	22.2	26	6.4	9	18.2	36	7.8	10	11	29	7.9	15	10.5	31	8.2	4
Freeman *et al.*, 1994[172]	4	–8.6	28	NA	9	–7.8	19	NA	NA	NA	NA	NA	NA	NA	NA	NA	2
Freeston *et al.*, 1997[173]	2	22	14	6	11	12.2	15	9.6	NA	NA	NA	NA	NA	NA	NA	NA	2
Goodman *et al.*, 1989[176]	1	28	21	7	4	19.4	21	7	NA	NA	NA	NA	NA	NA	NA	NA	2
Goodman *et al.*, 1996[177]	1	–1.71	78	4.88	4	–3.95	78	6.28	NA	NA	NA	NA	NA	NA	NA	NA	2
Greist *et al.*, 1995[126]	1	–3.41	84	6.19	6	–5.57	240	6.19	NA	NA	NA	NA	NA	NA	NA	NA	2
Greist *et al.*, 2002[178]	10	17.6	55	6.2	17	24.1	66	6.7	NA	NA	NA	NA	NA	NA	NA	NA	2
GlaxoSmithKline, 2005[174]	1	–4.61	75	7.53	5	–5.61	79	7.47	9	–7.73	78	7.42	NA	NA	NA	NA	3
GlaxoSmithKline, 2005[175]	5	–14.26	72	6.33	9	–13.19	69	6.48	NA	NA	NA	NA	NA	NA	NA	NA	2
Hollander *et al.*, 2003[180]	1	–5.6	120	7.67	4	–8.5	117	7.57	NA	NA	NA	NA	NA	NA	NA	NA	2

Study ID	t[i,1]	y[i,1]	n[i,1]	sd[i,1]	t[i,2]	y[i,2]	n[i,2]	sd[i,2]	t[i,3]	y[i,3]	n[i,3]	sd[i,3]	t[i,4]	y[i,4]	n[i,4]	sd[i,4]	Arms
Hollander *et al.*, 2003[181]	1	–3.33	89	NA	5	–4.14	88	NA	5	–6.35	86	NA	5	–7.34	85	NA	4
Jaurrieta *et al.*, 2008[182]	2	24.6	19	8.9	11	17.8	19	8.4	NA	NA	NA	NA	NA	NA	NA	NA	2
Jenike *et al.*, 1990[183]	1	22.3	9	7.8	6	20.6	10	9.2	NA	NA	NA	NA	NA	NA	NA	NA	2
Jenike *et al.*, 1990[184]	1	21.8	20	7.6	4	18.8	18	4	NA	NA	NA	NA	NA	NA	NA	NA	2
Jenike *et al.*, 1997[185]	1	18.7	18	6.1	3	16.2	19	6.3	NA	NA	NA	NA	NA	NA	NA	NA	2
Kamijima *et al.*, 2004[187]	1	20.3	94	7.38	5	15.8	94	8.09	NA	NA	NA	NA	NA	NA	NA	NA	2
Khodarahimi, 2009[188]	2	36.45	20	2.24	10	5.58	20	2.39	NA	NA	NA	NA	NA	NA	NA	NA	2
Kobak *et al.*, 2005[189]	1	19.87	30	7.46	13	19.75	30	7.46	NA	NA	NA	NA	NA	NA	NA	NA	2
Koran *et al.*, 1996[190]	4	17.8	34	7.7	9	17	39	8.55	NA	NA	NA	NA	NA	NA	NA	NA	2
Kronig *et al.*, 1999[191]	1	–4.14	79	NA	6	–8.5	85	NA	NA	NA	NA	NA	NA	NA	NA	NA	2
Lindsay *et al.*, 1997[192]	10	11	9	3.81	17	25.89	9	5.8	NA	NA	NA	NA	NA	NA	NA	NA	2
López-Ibor *et al.*, 1996[193]	3	–7.5	30	9.29	9	–8.9	24	7.13	NA	NA	NA	NA	NA	NA	NA	NA	2
McLean *et al.*, 2001[195]	12	16.1	31	6.7	10	13.2	32	7.2	NA	NA	NA	NA	NA	NA	NA	NA	2
Milanfranchi *et al.*, 1997[196]	4	18.4	13	9.2	9	16.5	12	11	NA	NA	NA	NA	NA	NA	NA	NA	2
Montgomery *et al.*, 1993[197]	1	–3.7	56	5.98	3	–5.13	52	6.41	3	–4.76	52	6.89	3	–6.07	54	6.92	4
Montgomery *et al.*, 2001[198]	1	–5.6	101	6.9	7	–8.4	102	7.3	7	–8.9	98	7	7	–10.4	100	6.9	4
Mundo *et al.*, 1997[199]	4	16.2	10	8.9	5	21.6	9	7.6	7	19.8	11	10.1	NA	NA	NA	NA	3
Mundo *et al.*, 2001[200]	4	–12.2	115	NA	9	–12	112	NA	NA	NA	NA	NA	NA	NA	NA	NA	2
Nakajima *et al.*, 1996[201]	1	–1.9	33	7.2	4	–7.1	60	7.03	NA	NA	NA	NA	NA	NA	NA	NA	2
Nakatani *et al.*, 2005[202]	4	20.2	10	9.4	10	12.9	10	4.9	17	28.4	8	5.5	NA	NA	NA	NA	3
O'Connor *et al.*, 1999[203]	2	17.5	6	4	11	13.3	6	8.6	NA	NA	NA	NA	NA	NA	NA	NA	2
O'Connor *et al.*, 2006[204]	1	25.4	10	3.5	4	24	11	4.7	NA	NA	NA	NA	NA	NA	NA	NA	2
Shareh *et al.*, 2010[206]	4	16.66	6	3.2	11	7	7	2.38	14	8.5	6	2.42	NA	NA	NA	NA	3
Sousa *et al.*, 2006[207]	6	–7.36	25	NA	11	–10.8	25	NA	NA	NA	NA	NA	NA	NA	NA	NA	2

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 16 Raw data used for the YBOCS analysis (adult subset) sorted by study ID and number of arms (*continued*)

Study ID	t[i,1]	y[i,1]	n[i,1]	sd[i,1]	t[i,2]	y[i,2]	n[i,2]	sd[i,2]	t[i,3]	y[i,3]	n[i,3]	sd[i,3]	t[i,4]	y[i,4]	n[i,4]	sd[i,4]	Arms
Stein *et al.*, 2007[124]	1	–8.46	113	8.08	5	–11.67	116	8.40	16	–11.43	112	8.25	16	–12.14	114	8.22	4
Tollefson *et al.*, 1994[127]	1	–0.8	89	5.66	3	–5.44	266	7.88	NA	NA	NA	NA	NA	NA	NA	NA	2
Van Oppen *et al.*, 1995[209]	10	17.9	29	9	12	13.4	28	9.4	NA	NA	NA	NA	NA	NA	NA	NA	2
Whittal *et al.*, 2005[211]	10	10.41	29	7.6	12	10.6	30	7.1	NA	NA	NA	NA	NA	NA	NA	NA	2
Whittal *et al.*, 2010[212]	12	6.43	37	4.77	17	9.1	30	6.48	NA	NA	NA	NA	NA	NA	NA	NA	2
Zohar and Judge, 1996[213]	1	–4.2	99	7.2	5	–6.4	201	7.1	9	–7	99	6.8	NA	NA	NA	NA	3

CCSG, Clomipramine Collaborative Study Group; NA, not applicable.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

TABLE 17 Summary raw YBOCS data per type of intervention (adult subset)

Intervention	Number of arms	Number of patients
Placebo	23	1515
Waitlist	6	97
Fluoxetine	8	633
Fluvoxamine	13	521
Paroxetine	10	902
Sertraline	7	565
Citalopram	4	311
Venlafaxine	2	98
Clomipramine	13	831
BT	11	287
CBT	9	231
CT	6	172
Hypericum	1	30
CBT + fluvoxamine	1	6
BT + clomipramine	1	31
Escitalopram	2	226
Psychological placebo	6	196
Total	123	6652

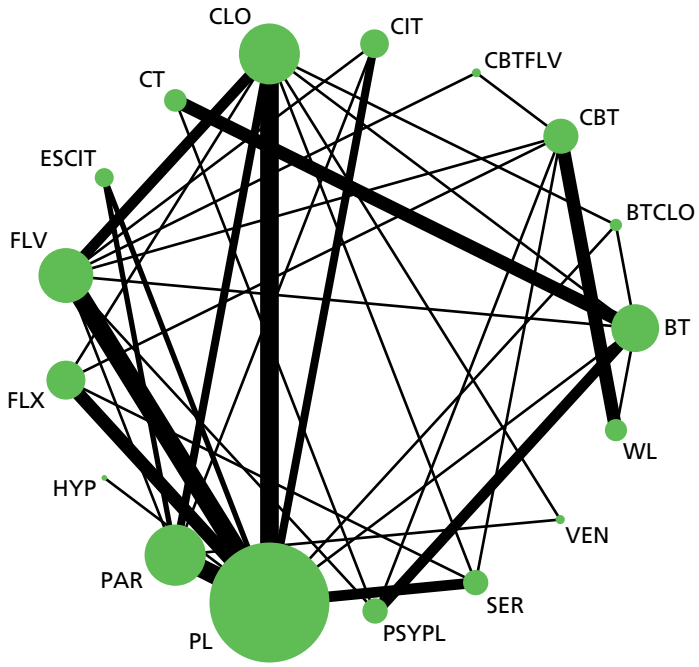


FIGURE 6 Network diagram for YBOCS analysis representing individual treatments (adult subset). BTCLO, BT + clomipramine; CBTFLV, CBT + fluvoxamine; CIT, citalopram; CLO, clomipramine; ESCIT, escitalopram; FLV, fluvoxamine; FLX, fluoxetine; HYP, hypericum; PAR, paroxetine; PL, placebo; PSYPL, psychological placebo; SER, sertraline; VEN, venlafaxine; WL, waitlist. Reproduced from Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, *et al*. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis [published online ahead of print June 15 2016]. *Lancet Psychiatry* 2016. © Skapinakis *et al*. Open Access article distributed under the terms of CC BY.[214]

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 18 Summary data per type of intervention for the YBOCS analysis, sorted by number of randomised patients (adult subset)

Intervention	Number of patients randomised	Number of pairwise comparisons (links)	Number of unique treatment comparisons
Placebo	1515	35	10
Clomipramine	831	17	8
Fluvoxamine	521	16	7
Paroxetine	902	15	6
BT	287	14	7
CBT	231	9	6
Fluoxetine	633	8	4
Sertraline	565	7	4
Psychological placebo	196	7	4
Waitlist	97	6	2
Citalopram	311	5	3
CT	172	5	2
Escitalopram	226	4	2
Venlafaxine	98	2	2
CBT + fluvoxamine	6	2	2
BT + clomipramine	31	2	3
Hypericum	30	1	1

Consistency of evidence

We examined model fit using the posterior mean of the residual deviance, the degree of between-study heterogeneity and the DIC. We compared a model assuming consistency of treatment effects with a model assuming independent treatment effects. *Table 19* presents the results of this comparison for the adult population.

The posterior mean of the residual deviance was 104.6 in the NMA, assuming consistency, compared with 107 data points (equivalent to the number of trial arms/data observations), suggesting adequate model fit. The posterior mean residual deviance from the independent treatment-effects model was 105.8. In addition, figures for the DIC are similar in both models (differences of < 3 or 5 are not considered important[145]), suggesting that the model assuming consistency has a similar fit to the model assuming independent treatment effects. However, we note a considerable reduction in heterogeneity when we relax the consistency assumption – the upper bound of the 95% CrI for the posterior median SD for the

TABLE 19 Posterior summaries from random-effects consistency and independent treatment-effect models (outcome: YBOCS; adult subset)

Model	Number of data points	Residual deviance (posterior mean)	SD, posterior median (95% CrI)	DIC
Random-effects consistency	107[a]	104.6[a]	3.10 (2.46 to 3.95)	480.8
Random-effects inconsistency	107[a]	105.8[a]	1.75 (1.18 to 2.53)	479.1

a Posterior mean residual deviance and number of data points are calculated for studies that reported a SD. SD is the between-trial variation in treatment effects (heterogeneity parameter).

independent effects model (upper credible limit 2.53) only just overlaps the lower bound of the 95% CrI for the consistency model (lower credible limit 2.46). We further explore this heterogeneity in subgroup and sensitivity analyses. As a further informal check, we note that the results of the NMA and the results of the pairwise comparisons (see *Table 20*) are in the same direction, with no evidence that the NMA effect estimate falls outside the 95% CrIs from the pairwise analysis. Overall, we conclude that there is no evidence for inconsistency in this network of trials, although heterogeneity may be moderate to high.

Data synthesis

The results of the NMA are presented in *Table 20*. We present the mean and 95% CrIs for the MD in YBOCS scores. We present both the direct, head-to-head and pairwise comparisons (as estimated from the independent effects model) and the results of the NMA (consistency model). All reported results for the NMA are at the class level, with the exception of the results for individual SSRIs, which are at the treatment level. Note that for treatments that did not form a class with multiple treatments (e.g. venlafaxine, clomipramine), the effect estimates from either the class or treatment level will be identical. For simplicity, we present only the MDs and 95% CrIs for all interventions compared with the reference intervention (drug placebo). A detailed table with all possible comparisons (both for the direct and NMA) is given in *Appendix 8*.

TABLE 20 Outcome 1: MD in YBOCS scores at end of study. Mean and 95% CrIs compared with drug placebo (adult subset)

	Posterior distribution of the treatment effect (mean YBOCS difference)				
	Direct		NMA		
Intervention	Mean	95% CrI	Mean	95% CrI	Posterior treatment rank, median (95% CrI)
Placebo					15 (14 to 16)
Waitlist	NA	NA	5.62	0.91 to 10.26	17 (16 to 17)
SSRIs (class effect)			–3.49	–5.12 to –1.81	
Fluoxetine	–2.66	–4.72 to –0.54	–3.46	–5.27 to –1.58	11 (6 to 14)
Fluvoxamine	–3.58	–5.51 to –1.70	–3.60	–5.29 to –1.95	10 (6 to 14)
Paroxetine	–2.84	–4.48 to –1.17	–3.42	–5.10 to –1.61	11 (6 to 14)
Sertraline	–2.85	–5.18 to –0.50	–3.50	–5.30 to –1.63	10 (6 to 14)
Citalopram	–3.65	–6.25 to –1.06	–3.49	–5.62 to –1.31	10 (5 to 14)
Escitalopram	–3.28	–6.38 to –0.20	–3.48	–5.61 to –1.23	10 (5 to 14)
Venlafaxine	NA	NA	–3.22	–8.26 to 1.88	12 (4 to 16)
Clomipramine	–6.28	–8.15 to –4.34	–4.72	–6.85 to –2.60	7 (4 to 13)
BT	–11.76	–16.87 to –6.62	–14.48	–18.61 to –10.23	1 (1 to 3)
CBT	NA	NA	–5.37	–9.10 to –1.63	6 (4 to 14)
CT	NA	NA	–13.36	–18.40 to –8.21	2 (1 to 4)
Hypericum	–0.08	–5.30 to 5.11	–0.15	–7.46 to 7.12	15 (4 to 17)
CBT + fluvoxamine	NA	NA	–7.50	–13.89 to –1.17	4 (2 to 14)
BT + clomipramine	–12.25	–17.29 to –7.09	–12.97	–19.18 to –6.74	3 (1 to 4)
Psychological placebo	NA	NA	–4.15	–8.65 to 0.49	8 (4 to 15)

NA, not applicable.
NMA MDs come from the class-level result, whereas treatment rankings are estimated from the individual-level treatment analysis.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Waitlist was the only group that showed a statistically significant worse effect than drug placebo. All active interventions, apart from venlafaxine and hypericum, had a greater effect than drug placebo on OCD symptom reduction (as measured by the total YBOCS scores). Venlafaxine showed a similar non-significant trend, whereas the effect of hypericum was indistinguishable from that of placebo.

Regarding the pharmacological interventions, SSRIs as a class had greater effects than drug placebo (class effect MD –3.49, 95% CrI –5.12 to –1.81). Regarding the individual effects of SSRIs, they were very similar with small differences between them. However, this was not unexpected because the grouping of treatments into a 'class' will have the effect of drawing individual treatment effects towards the class mean. All remaining treatments were analysed as individual treatments (within the class-level model). The relative effect of clomipramine was also greater than drug placebo (MD –4.72, 95% CrI –6.85 to –2.60). There was a trend for clomipramine to have a greater effect than SSRIs, but the 95% CrI included the null value (MD –1.23, 95% CrI –3.41 to 0.94). Venlafaxine showed a trend for a greater effect than drug placebo, but the 95% CrI also included the null value (MD –3.21, 95% CrI –8.26 to 1.88). It should be noted, however, that this result is based on two trials without direct comparison to placebo and a total number of 98 randomised patients. Therefore, this result should be interpreted with caution.

Regarding psychological interventions, all active psychotherapies had greater effects than drug placebo, with BT and CT having the largest effects, with small differences between them (MD –1.12, 95% CrI –1.95 to 4.19). Regarding the comparison between psychological interventions and psychological placebo, both BT and CT had greater effects (MD –10.33, 95% CrI –13.38 to –7.29 and MD –9.21, 95% CrI –13.1 to –5.34, respectively) but the effect of CBT was not significantly different from psychological placebo (MD –1.22, 95% CrI –5.54 to 3.03). In addition, both BT and CT had greater effects than CBT (MD –9.11, 95% CrI –13.18 to –4.97 and MD –7.99, 95% CrI –12.97 to –3.01, respectively). It should be noted, however, that CBT has not been compared directly with any of the psychological interventions and CT has been compared directly with BT only.

Regarding the comparison between psychological and pharmacological interventions, both BT and CT had greater effects than SSRIs as a class (MD –10.99, 95% CrI –15.14 to –6.75 for the comparison between BT and SSRIs; class effect MD –9.87, 95% CrI –14.91 to –4.74 for the comparison between CT and SSRIs). The difference with CBT was smaller and the 95% CrI included the null value (MD –1.88, 95% CrI –5.52 to 1.76) for the comparison between CBT and SSRIs. It should be noted, however, that of the three types of psychotherapy, CBT has been directly compared with SSRIs more extensively, whereas for CT there is no such direct comparison.

Similar results were observed for the comparison between different types of psychotherapy and clomipramine (MD –9.76, 95% CrI –14.02 to –5.40 for the comparison between BT and clomipramine; MD –8.63, 95% CrI –13.79 to –3.38 for the comparison between CT and clomipramine; MD –0.65, 95% CrI –4.60 to 3.29 for the comparison between CBT and clomipramine).

Combinations of medications and psychotherapy show large effects compared with placebo, with small differences between the effects of psychotherapy as monotherapy. It should be noted, however, that these results are based on a very limited number of patients and/or comparisons, especially for the combination of CBT with fluvoxamine. We recommend extreme caution in the interpretation of these results.

Table 20 also presents the median posterior treatment ranks with 95% CrIs. BT and CT were the most highly ranked treatments, followed by combinations of drug and psychotherapy, CBT and clomipramine.

Sensitivity analyses: outcome 1 – YBOCS (adult subset)

Low overall attrition and no evidence of imbalanced attrition

For this analysis, we excluded 21 studies in the adult subset for which overall levels of attrition were > 25% or differential attrition was > 15%. The 33 studies included[124,127,154,157–159,163,164,166,167,170,175,178,181–185,187,192,193,196,198–200,202,203,206,207,209,212] and the raw data used are presented in *Appendix 9*. Overall, 15 interventions (SSRIs were analysed individually and within a single class) were included and the total number of randomised patients was 3804 (57% of the patients originally used in our full analysis). MDs and 95% CrIs compared with placebo are presented in *Table 21*.

Compared with the results of the full data (see *Table 20*), there is a trend for a larger effect for SSRIs, clomipramine and CBT and a trend for a smaller effect for BT and CT. CBT (either as a monotherapy or in combination with fluvoxamine) has an effect that is very similar to the other psychological therapies. Clomipramine showed a non-statistically significant trend for superiority over SSRIs (MD –2.33, 95% CrI –4.94 to 0.29). All comparisons between clomipramine and psychological therapies had 95% CrIs that crossed zero (e.g. for the comparison between BT and clomipramine: MD –4.62, 95% CrI –4.63 to 1.46). However, the statistical power of these comparisons may be compromised as a result of the smaller number of studies/randomised patients included.

Low risk of bias in the domain: incomplete outcome assessment

Thirty-four studies from the adult subset were judged to be of 'low risk' in this domain (see *Table 12*) and were included in the analysis. The studies included and the raw data used are presented in *Appendix 9*. Overall, 15 interventions were included and the total number of randomised patients was 5074 (76% of the patients originally used in our full analysis). MDs and 95% CrIs relative to placebo are presented in *Table 22*.

TABLE 21 Sensitivity analysis (low overall attrition): outcome 1 – MD in YBOCS scores at end of study. Mean and 95% CrIs compared with drug placebo (adult subset)

Intervention	Posterior distribution of the treatment effect (mean YBOCS difference)		Posterior treatment rank, median (95% CrI)
	Mean	95% CrI	
Placebo	Reference	Reference	15 (13 to 15)
Waitlist	–3.32	–8.98 to 2.38	12 (5 to 15)
SSRIs (class effect)	–4.09	–6.07 to –2.06	
Fluoxetine	–4.10	–6.31 to –1.84	10 (6 to 14)
Fluvoxamine	–4.26	–6.64 to –2.00	9 (6 to 13)
Paroxetine	–4.10	–6.03 to –2.09	10 (6 to 13)
Sertraline	–4.05	–6.41 to –1.62	10 (6 to 14)
Citalopram	–4.01	–6.25 to –1.63	10 (6 to 14)
Escitalopram	–4.03	–6.30 to –1.61	10 (6 to 14)
Venlafaxine	–4.32	–8.72 to 0.12	9 (3 to 14)
Clomipramine	–6.42	–8.93 to –3.85	5 (3 to 10)
BT	–11.04	–16.84 to –5.19	2 (1 to 5)
CBT	–10.13	–14.52 to –5.69	3 (1 to 5)
CT	–10.63	–17.08 to –4.16	2 (1 to 7)
CBT + fluvoxamine	–10.31	–16.14 to –4.52	3 (1 to 7)
Psychological placebo	–2.85	–8.33 to 2.77	13 (5 to 15)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 22 Sensitivity analysis (low risk of bias in 'incomplete outcome assessment'): outcome 1 – MD in YBOCS scores at end of study. Mean and 95% CrIs compared with drug placebo (adult subset)

Intervention	Posterior distribution of the treatment effect (mean YBOCS difference)		Posterior treatment rank, median (95% CrI)
	Mean	95% CrI	
Placebo	Reference	Reference	13 (12 to 15)
Waitlist	2.06	–1.51 to 5.61	15 (12 to 15)
SSRIs (class effect)	–3.32	–4.25 to –2.46	
Fluoxetine	–3.37	–4.37 to –2.43	7 (4 to 11)
Fluvoxamine	–3.44	–4.48 to –2.53	7 (4 to 11)
Paroxetine	–3.04	–3.92 to –1.99	9 (5 to 12)
Sertraline	–3.49	–4.66 to –2.50	6 (4 to 11)
Citalopram	–3.37	–4.58 to –2.24	7 (4 to 11)
Escitalopram	–3.29	–4.45 to –2.07	7 (4 to 11)
Venlafaxine	–2.46	–5.49 to 0.57	11 (3 to 14)
Clomipramine	–3.16	–4.39 to –1.95	9 (4 to 12)
BT	–8.70	–11.78 to –5.75	2 (1 to 3)
CBT	–5.76	–8.23 to –3.31	3 (2 to 7)
Hypericum	–0.10	–4.34 to 4.11	13 (4 to 15)
BT + clomipramine	–10.67	–14.42 to –6.90	1 (1 to 2)
Psychological placebo	–0.92	–4.10 to 2.09	12 (4 to 14)

Compared with the results of the full data (see *Table 20*), there is a trend for a smaller effect for clomipramine, which is similar to the effect of the SSRIs. However, the combination of clomipramine with BT is now the highest ranked treatment, although the CrIs for ranks suggest that it may have a similar effectiveness to BT as monotherapy. It should be noted that in this analysis all CT studies have been excluded (eight out of nine CT studies have been assessed as being at high risk of incomplete outcome assessment bias, mainly because they had performed a completers analysis).

Low risk of bias in the domain: blinding of the outcome assessor

Seventeen studies that had reported the YBOCS outcome from the adult subset were judged to be at 'low risk' in this domain and were included in the analysis. The studies included and the raw data used are presented in *Appendix 9*. Overall, 15 interventions were included and the total number of randomised patients was 1461 (22% of the patients originally used in our full analysis). MDs and 95% CrI compared with placebo are presented in *Table 23*.

Compared with the results of the full data (see *Table 20*), there are small differences and the power of this analysis, owing to the small number of included studies, is low.

TABLE 23 Sensitivity analysis (low risk of bias in 'blinding of outcome assessor'): outcome 1 – MD in YBOCS scores at end of study. Mean and 95% CrIs compared with drug placebo (adult subset)

Intervention	Posterior distribution of the treatment effect (mean YBOCS difference)		Posterior treatment rank, median (95% CrI)
	Mean	95% CrI	
Placebo	Reference	Reference	13 (11 to 15)
Waitlist	3.23	–2.16 to 8.44	15 (12 to 15)
SSRIs (class effect)	–3.30	–5.59 to –0.65	
Fluoxetine	–3.42	–6.62 to 0.07	8 (4 to 12)
Fluvoxamine	–3.85	–5.99 to –1.95	7 (4 to 11)
Paroxetine	–3.20	–5.29 to –0.90	9 (5 to 12)
Sertraline	–2.71	–5.65 to 2.03	10 (5 to 13)
Citalopram	–3.27	–6.50 to 0.42	8 (4 to 13)
Escitalopram	–3.36	–5.38 to –1.21	8 (4 to 12)
Venlafaxine	–2.73	–5.97 to 0.47	10 (4 to 13)
Clomipramine	–4.05	–7.30 to –0.73	6 (4 to 12)
BT	–11.79	–15.17 to –8.28	2 (1 to 3)
CBT	–4.11	–7.63 to –0.34	5 (4 to 12)
CT	–12.23	–16.66 to –7.80	2 (1 to 3)
BT + clomipramine	–11.85	–16.07 to –7.82	2 (1 to 3)
Psychological placebo	2.33	–1.49 to 6.36	14 (13 to 15)

Acceptability (total dropouts)

Description of the data set

Table 24 presents the raw data used for the dropout analysis in the adult subset of the data. From the 64 studies eligible for inclusion in the NMA, 11 were excluded: eight studies either did not report dropout data or did not report dropout data separately for each arm;[179,182,187,188,194,201,204,208] and three studies were excluded because there were no dropouts (zero dropouts) in all arms.[183,192,199] Therefore, 53 studies were included in this analysis.[124,126,127,154–178,180,181,184–186,189–191,193,195–198,200,202,203,205–207,209–213]

Table 24 also presents raw dropout rates. It can be seen that the range of dropouts was 0–43%, with a median of 18%. *Table 25* presents summary dropout rate per type of intervention (minimum, maximum and median of raw dropout rates).

Network meta-analysis: results

Network geometry

Figure 7 shows the network geometry for total dropouts in the adult subset. Overall, of the 190 comparisons that can be made among the 20 treatment conditions, only 38 (20%) were studied directly in 53 studies involving 6743 randomised patients. It should be noted, however, that 24 of the 38 direct comparisons are made in single trials. As before, circles (treatment nodes) represent the interventions used in the network and are proportional to the number of participants randomised to a treatment. Placebo ($n = 1439$), clomipramine ($n = 937$), paroxetine ($n = 813$), fluoxetine ($n = 640$), sertraline ($n = 561$), fluvoxamine ($n = 497$), BT ($n = 366$), citalopram ($n = 300$), escitalopram ($n = 232$), CBT ($n = 221$), psychological placebo ($n = 200$) and venlafaxine ($n = 101$) had a sample size of > 100. Lines (network

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 24 Raw data used for the dropout analysis (adult subset)

Study ID	t[i,1], %	r[i,1], %	n[i,1], %	dr[i,1], %	t[i,2], %	r[i,2], %	n[i,2], %	dr[i,2], %	t[i,3], %	r[i,3], %	n[i,3], %	dr[i,3], %	t[i,4], %	r[i,4], %	n[i,4], %	dr[i,4], %
Albert *et al.*, 2002[155]	8	1	26	4	9	7	47	15	NA	NA	NA	NA	NA	NA	NA	NA
Ananth *et al.*, 1981[156]	9	1	10	10	13	2	10	20	NA	NA	NA	NA	NA	NA	NA	NA
Anderson and Rees, 2007[157]	2	3	17	18	11	4	21	19	NA	NA	NA	NA	NA	NA	NA	NA
Andersson *et al.*, 2012[158]	11	2	50	4	18	0	51	0	NA	NA	NA	NA	NA	NA	NA	NA
Belloch *et al.*, 2008[159]	10	2	15	13	12	2	18	11	NA	NA	NA	NA	NA	NA	NA	NA
Belotto-Silva *et al.*, 2012[160]	3	33	88	38	11	18	70	26	NA	NA	NA	NA	NA	NA	NA	NA
Bergeron *et al.*, 2002[161]	3	22	73	30	6	22	77	29	NA	NA	NA	NA	NA	NA	NA	NA
Bisserbe *et al.*, 1997[162]	6	23	86	27	9	35	82	43	NA	NA	NA	NA	NA	NA	NA	NA
CCSG1, 1991[154]	1	13	121	11	9	17	118	14	NA	NA	NA	NA	NA	NA	NA	NA
CCSG2, 1991[154]	1	12	139	9	9	14	142	10	NA	NA	NA	NA	NA	NA	NA	NA
Chouinard *et al.*, 1990[163]	1	4	44	9	6	6	43	14	NA	NA	NA	NA	NA	NA	NA	NA
Cordioli *et al.*, 2003[164]	2	1	24	4	11	1	23	4	NA	NA	NA	NA	NA	NA	NA	NA
Cottraux *et al.*, 1993[165]	4	7	20	35	10	5	20	25	14	4	20	20	NA	NA	NA	NA
Cottraux *et al.*, 2001[166]	10	3	33	9	12	2	32	6	NA	NA	NA	NA	NA	NA	NA	NA
Denys *et al.*, 2003[167]	5	9	75	12	8	4	75	5	NA	NA	NA	NA	NA	NA	NA	NA
Emmelkamp and Beens, 1991[168]	10	4	15	27	12	5	15	33	NA	NA	NA	NA	NA	NA	NA	NA

Study ID	t[i,1], %	r[i,1], %	n[i,1], %	dr[i,1], %	t[i,2], %	r[i,2], %	n[i,2], %	dr[i,2], %	t[i,3], %	r[i,3], %	n[i,3], %	dr[i,3], %	t[i,4], %	r[i,4], %	n[i,4], %	dr[i,4], %
Emmelkamp *et al.*, 1988[169]	10	1	10	10	12	1	10	10	NA	NA	NA	NA	NA	NA	NA	NA
Fals-Stewart *et al.*, 1993[170]	10	3	34	9	18	0	32	0	NA	NA	NA	NA	NA	NA	NA	NA
Foa *et al.*, 2005[171]	1	12	32	38	9	20	47	43	10	16	37	43	16	14	33	42
Freeman *et al.*, 1994[172]	4	6	34	18	9	13	32	41	NA	NA	NA	NA	NA	NA	NA	NA
Freeston *et al.*, 1997[173]	2	0	14	0	11	3	15	20	NA	NA	NA	NA	NA	NA	NA	NA
GlaxoSmithKline, 2005[174]	1	20	77	26	5	28	82	34	9	28	82	34	NA	NA	NA	NA
GlaxoSmithKline, 2005[175]	5	1	73	1	9	4	73	5	NA	NA	NA	NA	NA	NA	NA	NA
Goodman *et al.*, 1989[176]	1	6	23	26	4	2	23	9	NA	NA	NA	NA	NA	NA	NA	NA
Goodman *et al.*, 1996[177]	1	17	80	21	4	23	80	29	NA	NA	NA	NA	NA	NA	NA	NA
Greist *et al.*, 1995[126]	1	24	84	29	6	65	241	27	NA	NA	NA	NA	NA	NA	NA	NA
Greist *et al.*, 2002[178]	10	14	69	20	18	9	75	12	NA	NA	NA	NA	NA	NA	NA	NA
Hollander *et al.*, 2003[180]	1	31	126	25	4	43	127	34	NA	NA	NA	NA	NA	NA	NA	NA
Hollander *et al.*, 2003[181]	1	15	89	17	5	14	88	16	5	20	86	23	5	19	85	22
Jenike *et al.*, 1990[184]	1	0	20	0	4	2	20	10	NA	NA	NA	NA	NA	NA	NA	NA
Jenike *et al.*, 1997[185]	1	3	21	14	3	4	23	17	NA	NA	NA	NA	NA	NA	NA	NA

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 24 Raw data used for the dropout analysis (adult subset) (*continued*)

Study ID	t[i,1], %	r[i,1], %	n[i,1], %	dr[i,1], %	t[i,2], %	r[i,2], %	n[i,2], %	dr[i,2], %	t[i,3], %	r[i,3], %	n[i,3], %	dr[i,3], %	t[i,4], %	r[i,4], %	n[i,4], %	dr[i,4], %
Jones and Menzies, 1998[186]	2	1	11	9	12	1	12	8	NA	NA	NA	NA	NA	NA	NA	NA
Kobak *et al.*, 2005[189]	1	9	30	30	19	8	30	27	NA	NA	NA	NA	NA	NA	NA	NA
Koran *et al.*, 1996[190]	4	8	37	22	9	15	42	36	NA	NA	NA	NA	NA	NA	NA	NA
Kronig *et al.*, 1999[191]	1	25	81	31	6	25	86	29	NA	NA	NA	NA	NA	NA	NA	NA
López-Ibor *et al.*, 1996[193]	3	5	30	17	9	3	25	12	NA	NA	NA	NA	NA	NA	NA	NA
McLean *et al.*, 2001[195]	10	12	44	27	12	18	49	37	NA	NA	NA	NA	NA	NA	NA	NA
Milanfranchi *et al.*, 1997[196]	4	0	13	0	9	1	13	8	NA	NA	NA	NA	NA	NA	NA	NA
Montgomery *et al.*, 1993[197]	1	15	57	26	3	14	53	26	3	13	52	25	3	14	55	25
Montgomery *et al.*, 2001[198]	1	17	101	17	7	15	100	15	7	15	98	15	7	16	102	16
Mundo *et al.*, 2001[200]	4	19	115	17	9	26	112	23	NA	NA	NA	NA	NA	NA	NA	NA
Nakatani *et al.*, 2005[202]	4	1	11	9	10	1	11	9	18	1	9	11	NA	NA	NA	NA
O'Connor *et al.*, 1999[203]	2	0	6	0	11	1	7	14	NA	NA	NA	NA	NA	NA	NA	NA
Perse *et al.*, 1987[205]	1	2	10	20	4	2	10	20	NA	NA	NA	NA	NA	NA	NA	NA
Shareh *et al.*, 2010[206]	4	1	7	14	11	0	7	0	15	1	7	14	NA	NA	NA	NA
Sousa *et al.*, 2007[208]	6	3	28	11	11	3	28	11	NA	NA	NA	NA	NA	NA	NA	NA

Study ID	t[i,1], %	r[i,1], %	n[i,1], %	dr[i,1], %	t[i,2], %	r[i,2], %	n[i,2], %	dr[i,2], %	t[i,3], %	r[i,3], %	n[i,3], %	dr[i,3], %	t[i,4], %	r[i,4], %	n[i,4], %	dr[i,4], %
Stein *et al.*, 2007[124]	1	16	115	14	5	29	119	24	17	24	116	21	17	21	116	18
Tollefson *et al.*, 1994[127]	1	13	89	15	3	12	87	14	3	22	89	25	3	22	90	24
Van Oppen *et al.*, 1995[209]	10	7	36	19	12	7	35	20	NA	NA	NA	NA	NA	NA	NA	NA
Volavka *et al.*, 1985[210]	9	3	11	27	20	4	12	33	NA	NA	NA	NA	NA	NA	NA	NA
Whittal *et al.*, 2005[211]	10	13	42	31	12	11	41	27	NA	NA	NA	NA	NA	NA	NA	NA
Whittal *et al.*, 2010[212]	12	3	40	8	18	3	33	9	NA	NA	NA	NA	NA	NA	NA	NA
Zohar and Judge, 1996[213]	1	40	100	40	5	53	205	26	9	36	101	36	NA	NA	NA	NA

CCSG, Clomipramine Collaborative Study Group; NA, not applicable.

Notes

t[i], type of treatment per arm [i] (1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = amitriptyline, 14 = fluvoxamine and BT, 15 = fluvoxamine and CBT, 16 = clomipramine and BT, 17 = escitalopram, 18 = psychological placebo, 19 = hypericum, 20 = imipramine); r[i], number of dropouts in arm[i]; n[i], total number of patients in arm [i]; dr[i], dropout rate (%) in arm[i].

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 25 Summary raw dropout rates per type of intervention (adult subset)

Intervention	Dropout rates (%)			Number of arms
	Minimum	Maximum	Median	
Placebo	0	40	21	20
Waitlist	0	18	4	5
Fluoxetine	14	38	25	10
Fluvoxamine	0	35	17	12
Paroxetine	1	34	23	8
Sertraline	11	29	27	6
Citalopram	15	16	15	3
Venlafaxine	4	5	4.5	2
Clomipramine	5	43	23	15
BT	9	43	20	12
CBT	0	26	12.5	8
CT	6	37	11	9
Amitriptyline	20	20	NA	1
BT + fluvoxamine	20	20	NA	1
CBT + fluvoxamine	14	14	NA	1
BT + clomipramine	42	42	NA	1
Escitalopram	18	21	19.5	2
Psychological placebo	0	12	9	5
Hypericum	27	27	NA	1
Imipramine	33	33	NA	1

NA, not available.

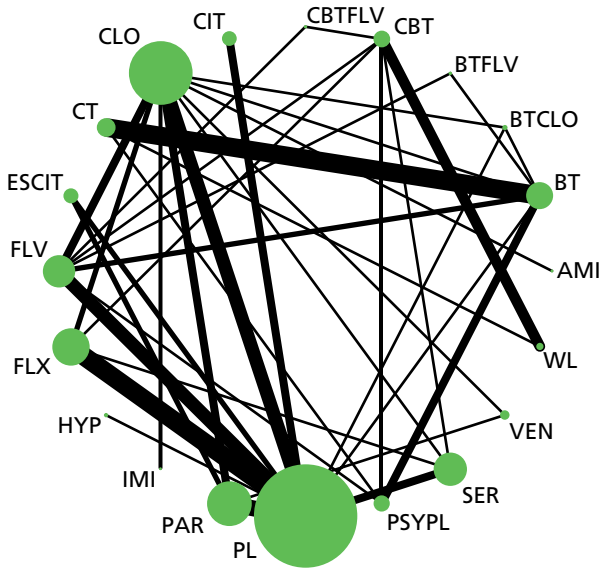


FIGURE 7 Network diagram for dropouts representing individual treatments (adult subset). AMI, amitriptyline; BTCLO, BT + clomipramine; BTFLV, BT + fluvoxamine; CBTFLV, CBT + fluvoxamine; CIT, citalopram; CLO, clomipramine; ESCIT, escitalopram; FLV, fluvoxamine; FLX, fluoxetine; HYP, hypericum; IMI, imipramine; PAR, paroxetine; PL, placebo; PSYPL, psychological placebo; SER, sertraline; VEN, venlafaxine; WL, waitlist.

edges) are proportional to the number of direct randomised comparisons. *Figure 7* includes 79 randomised pairwise comparisons and the most common comparisons are those between placebo versus fluoxetine ($n = 7$) and BT versus CT ($n = 7$). Nodes with the most connections (links) in the network are drug placebo ($n = 33$ links), clomipramine ($n = 19$ links), BT ($n = 16$ links), fluvoxamine ($n = 15$ links), paroxetine ($n = 11$ links), fluoxetine ($n = 10$ links), CBT ($n = 9$ links) and CT ($n = 9$ links).

Consistency of evidence

We examined model fit using the posterior mean of the residual deviance, the degree of between-study heterogeneity and the DIC. We compared a model assuming consistency of treatment effects with a model assuming independent treatment effects. For the 'consistency' model all SSRIs were analysed as a class and individually. *Table 26* presents the results of this comparison for the adult set.

The posterior mean of the residual deviance was 118.2 in model assuming consistency compared with the number of data points ($n = 123$), suggesting adequate model fit. The posterior mean residual deviance from the independent treatment-effects model was 120.3 In addition, the lower value of the DIC for the consistency model suggests that it is preferred over the independent effects model. In addition, the results of the NMA and the results of the pairwise comparisons (see *Table 27*) are in the same direction, with no evidence that the NMA effect estimate falls outside the 95% CrIs from the pairwise analysis. Overall, there is no evidence for inconsistency.

Data synthesis

The results of the NMA are presented in *Table 27*. We present posterior median ORs for dropouts relative to drug placebo (reference treatment). We present both the direct head-to-head comparisons from pairwise meta-analysis (from independent effects model) and the results of the NMA from the model assuming consistency. For simplicity, we present only the ORs compared with the drug placebo. A more detailed table with all possible comparisons (both for the direct and NMA) is given in *Appendix 8*.

Clomipramine was the only intervention with a statistically significant higher likelihood of dropout than placebo, with an OR of 1.52 (95% CrI 1.16 to 2.01). Amitriptyline, imipramine and the combination of CBT with fluvoxamine had larger ORs than clomipramine, suggesting increased odds of dropout. However, these results are based on just one trial, the 95% CrIs are wide and include the null value of no difference. Therefore, these results should be interpreted with caution. SSRIs as a class were not more likely than placebo to lead to attrition. Differences with individual SSRIs were very small and insignificant. There was a non-significant trend for venlafaxine to be associated with a lower dropout rate than placebo but this was based on only two trials. All psychological therapies were not more likely than placebo to lead to dropout.

Table 27 also presents the posterior median treatment ranks with 95% CrIs. As before, it is the tricyclics, particularly clomipramine, that are ranked lowest (i.e. they are less tolerable). In general, all psychological therapies delivered as monotherapy are ranked more highly than pharmacological treatments. Combinations of psychological treatments with medication result in lower ranks than psychological monotherapy, but the evidence is based on single trials with small sample sizes. We again suggest caution in the interpretation of these findings.

TABLE 26 Posterior summaries from random-effects consistency and independent treatment-effect models (outcome: dropouts; adult subset)

Model	Number of data points	Residual deviance, posterior mean	SD,[a] posterior median, (95% CrI)	DIC
Random-effects consistency	123	118.2	0.13 (0.01 to 0.32)	610.3
Random-effects independent effect	123	120.3	0.12 (0.01 to 0.32)	626.0

a SD is the between-trial variation in treatment effects (heterogeneity parameter).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 27 Outcome 2: dropouts. Median ORs (95% CrI) compared with drug placebo (adult subset)

Intervention	Direct		NMA		Posterior treatment rank (median and 95% CrI)
	Median OR	95% CrI	Median OR	95% CrI	
Placebo	Reference	Reference	Reference	Reference	9 (5 to 16)
Waitlist	NA	NA	0.40	0.10 to 1.50	2 (1 to 17)
Psychological placebo	NA	NA	0.52	0.19 to 1.45	4 (1 to 15)
SSRIs (class effect)			1.08	0.85 to 1.36	
Fluoxetine	1.25	0.79 to 2.03	1.12	0.88 to 1.54	13 (7 to 18)
Fluvoxamine	1.38	0.88 to 2.18	1.09	0.85 to 1.41	12 (6 to 17)
Paroxetine	1.08	0.78 to 1.52	1.09	0.86 to 1.38	12 (6 to 17)
Sertraline	0.98	0.63 to 1.55	1.04	0.78 to 1.33	10 (5 to 16)
Citalopram	0.90	0.49 to 1.75	1.06	0.74 to 1.41	11 (5 to 17)
Escitalopram	1.09	0.64 to 1.97	1.08	0.80 to 1.46	12 (5 to 17)
Venlafaxine	NA	NA	0.39	0.11 to 1.15	2 (1 to 13)
Clomipramine	1.25	0.88 to 1.76	1.52	1.16 to 2.01	17 (13 to 19)
Amitriptyline	NA	NA	4.51	0.30 to 138.6	19 (2 to 20)
Imipramine	NA	NA	1.96	0.29 to 16.07	18 (2 to 20)
Hypericum	0.83	0.25 to 2.80	0.85	0.25 to 2.73	7 (1 to 19)
BT	1.27	0.52 to 3.08	1.04	0.52 to 2.08	10 (4 to 18)
CBT	NA	NA	0.77	0.40 to 1.59	6 (2 to 17)
CT	NA	NA	1.01	0.43 to 2.30	9 (3 to 19)
BT + fluvoxamine	NA	NA	0.61	0.13 to 2.35	4 (1 to 19)
CBT + fluvoxamine	NA	NA	2.13	0.04 to 74.15	18 (1 to 20)
BT + clomipramine	1.23	0.48 to 3.05	1.27	0.53 to 2.93	15 (4 to 19)

NA, not applicable.

Sensitivity analyses: outcome 2, dropouts – adult subset

Low overall attrition and no evidence of imbalanced attrition

For this analysis we included 40[124,127,154,156–160,163,164,166,167,169–171,175,177,178,180,181,184–186,189,193,195–198,200,202,203,205–207,209–212] and excluded 13 studies. The studies included and the raw data used are presented in *Appendix 9*. Overall, 18 interventions were included and the total number of randomised patients was 4767 (70.7% of the patients originally used in our full analysis). MDs and 95% CrIs compared with placebo are presented in *Table 28*. It can be seen that compared with the full data set reported in *Table 27*, the results are essentially similar, with the tricyclic drugs, in particular clomipramine, being most poorly tolerated.

Low risk of bias in the domain: incomplete outcome assessment

For this analysis we included 29[124,127,157,158,160–164,167,171–174,176–178,180,181,185,189–191,193,197,198,200,207,213] and excluded 24 studies. The studies included and the raw data used are presented in *Appendix 9*. Overall, 15 interventions were included and the total number of randomised patients was 4868 (72% of the patients originally used in our full analysis). MDs and 95% CrIs compared with placebo are presented in *Table 29*. It can be seen that compared with the full data set reported in *Table 27*, the results are essentially similar.

TABLE 28 Sensitivity analysis (low overall attrition): outcome 2 – dropouts. Median ORs (95% CrI) compared with drug placebo (adult subset)

Intervention	Posterior distribution of the treatment effect (mean YBOCS difference)		Posterior treatment rank, median (95% CrI)
	Median OR	95% CrI	
Placebo	Reference	Reference	8 (4 to 12)
Waitlist	0.36	0.09 to 1.43	3 (1 to 13)
SSRIs (class effect)	1.28	0.94 to 1.73	
Fluoxetine	1.32	0.95 to 1.87	12 (7 to 17)
Fluvoxamine	1.31	0.98 to 1.76	12 (7 to 16)
Paroxetine	1.34	0.97 to 1.90	13 (7 to 17)
Sertraline	1.28	0.80 to 1.97	12 (6 to 17)
Citalopram	1.22	0.75 to 1.67	11 (5 to 16)
Escitalopram	1.27	0.88 to 1.79	11 (6 to 16)
Venlafaxine	0.52	0.10 to 1.84	5 (1 to 16)
Clomipramine	1.58	1.04 to 2.59	15 (8 to 18)
BT	0.44	0.05 to 2.77	4 (2 to 17)
CBT	0.84	0.42 to 1.62	7 (3 to 15)
CT	0.45	0.06 to 2.70	4 (1 to 16)
Amitriptyline	3.94	0.23 to 162.7	17 (2 to 18)
CBT + fluvoxamine	1.94	0.06 to 79.68	16 (1 to 18)
Psychological placebo	0.24	0.02 to 1.46	2 (1 to 11)
Hypericum	0.83	0.23 to 2.91	7 (1 to 17)
Imipramine	2.05	0.27 to 15.90	16 (2 to 18)

TABLE 29 Sensitivity analysis (low risk of bias in 'incomplete outcome assessment'): outcome 2 – dropouts. Median ORs (95% CrI) compared with drug placebo (adult subset)

Intervention	Posterior distribution of the treatment effect (mean YBOCS difference)		Posterior treatment rank, median (95% CrI)
	Median OR	95% CrI	
Placebo	Reference	Reference	7 (3 to 12)
Waitlist	0.39	0.08 to 1.81	2 (1 to 14)
SSRIs (class effect)	1.10	0.84 to 1.43	
Fluoxetine	1.15	0.88 to 1.59	10 (5 to 14)
Fluvoxamine	1.09	0.81 to 1.43	9 (4 to 13)
Paroxetine	1.12	0.86 to 1.48	10 (5 to 14)
Sertraline	1.07	0.76 to 1.42	8 (4 to 13)
Citalopram	1.08	0.72 to 1.49	9 (3 to 14)
Escitalopram	1.10	0.78 to 1.52	9 (4 to 14)
Venlafaxine	0.44	0.10 to 1.61	2 (1 to 14)
Clomipramine	1.55	1.10 to 2.17	14 (10 to 15)
BT	1.23	0.50 to 2.91	12 (3 to 15)
CBT	0.80	0.37 to 1.73	5 (2 to 14)
BT + clomipramine	1.33	0.52 to 3.39	13 (3 to 15)
Psychological placebo	0.51	0.14 to 1.82	3 (1 to 14)
Hypericum	0.84	0.25 to 2.90	5 (1 to 15)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Low risk of bias in the domain: blinding of the outcome assessor

For this analysis we included 18[124,155,158–160,164,166–169,171,175,184,202,203,205,207,211] and excluded 35 studies. The studies included and the raw data used are presented in *Appendix 9*. Overall, 14 interventions were included and the total number of randomised patients was 1581 (23.5% of the patients originally used in our full analysis). MDs and 95% CrIs compared with placebo are presented in *Table 30*. The power of the analysis is compromised, but the results show the same trends with the full analysis.

Rankograms (both outcomes)

Table 31 presents the probabilities that each treatment is among the best three or worst three for both outcomes (YBOCS/dropouts) – a dropout rate that is among the top three means better tolerability (i.e. fewer dropouts). In *Appendix 8* we present complete data for all rank probabilities for both outcomes. Based on these data, we also present rankograms (plots of the probabilities for each treatment taking each possible rank) in *Figure 8*. These results show that there is a great deal of uncertainty surrounding the overall rankings of the active treatments used to treat OCD in adults. Although we observe that BT has a 50% probability of being the most effective treatment for reducing OCD symptoms, there is a 50% probability that it is not the best treatment, which represents a large degree of uncertainty.

TABLE 30 Sensitivity analysis (low risk of bias in 'blinding of the outcome assessor'): outcome 2 – dropouts. Median ORs (95% CrI) compared with drug placebo (adult subset)

Intervention	Posterior distribution of the treatment effect (mean YBOCS difference)		Posterior treatment rank, median (95% CrI)
	Median OR	95% CrI	
Placebo	Reference	Reference	6 (2 to 12)
Waitlist	0.45	0.01 to 31.84	2 (1 to 14)
SSRIs (class effect)	1.39	0.46 to 8.44	
Fluoxetine	1.60	0.45 to 47.92	11 (4 to 14)
Fluvoxamine	1.11	0.36 to 2.71	7 (2 to 13)
Paroxetine	1.55	0.67 to 3.74	10 (4 to 14)
Sertraline	1.38	0.31 to 31.95	10 (2 to 14)
Escitalopram	1.34	0.62 to 3.05	9 (3 to 14)
Venlafaxine	0.48	0.10 to 1.79	3 (1 to 11)
Clomipramine	1.36	0.46 to 4.24	9 (3 to 14)
BT	1.23	0.39 to 3.83	8 (3 to 14)
CBT	1.13	0.27 to 32.32	7 (2 to 14)
CT	1.10	0.27 to 4.30	7 (2 to 14)
BT + clomipramine	1.24	0.36 to 4.26	8 (2 to 14)
Psychological placebo	0.31	0.01 to 4.51	2 (1 to 14)

TABLE 31 Summary of rank probabilities (top three/bottom three): adult subset

		Probability treatment being in:	
Outcome[a]	Treatment	Top three	Bottom three
YBOCS	Placebo	0.00	0.92
Dropout	Placebo	0.00	0.00
YBOCS	Waitlist	0.00	1.00
Dropout	Waitlist	0.66	0.02
YBOCS	Fluoxetine	0.00	0.02
Dropout	Fluoxetine	0.00	0.03
YBOCS	Fluvoxamine	0.00	0.01
Dropout	Fluvoxamine	0.00	0.01
YBOCS	Paroxetine	0.00	0.02
Dropout	Paroxetine	0.00	0.01
YBOCS	Sertraline	0.00	0.02
Dropout	Sertraline	0.00	0.00
YBOCS	Citalopram	0.00	0.02
Dropout	Citalopram	0.01	0.01
YBOCS	Venlafaxine	0.01	0.19
Dropout	Venlafaxine	0.69	0.00
YBOCS	Clomipramine	0.00	0.00
Dropout	Clomipramine	0.00	0.39
YBOCS	BT	1.00	0.00
Dropout	BT	0.01	0.06
YBOCS	CBT	0.00	0.01
Dropout	CBT	0.12	0.02
YBOCS	CT	0.95	0.00
Dropout	CT	0.03	0.08
YBOCS	Hypericum	0.00	0.66
Dropout	Hypericum	0.21	0.13
YBOCS	CBT + fluvoxamine	0.14	0.02
Dropout	CBT + fluvoxamine	0.20	0.56
YBOCS	BT + clomipramine	0.89	0.00
Dropout	BT + clomipramine	0.02	0.24
YBOCS	Escitalopram	0.00	0.02
Dropout	Escitalopram	0.01	0.02
YBOCS	Psychological placebo	0.00	0.09
Dropout	Psychological placebo	0.50	0.00
Dropout	Amitriptyline	0.06	0.76
Dropout	BT + fluvoxamine	0.41	0.06
Dropout	Imipramine	0.07	0.59

a For dropouts, being in the top three means better tolerability (i.e. fewer dropouts).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

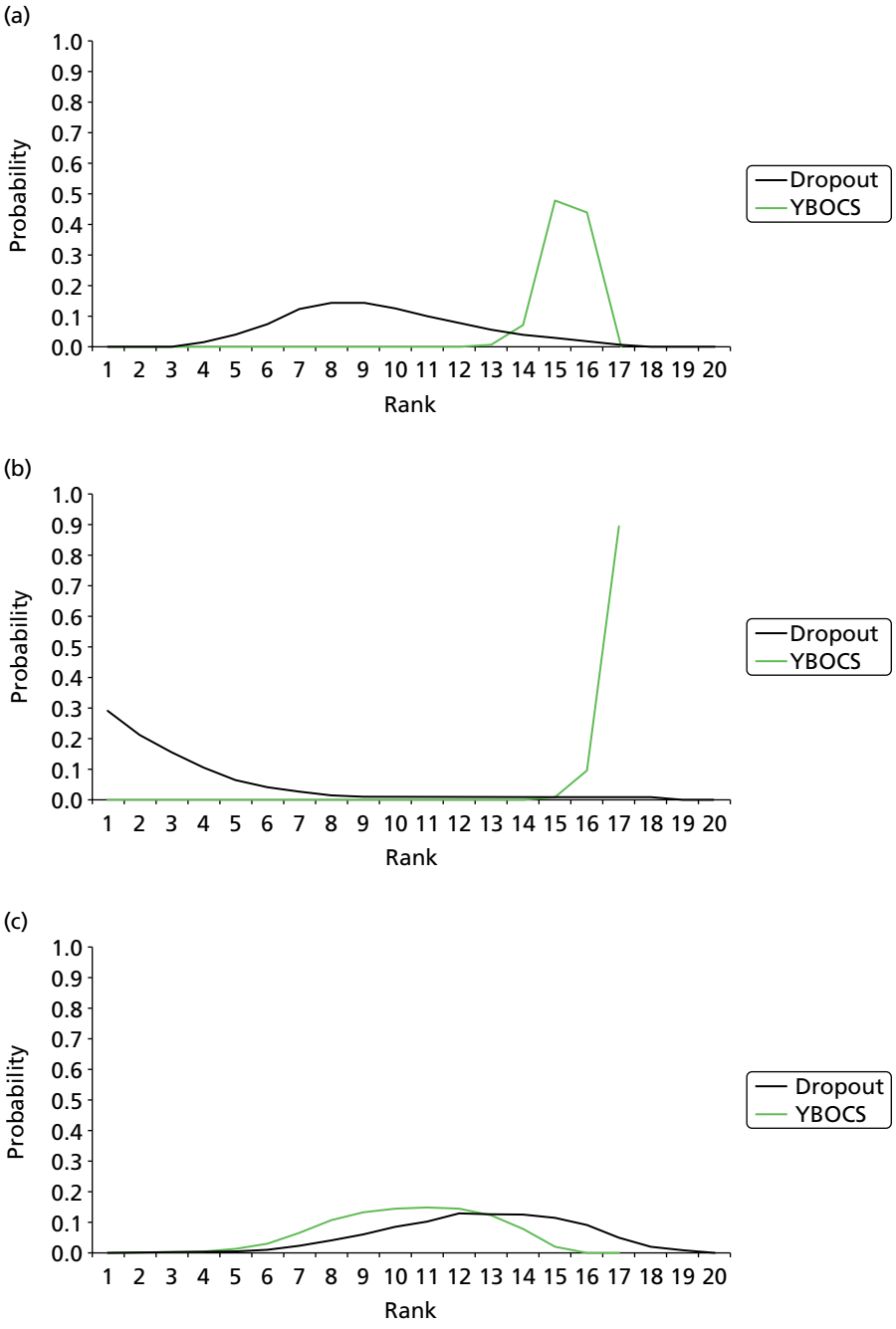


FIGURE 8 Rankograms for adults: dropout (black lines); YBOCS (green lines). (a) placebo; (b) waitlist; (c) fluoxetine; (d) fluvoxamine; (e) paroxetine; (f) sertraline; (g) citalopram; (h) venlafaxine; (i) clomipramine; (j) BT; (k) CBT; (l) CT; (m) hypericum; (n) CBT + fluvoxamine; (o) BT + clomipramine; (p) escitalopram; (q) psychological placebo; (r) amitriptyline; (s) BT + fluvoxamine; and (t) imipramine. Reproduced from Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, *et al*. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis [published online ahead of print June 15 2016]. *Lancet Psychiatry* 2016. © Skapinakis *et al*. Open Access article distributed under the terms of CC BY.[214] (*continued*)

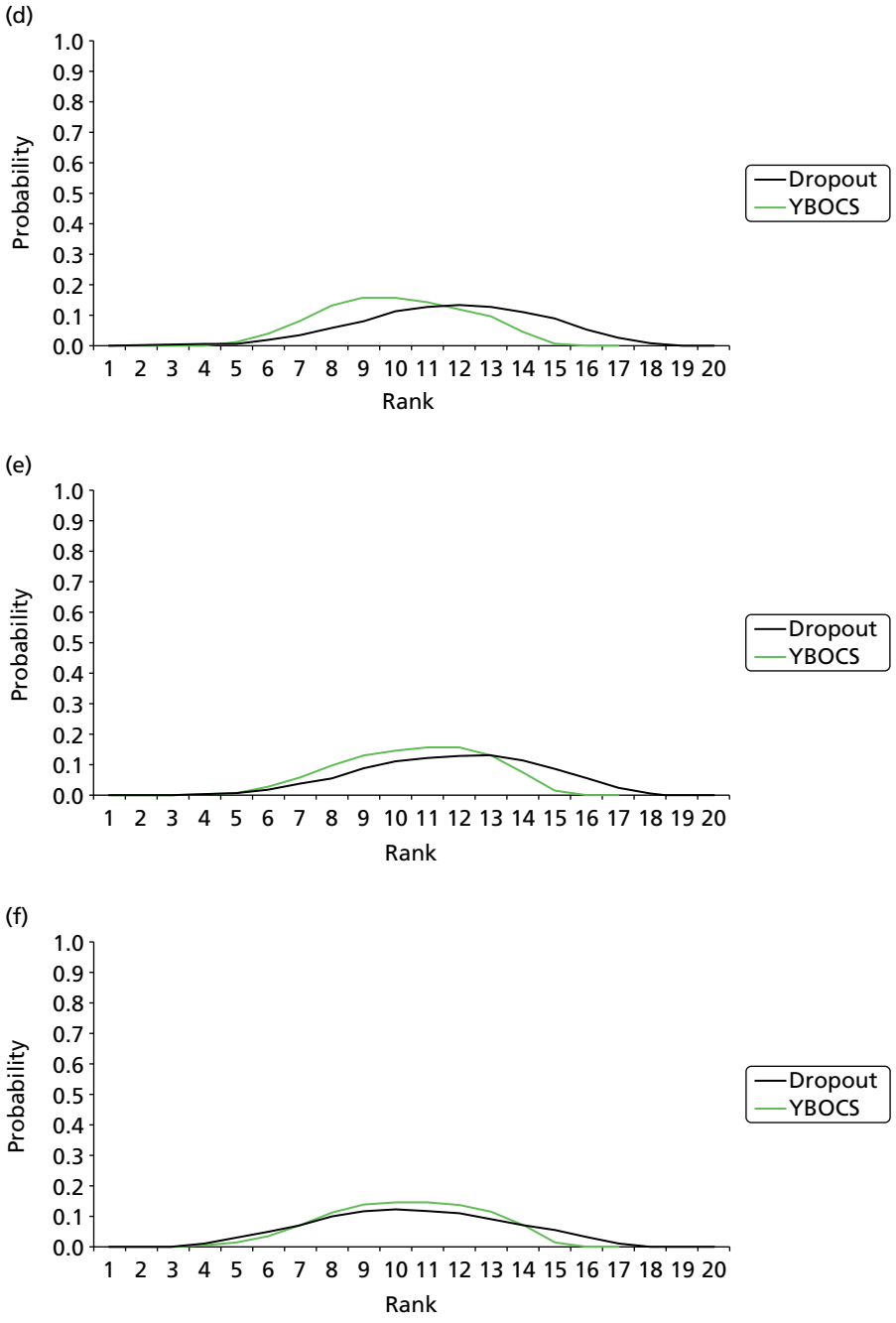


FIGURE 8 Rankograms for adults: dropout (black lines); YBOCS (green lines). (a) placebo; (b) waitlist; (c) fluoxetine; (d) fluvoxamine; (e) paroxetine; (f) sertraline; (g) citalopram; (h) venlafaxine; (i) clomipramine; (j) BT; (k) CBT; (l) CT; (m) hypericum; (n) CBT + fluvoxamine; (o) BT + clomipramine; (p) escitalopram; (q) psychological placebo; (r) amitriptyline; (s) BT + fluvoxamine; and (t) imipramine. Reproduced from Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, *et al*. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis [published online ahead of print June 15 2016]. *Lancet Psychiatry* 2016. © Skapinakis *et al*. Open Access article distributed under the terms of CC BY.[214] (*continued*)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

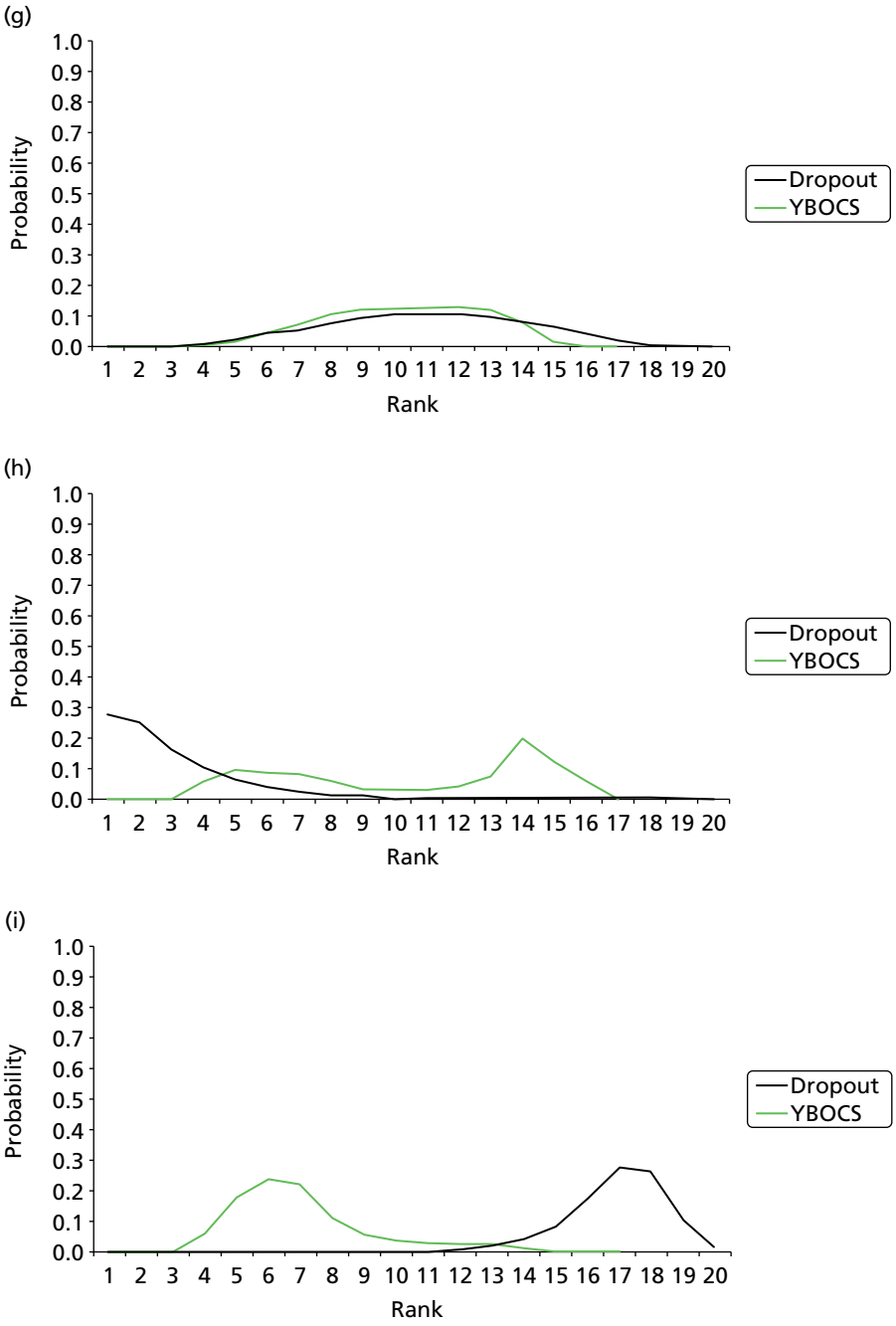


FIGURE 8 Rankograms for adults: dropout (black lines); YBOCS (green lines). (a) placebo; (b) waitlist; (c) fluoxetine; (d) fluvoxamine; (e) paroxetine; (f) sertraline; (g) citalopram; (h) venlafaxine; (i) clomipramine; (j) BT; (k) CBT; (l) CT; (m) hypericum; (n) CBT + fluvoxamine; (o) BT + clomipramine; (p) escitalopram; (q) psychological placebo; (r) amitriptyline; (s) BT + fluvoxamine; and (t) imipramine. Reproduced from Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, *et al*. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis [published online ahead of print June 15 2016]. *Lancet Psychiatry* 2016. © Skapinakis *et al*. Open Access article distributed under the terms of CC BY.[214] (*continued*)

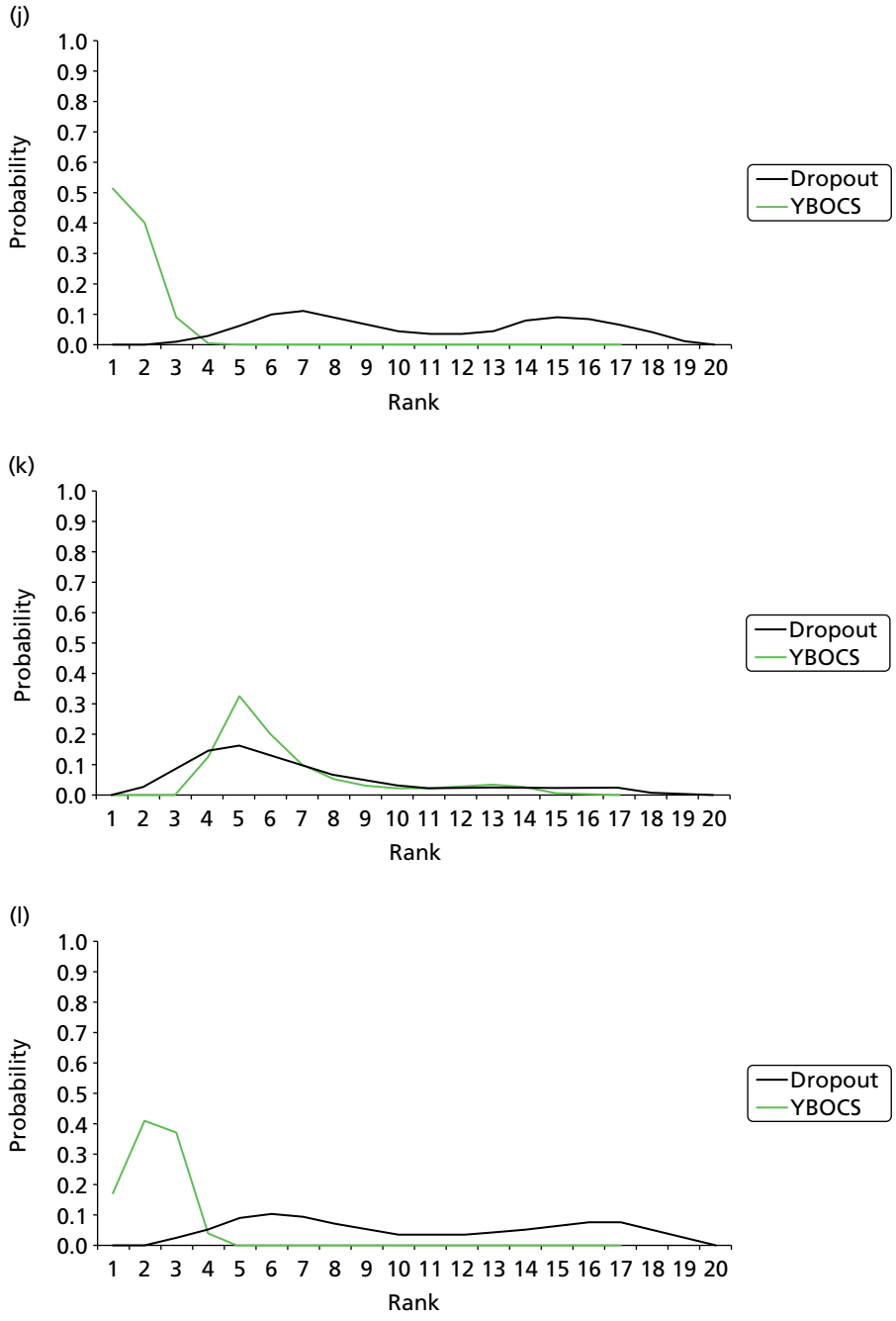


FIGURE 8 Rankograms for adults: dropout (black lines); YBOCS (green lines). (a) placebo; (b) waitlist; (c) fluoxetine; (d) fluvoxamine; (e) paroxetine; (f) sertraline; (g) citalopram; (h) venlafaxine; (i) clomipramine; (j) BT; (k) CBT; (l) CT; (m) hypericum; (n) CBT + fluvoxamine; (o) BT + clomipramine; (p) escitalopram; (q) psychological placebo; (r) amitriptyline; (s) BT + fluvoxamine; and (t) imipramine. Reproduced from Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, *et al*. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis [published online ahead of print June 15 2016]. *Lancet Psychiatry* 2016. © Skapinakis *et al*. Open Access article distributed under the terms of CC BY.[214] (*continued*)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

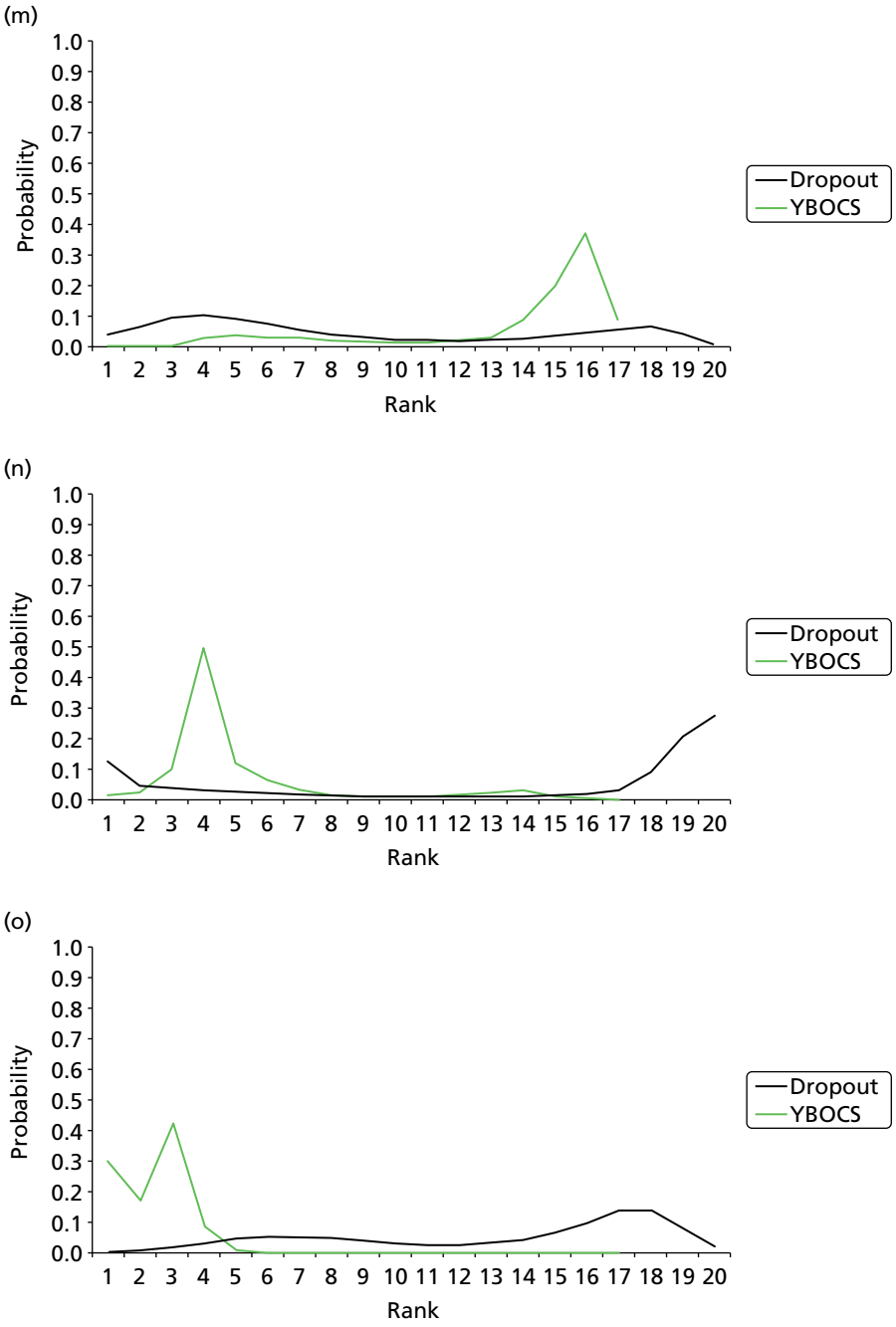


FIGURE 8 Rankograms for adults: dropout (black lines); YBOCS (green lines). (a) placebo; (b) waitlist; (c) fluoxetine; (d) fluvoxamine; (e) paroxetine; (f) sertraline; (g) citalopram; (h) venlafaxine; (i) clomipramine; (j) BT; (k) CBT; (l) CT; (m) hypericum; (n) CBT + fluvoxamine; (o) BT + clomipramine; (p) escitalopram; (q) psychological placebo; (r) amitriptyline; (s) BT + fluvoxamine; and (t) imipramine. Reproduced from Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, *et al*. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis [published online ahead of print June 15 2016]. *Lancet Psychiatry* 2016. © Skapinakis *et al*. Open Access article distributed under the terms of CC BY.[214] (*continued*)

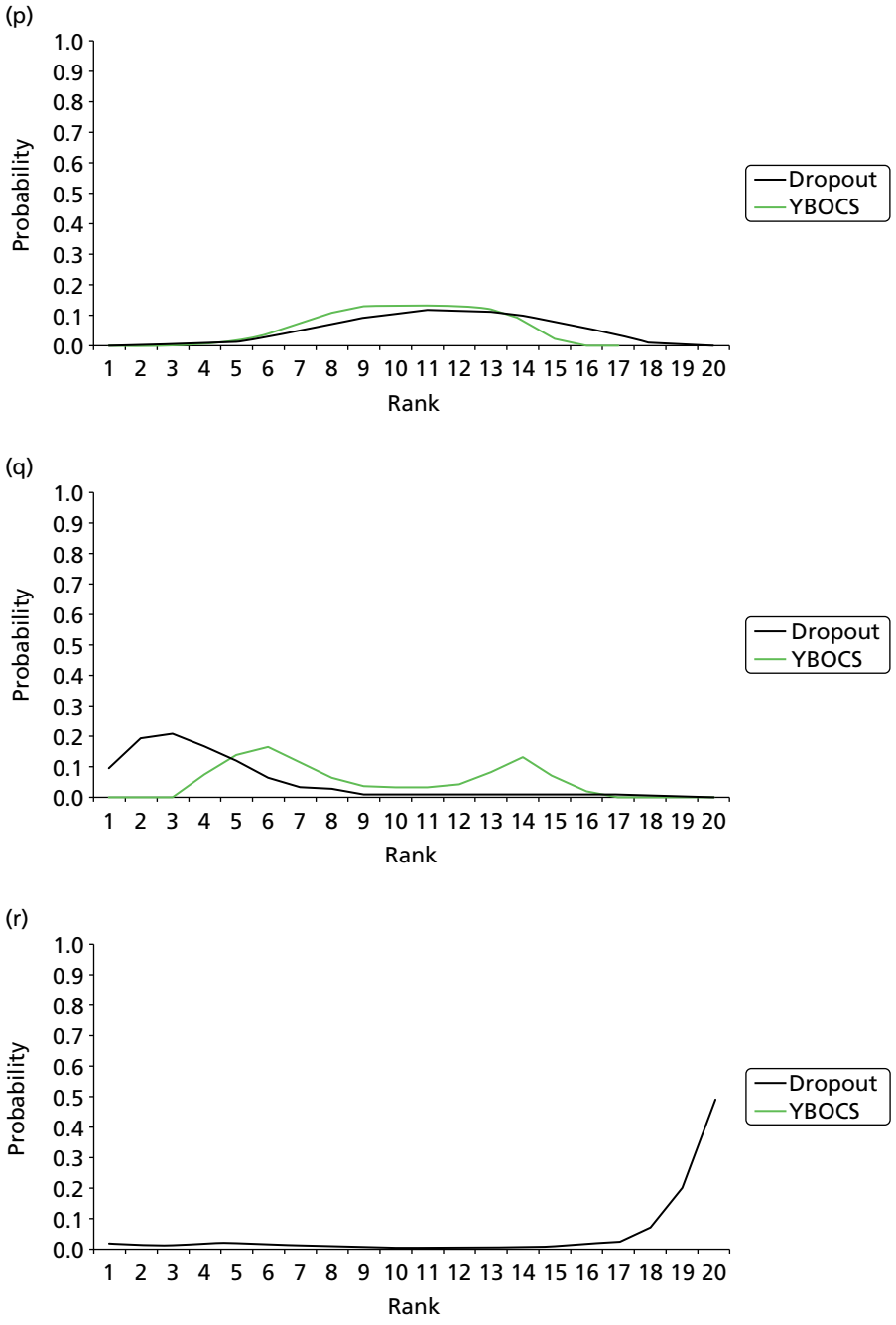


FIGURE 8 Rankograms for adults: dropout (black lines); YBOCS (green lines). (a) placebo; (b) waitlist; (c) fluoxetine; (d) fluvoxamine; (e) paroxetine; (f) sertraline; (g) citalopram; (h) venlafaxine; (i) clomipramine; (j) BT; (k) CBT; (l) CT; (m) hypericum; (n) CBT + fluvoxamine; (o) BT + clomipramine; (p) escitalopram; (q) psychological placebo; (r) amitriptyline; (s) BT + fluvoxamine; and (t) imipramine. Reproduced from Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, *et al*. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis [published online ahead of print June 15 2016]. *Lancet Psychiatry* 2016. © Skapinakis *et al*. Open Access article distributed under the terms of CC BY.[214] (*continued*)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

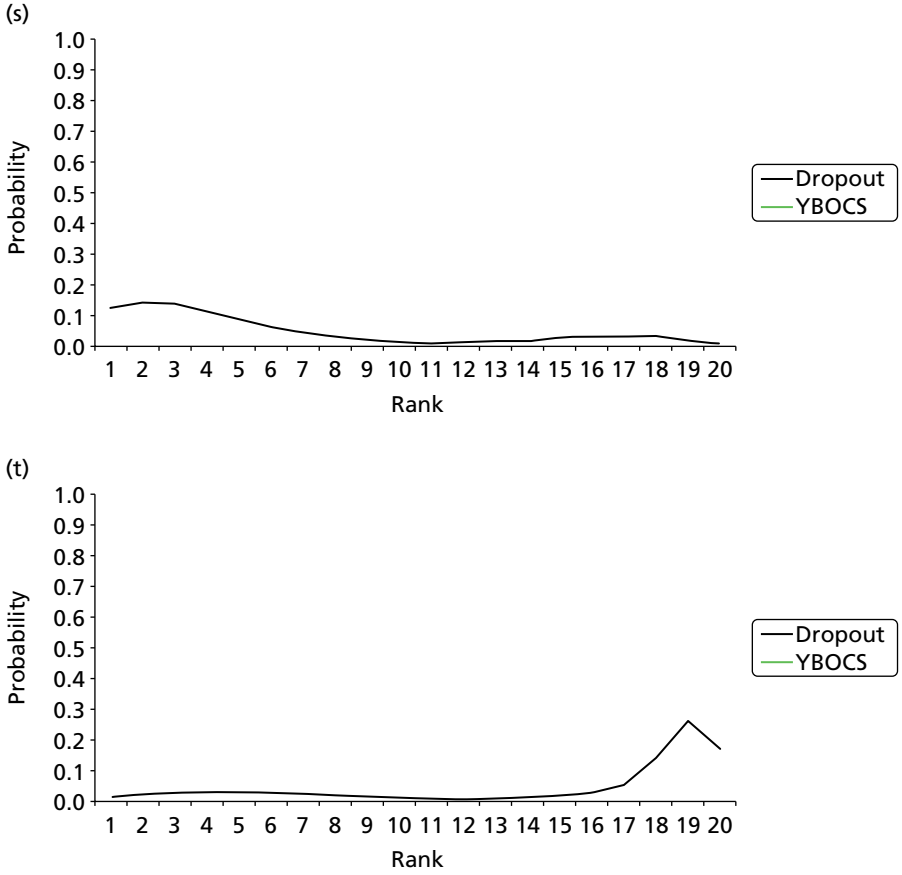


FIGURE 8 Rankograms for adults: dropout (black lines); YBOCS (green lines). (a) placebo; (b) waitlist; (c) fluoxetine; (d) fluvoxamine; (e) paroxetine; (f) sertraline; (g) citalopram; (h) venlafaxine; (i) clomipramine; (j) BT; (k) CBT; (l) CT; (m) hypericum; (n) CBT + fluvoxamine; (o) BT + clomipramine; (p) escitalopram; (q) psychological placebo; (r) amitriptyline; (s) BT + fluvoxamine; and (t) imipramine. Reproduced from Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, *et al*. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis [published online ahead of print June 15 2016]. *Lancet Psychiatry* 2016. © Skapinakis *et al*. Open Access article distributed under the terms of CC BY.[214]

Meta-regression

Table 32 presents the study-level covariates that could potentially influence the treatment effect (effect modification). It can be seen that the meta-regressions do not suggest an effect of adjusting for each covariate and the 95% CrIs all cross the null value. In addition, model fit was not improved and heterogeneity was not reduced in the covariate models when compared with the main consistency model reported in *Table 20*.

TABLE 32 Meta-regression of effect modifiers

Included covariate	Coefficient (95% CrI)
Subset: adults (outcome: YBOCS)	
Publication date (continuous)	0.14 (–0.11 to 0.39)
Trial length (continuous)	0.31 (–0.26 to 0.86)
Comorbid depression (binary, 1 = yes)	–1.24 (–4.34 to 1.78)
Pharmaceutical industry sponsorship (binary, 1 = yes)	–0.40 (–4.33 to 3.41)
Subset: adult (outcome: dropouts)	
Publication date	0.03 (–0.01 to 0.06)
Trial length	0.05 (–0.07 to 0.18)
Comorbid depression (yes/no)	–0.13 (–0.68 to 0.36)
Pharmaceutical industry sponsorship (binary, 1 = yes)	0.27 (–0.54 to 1.04)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Chapter 6 Network meta-analysis results (children and adolescents)

Clinical effectiveness: symptom reduction (Children's Yale–Brown Obsessive–Compulsive Scale)

Description of the data set

Table 33 presents the raw data used for the dropout analysis in the children and adolescents subset of the data (for a complete copy of the data extraction, see *Appendix 5*). Of the 22 studies eligible for inclusion in the NMA,[215–236] four were excluded: Flament *et al.* did not use the CYBOCS scale; March *et al.*[228] contained a population of 10- to 18-year-olds and used the adult YBOCS rather than the CYBOCS to assess symptoms; Asbahr *et al.*[216] did not report the follow-up measures; Alaghband-Rad and Hakimshooshtary[215] did not report the number at follow-up or any uncertainty around the CYBOCS; and GlaxoSmithKline[225] did not report a follow-up CYBOCS or a change from baseline. The studies excluded from the analysis involved a total of 311 randomised patients, but 207 of whom were included in the GlaxoSmithKline[225] paroxetine versus placebo study, whereas 104 patients were included in the remaining four studies. In total, 17 studies were included in the analysis.[217–221,223,224,228–236]

Table 34 presents summary data per type of intervention for the studies included in the NMA (number of arms and number of randomised patients per intervention).

Network meta-analysis: results

Network geometry

Figure 9 shows the network geometry of the CYBOCS comparison in the children and adolescent subsets and *Table 35* presents summary data per type of intervention (number of patients randomised, total number of links with other treatments, number of unique treatments compared). Overall, of the 66 pairwise comparisons that can be made among the 12 treatment conditions, only 15 (23%) were studied directly by head-to-head comparison in 17 studies involving 991 randomised patients. It should be noted, however, that 11 of these 15 direct comparisons were made in single trials. *Figure 9* includes 22 randomised pairwise comparisons and the most common comparisons are those between CBT and waitlist ($n = 4$), fluoxetine and placebo ($n = 3$), sertraline and placebo ($n = 2$), and CBT and psychological placebo ($n = 2$). Placebo ($n = 275$), CBT ($n = 184$), sertraline ($n = 120$) and fluoxetine ($n = 99$) had a sample approximately ≥ 100 (*Table 35*). Nodes with the most connections (links) in the network (*Table 35*) are drug placebo ($n = 9$ links with six different interventions), CBT ($n = 9$ links with five different interventions), waitlist ($n = 5$ links with two different interventions), sertraline ($n = 4$ links with three different interventions), the combination of sertraline and CBT ($n = 4$ links with four different interventions) and fluoxetine ($n = 3$ links with placebo).

Consistency of evidence

We examined model fit using the posterior mean of the residual deviance, the degree of between-study heterogeneity and the DIC. We compared a model assuming consistency of treatment effects with a model assuming independent treatment effects. For the consistency model, all SSRIs were analysed as a class and individually. *Table 36* presents the results of this comparison for the children and adolescents subset.

The posterior mean of the residual deviance was 35.04 compared with the number of data points ($n = 34$), suggesting adequate model fit. The posterior mean residual deviance was 34.27 in the independent effects model; however, heterogeneity was not reduced and may be considered low to moderate. In addition, the DIC suggests that we can select the model assuming consistency as our preferred choice. The results

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 33 Raw data used for the CYBOCS analysis (children and adolescent subset) sorted by study ID and number of arms

Study ID	t[,1]	y[,1]	n[,1]	sd[,1]	t[,2]	y[,2]	n[,2]	sd[,2]	t[,3]	y[,3]	n[,3]	sd[,3]	t[,4]	y[,4]	n[,4]	sd[,4]	Arms
Barrett *et al.*, 2004[217]	2	24.04	24	4.14	9	8.36	22	6.93	NA	NA	NA	NA	NA	NA	NA	NA	2
Bolton and Perrin, 2008[218]	2	21.1	10	5.9	8	13.9	10	10.74	NA	NA	NA	NA	NA	NA	NA	NA	2
Bolton *et al.*, 2011[219]	2	23.3	24	8.3	9	9.5	36	8	NA	NA	NA	NA	NA	NA	NA	NA	2
de Haan *et al.*, 1998[220]	7	17.6	10	11.8	8	9.1	12	9.1	NA	NA	NA	NA	NA	NA	NA	NA	2
DeVeaugh-Geiss *et al.*, 1992[221]	1	–2.4	29	NA	7	–10	31	NA	NA	NA	NA	NA	NA	NA	NA	NA	2
Freeman *et al.*, 2008[223]	3	17.1	20	7.57	9	14.45	22	8.16	NA	NA	NA	NA	NA	NA	NA	NA	2
Geller *et al.*, 2001[224]	1	–5.2	32	7.4	4	–9.5	71	9.2	NA	NA	NA	NA	NA	NA	NA	NA	2
Liebowitz *et al.*, 2002[226]	1	18.55	22	11.44	4	14.71	21	8.73	NA	NA	NA	NA	NA	NA	NA	NA	2
March *et al.*, 1998[228]	1	–3.4	95	7.99	6	–6.8	92	8.34	NA	NA	NA	NA	NA	NA	NA	NA	2
Neziroglu *et al.*, 2000[229]	5	19.2	5	3.56	10	16.4	5	5.18	NA	NA	NA	NA	NA	NA	NA	NA	2
Piacentini *et al.*, 2011[230]	3	17.2	22	10.04	9	13.3	49	9.31	NA	NA	NA	NA	NA	NA	NA	NA	2
Riddle *et al.*, 1992[231]	1	14.8	6	7	4	13.6	7	5.7	NA	NA	NA	NA	NA	NA	NA	NA	2
Riddle *et al.*, 2001[232]	1	20.9	63	8.5	5	18.2	57	8.6	NA	NA	NA	NA	NA	NA	NA	NA	2
Storch *et al.*, 2011[233]	2	18.53	15	8.11	9	11.13	16	10.53	NA	NA	NA	NA	NA	NA	NA	NA	2
Storch *et al.*, 2013[234]	11	15.43	14	9.72	12	15.56	16	6.62	NA	NA	NA	NA	NA	NA	NA	NA	2
Williams *et al.*, 2010[235]	2	19.6	10	6.42	9	12.09	11	7.46	NA	NA	NA	NA	NA	NA	NA	NA	2
The Pediatric OCD Treatment Study, 2004[236]	1	21.5	28	5.4	6	16.5	28	9.1	9	14	28	9.5	11	11.2	28	8.6	4

NA, not applicable.

Notes

[i]: type of treatment per arm [i] (1 = placebo, 2 = waitlist, 3 = psychological placebo, 4 = fluoxetine, 5 = fluvoxamine, 6 = sertraline, 7 = clomipramine, 8 = behavioural therapy, 9 = CBT, 10 = fluvoxamine and BT, 11 = sertraline and CBT, 12 = placebo and CBT); y[i]:total mean CYBOCS scores at end of study (positive) or mean change from baseline (negative); n[i]: total number of patients in arm [i]; sd[i]: SD of mean total score or change from baseline [i].

TABLE 34 Summary raw CYBOCS data per type of intervention (children and adolescents subset)

Intervention	Number of arms	Number of patients
Placebo	7	275
Waitlist	5	83
Psychological placebo	2	42
Fluoxetine	3	99
Fluvoxamine	2	62
Sertraline	2	120
Clomipramine	2	41
BT	2	22
CBT	7	184
BT + fluvoxamine	1	5
CBT + sertraline	2	42
CBT + placebo	1	16
Total	36	991

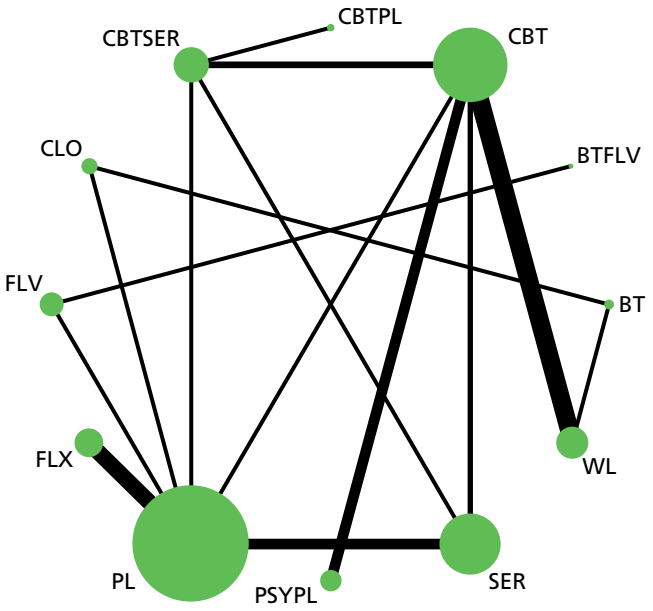


FIGURE 9 Network diagram for CYBOCS analysis representing individual treatments (children and adolescents subset). Circles (nodes) represent the types of interventions compared in the network and they are proportional to the number of participants randomised to a treatment. Lines are proportional to the number of direct randomised comparisons. BTFLV, BT + fluvoxamine; CBTPL, CBT + placebo; CBTSER, CBT + sertraline; CLO, clomipramine; FLV, fluvoxamine; FLX, fluoxetine; PL, placebo; PSYPL, psychological placebo; SER, sertraline; WL, waitlist.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 35 Summary data per type of intervention for the CYBOCS analysis, sorted by number of randomised patients (children and adolescents subset)

Intervention	Number of patients randomised	Number of pairwise comparisons (links)	Number of unique treatment comparisons
Placebo	275	9	6
CBT	184	9	5
Sertraline	120	4	3
Fluoxetine	99	3	1
Waitlist	83	5	2
Fluvoxamine	62	2	2
Psychological placebo	42	2	1
CBT + sertraline	42	4	4
Clomipramine	41	2	2
BT	22	2	2
CBT + placebo	16	1	1
BT + fluvoxamine	5	1	1

TABLE 36 Posterior summaries from random-effects consistency and inconsistency models (outcome: CYBOCS – children and adolescents subset)

Model	Number of data points	Residual deviance, posterior mean[a]	SD,[b] posterior median (95% CrI)	DIC
Random-effects consistency	34	35.04	1.88 (0.13 to 5.23)	64.2
Random-effects inconsistency	34	34.27	1.81 (0.08 to 5.78)	64.4

a The posterior mean residual deviance and number of data points are calculated for studies that reported a SD. Studies for which we predicted a SD could not be included in the residual deviance calculation. The DIC was calculated externally to OpenBUGS and does not include trials where SD was estimated.
b The SD is the between-trial variation in treatment effects (heterogeneity parameter).

of the NMA and the results of the pairwise comparisons (see *Table 37*) are in the same direction, with no evidence that the NMA effect estimate falls outside the 95% CrIs from the pairwise analysis. Overall, we conclude that there is no evidence of inconsistency in this network of evidence.

Data synthesis

The results of the NMA are presented in *Table 37*. We present the mean and 95% CrIs for the MD in CYBOCS scores at the end of study between the treatments compared. We present both the direct, head-to-head and pairwise comparisons (from the model assuming independent effects) and the results of the NMA (consistency model). For simplicity, we present only the MD and 95% CrIs for all interventions compared with the reference intervention (drug placebo). A more detailed table with all possible comparisons (both for the direct analysis and NMA) is given in *Appendix 8*.

Selective serotonin reuptake inhibitors as a class showed a trend for a greater effect than drug placebo, but the 95% CrIs included the null value. Individual SSRIs, however, reached marginal statistical significance, in particular sertraline (MD –3.90, 95% CrI –7.47 to –0.60). Although clomipramine showed a greater effect in the direct pairwise analysis (MD –7.62, 95% CrI –14.21 to –0.97), in the network analysis this effect was attenuated (MD –5.64, 95% CrI –11.36 to 0.64). It should be noted, however, that this result is based on two small studies with 41 patients randomised to clomipramine.

TABLE 37 Outcome 1: MD in CYBOCS scores at end of study. Mean and 95% CrIs compared with drug placebo (children and adolescents subset)

	Direct		NMA		Posterior treatment rank, median (95% CrI)
Intervention	Mean CYBOCS score	95% CrI	Mean CYBOCS score	95% CrI	
Placebo	Reference	Reference	Reference	Reference	11 (9 to 12)
Waitlist	NA	NA	3.10	–3.79 to 9.03	12 (8 to 12)
Psychological placebo	NA	NA	–5.37	–12.9 to 2.01	6 (2 to 11)
SSRIs (class effect)			–3.57	–8.57 to 1.51	
Fluoxetine	–3.52	–7.59 to 0.81	–3.58	–7.01 to –0.08	8 (4 to 11)
Fluvoxamine	–2.69	–8.73 to 3.35	–3.27	–7.39 to 1.13	9 (4 to 11)
Sertraline	–3.99	–8.45 to 0.21	–3.90	–7.47 to –0.60	8 (4 to 10)
Clomipramine	–7.62	–14.21 to –0.97	–5.64	–11.36 to 0.64	6 (2 to 11)
BT	NA	NA	–8.47	–16.98 to –0.39	4 (1 to 10)
CBT	–7.30	–13.95 to –0.88	–8.66	–14.38 to –3.14	3 (1 to 7)
BT + fluvoxamine	NA	NA	–6.12	–14.49 to 2.45	6 (1 to 12)
CBT + sertraline	–10.12	–16.58 to –3.84	–10.30	–16.16 to –4.58	2 (1 to 6)
CBT + placebo	NA	NA	–10.22	–19.84 to –0.61	2 (1 to 10)

NA, not applicable.

Behavioural therapy and CBT had greater effects than drug placebo (MD –8.47, 95% CrI –16.98 to –0.39 and MD –8.66, 95% CrI –14.38 to –3.14, respectively). Compared with psychological placebo, there was a trend for a greater effect, especially in CBT, but the 95% CrIs included the null value.

Compared with SSRIs as a class, both psychological therapies (BT and CBT) showed a trend for a greater effect, although the 95% CrIs included the null value (BT: MD –4.89, 95% CrI –14.6 to 4.28; CBT: MD –5.09, 95% CrI –12.33 to 1.86). Similar results were found for clomipramine.

The combination of sertraline with CBT was compared in four arms within two studies with a total number of 42 randomised patients. This was associated with the largest effect compared with drug placebo (MD –10.30, 95% CrI –16.16 to –4.58), but the same was observed for the combination of CBT with placebo (MD –10.22, 95% CrI –19.84 to –0.61). Compared with sertraline as monotherapy, the combination of sertraline and CBT had a greater effect (MD –6.40, 95% CrI –12.35 TO –0.40), but compared with CBT as monotherapy, the combination had similar effects (MD –1.64, 95% CrI –8.26 to 5.06). The combination of CBT with sertraline showed a trend for a greater effect than psychological placebo but the 95% CrI included the null value.

Table 37 also presents the posterior median treatment ranks with 95% CrIs. CBT as monotherapy or combined with sertraline or drug placebo were ranked as the highest performing treatments, followed by BT.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Sensitivity analyses: outcome 1, CYBOCS – subset (children and adolescents)

Low overall attrition and no evidence of imbalanced attrition

For this analysis, we excluded the five studies in the children and adolescents subset for which overall levels of attrition were > 25% or differential attrition was > 15%. The remaining 12 studies[217,219–221,226–231,233,235,236] included and the raw data used are presented in *Appendix 9*. Overall, 11 interventions were included and the total number of randomised patients was 686 (69% of the patients originally used in our full analysis). MDs and 95% CrIs compared with placebo are presented in *Table 38*. The results are essentially similar to the original analysis with the full data reported in *Table 37*, but the power of the analysis is low owing to the small number of included studies.

Low risk of bias in the domain: incomplete outcome assessment

For this analysis, we included 15[218–221,223,224,226,228,230–236] and excluded two studies. The studies included and the raw data used are presented in *Appendix 9*. Overall, 12 interventions were included and the total number of randomised patients was 935 (94% of the patients originally used in our full analysis). MDs and 95% CrIs compared with placebo are presented in *Table 39*. It can be seen from the table that the results are essentially similar to the original analysis, with the full data reported in *Table 37*.

Low risk of bias in the domain: blinding of the outcome assessor

For this analysis, we included nine[219,223,226–230,232–236] and excluded eight studies. The studies included and the raw data used are presented in *Appendix 9*. Overall, nine interventions were included and the total number of randomised patients was 530 (53% of the patients originally used in our full analysis). MDs and 95% CrIs compared with placebo are presented in *Table 40*. Owing to the small number of studies included, the power is compromised but the results show the same trends with the full analysis reported in *Table 37*.

TABLE 38 Sensitivity analysis (low overall attrition): outcome 1 – MD in CYBOCS scores at end of study. Mean and 95% CrIs compared with drug placebo (children and adolescent subset)

Intervention	Posterior distribution of the treatment effect (mean CYBOCS difference)		Posterior treatment rank, median (95% CrI)
	Mean	95% CrI	
Placebo	Reference	Reference	9 (6 to 11)
Waitlist	2.47	–6.72 to 10.43	10 (6 to 11)
Psychological placebo	–4.88	–16.98 to 6.95	6 (1 to 10)
SSRIs (class effect)	–3.65	–12.37 to 5.01	
Fluoxetine	–3.18	–9.12 to 2.87	7 (3 to 10)
Fluvoxamine	–3.64	–17.44 to 10.31	7 (1 to 11)
Sertraline	–4.10	–9.47 to 1.10	6 (3 to 9)
Clomipramine	–5.28	–12.97 to 3.28	5 (2 to 10)
BT	–8.75	–19.24 to 1.43	3 (1 to 9)
CBT	–8.82	–16.67 to –1.38	3 (1 to 7)
BT + fluvoxamine	Not estimable		
CBT + sertraline	–10.37	–18.48 to –2.396	2 (1 to 7)

TABLE 39 Sensitivity analysis (low risk of bias in 'incomplete outcome assessment'): outcome 1 – MD in CYBOCS scores at end of study. Mean and 95% CrIs compared with drug placebo (children and adolescents subset)

Intervention	Posterior distribution of the treatment effect (mean CYBOCS difference)		Posterior treatment rank, median (95% CrI)
	Mean	95% CrI	
Placebo	Reference	Reference	11 (9 to 12)
Waitlist	1.36	–5.01 to 7.12	11 (7 to 12)
Psychological placebo	–5.08	–11.91 to 1.57	6 (3 to 11)
SSRIs (class effect)	–3.55	–8.16 to 1.16	
Fluoxetine	–3.59	–6.53 to –0.56	8 (4 to 10)
Fluvoxamine	–3.21	–6.80 to 0.57	8 (5 to 11)
Sertraline	–3.85	–6.92 to –1.01	8 (4 to 10)
Clomipramine	–6.14	–11.25 to –0.59	6 (2 to 10)
BT	–9.58	–17.62 to –1.61	3 (1 to 9)
CBT	–8.36	–13.52 to –3.48	4 (1 to 7)
BT + fluvoxamine	Not estimable		
CBT + sertraline	–10.23	–15.40 to –5.20	3 (1 to 6)
CBT + placebo	–10.06	–18.84 to –1.32	3 (1 to 10)

TABLE 40 Sensitivity analysis (low risk of bias in 'blinding of outcome assessor'): outcome 1 – MD in CYBOCS scores at end of study. Mean and 95% CrIs compared with drug placebo (children and adolescents subset)

Intervention	Posterior distribution of the treatment effect (mean CYBOCS difference)		Posterior treatment rank, median (95% CrI)
	Mean	95% CrI	
Placebo	Reference	Reference	8 (5 to 9)
Waitlist	3.10	–5.74 to 11.54	9 (5 to 9)
Psychological placebo	–3.94	–13.04 to 5.26	5 (1 to 8)
SSRIs (class effect)	–3.79	–10.55 to 2.97	
Fluoxetine	–3.85	–10.08 to 2.40	5 (2 to 8)
Fluvoxamine	–3.27	–8.81 to 2.22	6 (2 to 8)
Sertraline	–4.27	–9.96 to 1.42	5 (2 to 8)
CBT	–7.18	–14.33 to 0.09	3 (1 to 6)
CBT + sertraline	–9.97	–16.91 to –2.86	2 (1 to 5)
CBT + placebo	–9.76	–20.78 to 1.46	2 (1 to 8)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Acceptability (dropouts)

Description of the data set

Table 41 presents the raw data used for the dropout analysis in the children and adolescents subset of the data. Of the 22 studies eligible for inclusion in the NMA,[215–236] four were excluded: three studies either did not report dropout data or did not report dropout data separately for each arm;[215,217] and one study was excluded because there were no dropouts (zero dropouts) in all arms.[229] Therefore, 18 studies were included in this analysis.[216,218–221,223–228,230–236]

Table 41 also presents raw dropout rates. It can be seen that the range of dropouts was 0–43%, with a median of 14%. *Table 42* presents summary dropout rate per type of intervention (minimum, maximum and median of raw dropout rates).

Network meta-analysis: results

Network geometry

Figure 10 shows the network geometry for total dropouts in the children and adolescents subset. Overall, of the 66 comparisons that can be made among the 12 treatment conditions, only 15 (23%) were studied directly by head-to-head evidence in 18 studies involving 1199 randomised patients. It should be noted, however, that 9 of the 15 direct comparisons are associated with one study each. Placebo ($n = 390$), CBT ($n = 182$), sertraline ($n = 140$), paroxetine ($n = 100$) and fluoxetine ($n = 99$) are the treatments with the largest sample size. *Figure 10* includes 23 randomised pairwise comparisons and the most common comparisons are those between placebo and fluoxetine ($n = 3$) and CBT and waitlist ($n = 3$). Nodes with the most connections (links) in the network are drug placebo ($n = 11$ links with seven different treatments), CBT ($n = 9$ links with four different treatments), sertraline ($n = 5$ links with three different treatments), combination of sertraline and CBT ($n = 4$ links with three different treatments) and waitlist ($n = 4$ links with two different treatments).

Consistency of evidence

We examined model fit using the posterior mean of the residual deviance, the degree of between-study heterogeneity and the DIC. We compared a model assuming consistency of treatment effects with a model assuming independent treatment effects. For the consistency model, all SSRIs were analysed as a class and individually. *Table 43* presents the results of this comparison for the children and adolescents subset.

The posterior mean of the residual deviance was 42.0 in the NMA (the consistency model) compared with the number of data points ($n = 38$), suggesting adequate model fit. The posterior mean residual deviance was 41.4 in the independent effect model. The DIC does not differentiate between the two models. In addition, the results of the NMA and the results of the pairwise comparisons (*Table 44*) are in the same direction, with no evidence that the NMA effect estimate falls outside the 95% CrIs from the pairwise analysis. Overall, we conclude that there is no evidence of inconsistency.

Data synthesis

The results of the NMA are presented in *Table 44*. We present posterior median ORs for dropouts compared with drug placebo, which is the reference treatment. We present both pairwise comparisons (from the independent effects model) for the direct head-to-head comparisons and the results of the NMA. For simplicity, we present only the ORs compared with drug placebo. A more detailed table with all possible comparisons (both for the direct and NMA) is given in *Appendix 8*.

There were no interventions with a statistically significant higher dropout than placebo. However, clomipramine and BT were associated with the largest median ORs. It should be noted, however, that the evidence for this comes from three[220,221,227] and two studies,[218,220] respectively, with small sample sizes ($n = 49$ for clomipramine and $n = 23$ for BT), and in the case of BT, there is no direct comparison with placebo.

TABLE 41 Raw data used for the dropout analysis (children and adolescent subset)

Study	t[,1]	r[,1]	n[,1]	dr[,]1, %	t[,2]	r[,2]	n[,2]	dr[,2], %	t[,3]	r[,3]	n[,3]	dr[,3], %	t[,4]	r[,4]	n[,4]	dr[,4], %
Asbahr *et al.*, 2005[216]	7	1	20	5	10	0	20	0	NA	NA	NA	NA	NA	NA	NA	NA
Bolton and Perrin, 2008[218]	2	0	10	0	9	2	10	20	NA	NA	NA	NA	NA	NA	NA	NA
Bolton *et al.*, 2011[219]	2	3	24	13	10	2	36	6	NA	NA	NA	NA	NA	NA	NA	NA
DeVeaugh-Geiss *et al.*, 1992[221]	1	2	29	7	8	4	31	13	NA	NA	NA	NA	NA	NA	NA	NA
Freeman *et al.*, 2008[223]	3	5	20	25	10	6	22	27	NA	NA	NA	NA	NA	NA	NA	NA
Geller *et al.*, 2001[224]	1	12	32	38	4	22	71	31	NA	NA	NA	NA	NA	NA	NA	NA
GlaxoSmithKline, 2001[225]	1	27	107	25	6	35	100	35	NA	NA	NA	NA	NA	NA	NA	NA
de Haan *et al.*, 1998[220]	8	0	10	0	9	1	13	8	NA	NA	NA	NA	NA	NA	NA	NA
Liebowitz *et al.*, 2002[226]	1	4	22	18	4	1	21	5	NA	NA	NA	NA	NA	NA	NA	NA
March *et al.*, 1990[227]	1	0	8	0	8	2	8	25	NA	NA	NA	NA	NA	NA	NA	NA
March *et al.*, 1998[228]	1	13	95	14	7	18	92	20	NA	NA	NA	NA	NA	NA	NA	NA
Piacentini *et al.*, 2011[230]	3	5	22	23	10	8	49	16	NA	NA	NA	NA	NA	NA	NA	NA
Riddle *et al.*, 1992[231]	1	1	6	17	4	1	7	14	NA	NA	NA	NA	NA	NA	NA	NA
Riddle *et al.*, 2001[232]	1	27	63	43	5	19	57	33	NA	NA	NA	NA	NA	NA	NA	NA
Storch *et al.*, 2011[233]	2	0	15	0	10	2	16	13	NA	NA	NA	NA	NA	NA	NA	NA
Storch *et al.*, 2013[234]	11	6	14	43	12	3	16	19	NA	NA	NA	NA	NA	NA	NA	NA
Williams *et al.*, 2010[235]	2	1	10	10	10	1	11	9	NA	NA	NA	NA	NA	NA	NA	NA
The Pediatric OCD Treatment Study, 2004[236]	1	7	28	25	7	2	28	7	10	3	28	11	11	3	28	11

NA, not applicable.

Notes

t[i]: type of treatment per arm [i] (1 = placebo, 2 = waitlist, 3 = psychological placebo, 4 = fluoxetine, 5 = fluvoxamine, 6 = paroxetine, 7 = sertraline, 8 = clomipramine, 9 = BT, 10 = CBT, 11 = sertraline + CBT, 12 = placebo + CBT); r[i]: number of dropouts in arm[i]; n[i]: total number of patients in arm [i]; dr [i]: dropout rate (%) in arm[i].

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 42 Summary raw dropout rates per type of intervention (children and adolescents subset)

Intervention	Dropout rates (%)			Number of arms
	Minimum	Maximum	Median	
Placebo	0	43	18	9
Waitlist	0	12.5	5	4
Psychological placebo	23	25	24	2
Fluoxetine	5	31	14	3
Fluvoxamine	33	33	NA	1
Paroxetine	35	35	NA	1
Sertraline	5	20	7	3
Clomipramine	0	25	13	3
BT	8	20	14	2
CBT	0	27	11	7
CBT + sertraline	11	43	27	2
CBT + placebo	19	19	NA	1

NA, not applicable.

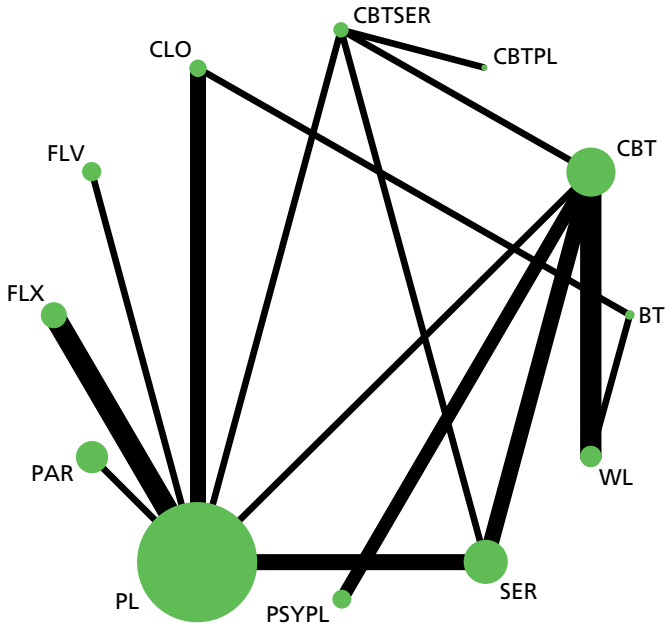


FIGURE 10 Network diagram for dropouts representing individual treatments (children and adolescent subset). Circles represent the types of interventions used in the network and they are proportional to the number of participants randomised to a treatment. Lines (edges) are proportional to the number of direct randomised comparisons. CBTPL, CBT + placebo; CBTSER, CBT + sertraline; CLO, clomipramine; FLV, fluvoxamine; FLX, fluoxetine; PAR, paroxetine; PL, placebo; PSYPL, psychological placebo; SER, sertraline; WL, waitlist.

TABLE 43 Posterior summaries from random-effects consistency and inconsistency models (outcome: dropouts – children and adolescents subset)

Model	Number of data points	Residual deviance (posterior mean)	SD,[a] posterior median (95% CrI)	DIC
Random-effects consistency	38	42.0	0.36 (0.02 to 1.19)	169.3
Random-effects independent effects	38	41.4	0.58 (0.04 to 1.92)	170.9

a SD is the between-trial variation in treatment effects (heterogeneity parameter).

TABLE 44 Outcome 2: dropouts. Median ORs (95% CrI) compared with drug placebo (children and adolescents subset)

	Direct		NMA		
Intervention	Median OR	95% CrI	Median OR	95% CrI	Posterior treatment rank, median (95% CrI)
Placebo	Reference	Reference	Reference	Reference	8 (3 to 11)
Waitlist	NA	NA	0.53	0.05 to 4.33	4 (1 to 11)
Psychological placebo	NA	NA	0.58	0.07 to 4.44	5 (1 to 11)
SSRIs (class effect)			0.87	0.23 to 3.00	
Fluoxetine	0.56	0.09 to 2.57	0.74	0.25 to 1.68	6 (1 to 10)
Fluvoxamine	0.66	0.06 to 6.95	0.79	0.24 to 2.07	6 (1 to 11)
Paroxetine	1.59	0.16 to 16.65	1.12	0.37 to 3.42	9 (3 to 12)
Sertraline	0.81	0.10 to 3.78	0.89	0.32 to 2.07	7 (2 to 11)
Clomipramine	3.44	0.41 to 41.35	3.06	0.54 to 21.69	11 (4 to 12)
BT	NA	NA	7.64	0.41 to 423.7	12 (4 to 12)
CBT	0.44	0.02 to 5.08	0.49	0.09 to 2.41	4 (1 to 10)
Sertraline + CBT	0.43	0.02 to 4.91	0.54	0.08 to 3.15	4 (1 to 11)
Placebo + CBT	NA	NA	0.15	0.01 to 2.26	1 (1 to 10)

NA, not available.

Paroxetine was the only SSRI with an OR greater than 1, but this was not statistically significant. SSRIs as a class were not more likely than placebo to lead to dropout.

Sensitivity analyses: outcome 2 – dropouts, children and adolescents subset

Low overall attrition and no evidence of imbalanced attrition

For this analysis, we included 13[216,218–221,226–228,230,231,233,235,236] and excluded five studies. The studies included and the raw data used are presented in *Appendix 9*. Overall, nine interventions were included and the total number of randomised patients was 707 (59% of the patients originally used in our full analysis). MDs and 95% CrI compared with placebo are presented in *Table 45*. Compared with the full data set reported in *Table 44*, the results are essentially similar.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 45 Sensitivity analysis (low overall attrition): outcome 2 – dropouts. Median ORs (95% CrI) compared with drug placebo (children and adolescents subset)

Intervention	Median OR	95% CrI	Posterior treatment rank, median (95% CrI)
Placebo	Reference	Reference	6 (2 to 8)
Waitlist	0.46	0.02 to 7.38	3 (1 to 8)
Psychological placebo	0.68	0.02 to 23.59	4 (1 to 9)
SSRIs (class effect)	0.58	0.0005 to 448.1	
Fluoxetine	0.41	0.03 to 3.62	3 (1 to 8)
Sertraline	0.79	0.12 to 4.08	5 (1 to 8)
Clomipramine	3.12	0.36 to 36.01	8 (2 to 9)
BT	8.09	0.23 to 695.2	9 (3 to 9)
CBT	0.47	0.04 to 4.39	3 (1 to 7)
CBT + sertraline	0.54	0.03 to 7.33	4 (1 to 9)

Low risk of bias in the domain: incomplete outcome assessment

For this analysis, we included 16[216,218–221,223,224,226,228,230–236] and excluded two studies. The studies included and the raw data used are presented in *Appendix 9*. Overall, 11 interventions were included and the total number of randomised patients was 984 (82% of the patients originally used in our full analysis). MDs and 95% CrIs compared with placebo are presented in *Table 46*. Compared with the full data set, reported in *Table 44*, the results show the same trends.

TABLE 46 Sensitivity analysis (low risk of bias in 'incomplete outcome assessment'): outcome 2 – dropouts. Median ORs (95% CrI) compared with drug placebo (children and adolescents subset)

Intervention	Median	95% CrI	Posterior treatment rank, median (95% CrI)
Placebo	Reference	Reference	8 (4 to 11)
Waitlist	0.48	0.04 to 4.17	4 (1 to 10)
Psychological placebo	0.55	0.05 to 4.71	5 (1 to 10)
SSRIs (class effect)	0.70	0.06 to 7.78	
Fluoxetine	0.64	0.19 to 1.70	5 (1 to 10)
Fluvoxamine	0.69	0.18 to 2.31	6 (1 to 10)
Sertraline	0.80	0.25 to 2.18	7 (2 to 10)
Clomipramine	2.01	0.23 to 20.91	10 (2 to 11)
BT	5.95	0.27 to 307.3	11 (3 to 11)
CBT	0.48	0.07 to 2.39	4 (1 to 9)
CBT + sertraline	0.52	0.06 to 3.50	5 (1 to 10)
CBT + placebo	0.14	0.01 to 2.59	1 (1 to 10)

Low risk of bias in the domain: blinding of the outcome assessor

For this analysis, we included 10[216,219,223,226,230,232–236] and excluded eight studies. The studies included and the raw data used are presented in *Appendix 9*. Overall, nine interventions were included and the total number of randomised patients was 574 (48% of the patients originally used in our full analysis). MDs and 95% CrIs compared with placebo are presented in *Table 47*. Compared with the full data set reported in *Table 44*, the results show similar trends for the included interventions.

Rankograms (both outcomes)

Table 48 presents the probabilities that each treatment is among the best three or worst three for both outcomes (CYBOCS/dropouts: for dropouts, being in the top three means better tolerability, i.e. lower dropouts). In *Appendix 8* we present complete data for all rank probabilities for both outcomes. Based on these data, we also present rankograms (plots of the probabilities for each treatment taking each possible rank) in *Figure 11*.

Meta-regression

We were not able to explore fully the impact of effect modifiers as we had originally planned, because in the children and adolescent networks, there were an insufficient number of studies (CYBOCS) and/or insufficient data (dropouts) for the analysis to be feasible. Therefore, these analyses were not undertaken.

TABLE 47 Sensitivity analysis (low risk of bias in 'blinding of the outcome assessor'): outcome 2 – dropouts. Median ORs (95% CrI) compared with drug placebo (children and adolescent subset)

Intervention	Median OR	95% CrI	Posterior treatment rank, median (95% CrI)
Placebo	Reference	Reference	8 (4 to 9)
Waitlist	0.26	0.01 to 4.36	4 (1 to 9)
Psychological placebo	0.32	0.01 to 5.32	5 (1 to 9)
SSRIs (class effect)	0.38	0.01 to 15.56	
Fluoxetine	0.30	0.01 to 2.50	4 (1 to 9)
Fluvoxamine	0.54	0.06 to 3.52	7 (2 to 9)
Sertraline	0.33	0.03 to 2.43	5 (1 to 9)
CBT	0.27	0.02 to 2.50	4 (1 to 8)
CBT + sertraline	0.36	0.02 to 4.28	5 (2 to 9)
CBT + placebo	0.10	0.01 to 4.01	1 (1 to 9)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 48 Summary of rank probabilities (top three/bottom three): children and adolescents subset

		Probability of treatment being in the	
Outcome[a]	Treatment	Top three	Bottom three
CYBOCS	Placebo	0.00	0.95
Dropout	Placebo	0.03	0.18
CYBOCS	Waitlist	0.00	0.96
Dropout	Waitlist	0.42	0.14
CYBOCS	Psychological placebo	0.11	0.17
Dropout	Psychological placebo	0.36	0.15
CYBOCS	Fluoxetine	0.01	0.19
Dropout	Fluoxetine	0.21	0.06
CYBOCS	Fluvoxamine	0.01	0.26
Dropout	Fluvoxamine	0.17	0.09
Dropout	Paroxetine	0.05	0.35
CYBOCS	Sertraline	0.01	0.13
Dropout	Sertraline	0.07	0.12
CYBOCS	Clomipramine	0.14	0.11
Dropout	Clomipramine	0.02	0.84
CYBOCS	BT	0.48	0.05
Dropout	BT	0.02	0.89
CYBOCS	CBT	0.53	0.00
Dropout	CBT	0.43	0.03
CYBOCS	CBT + sertraline	0.78	0.00
Dropout	CBT + sertraline	0.40	0.11
CYBOCS	CBT + placebo	0.66	0.04
Dropout	CBT + placebo	0.82	0.04
CYBOCS	BT + fluvoxamine	0.27	0.14

a For dropouts, being in the top three means better tolerability (i.e. fewer dropouts).

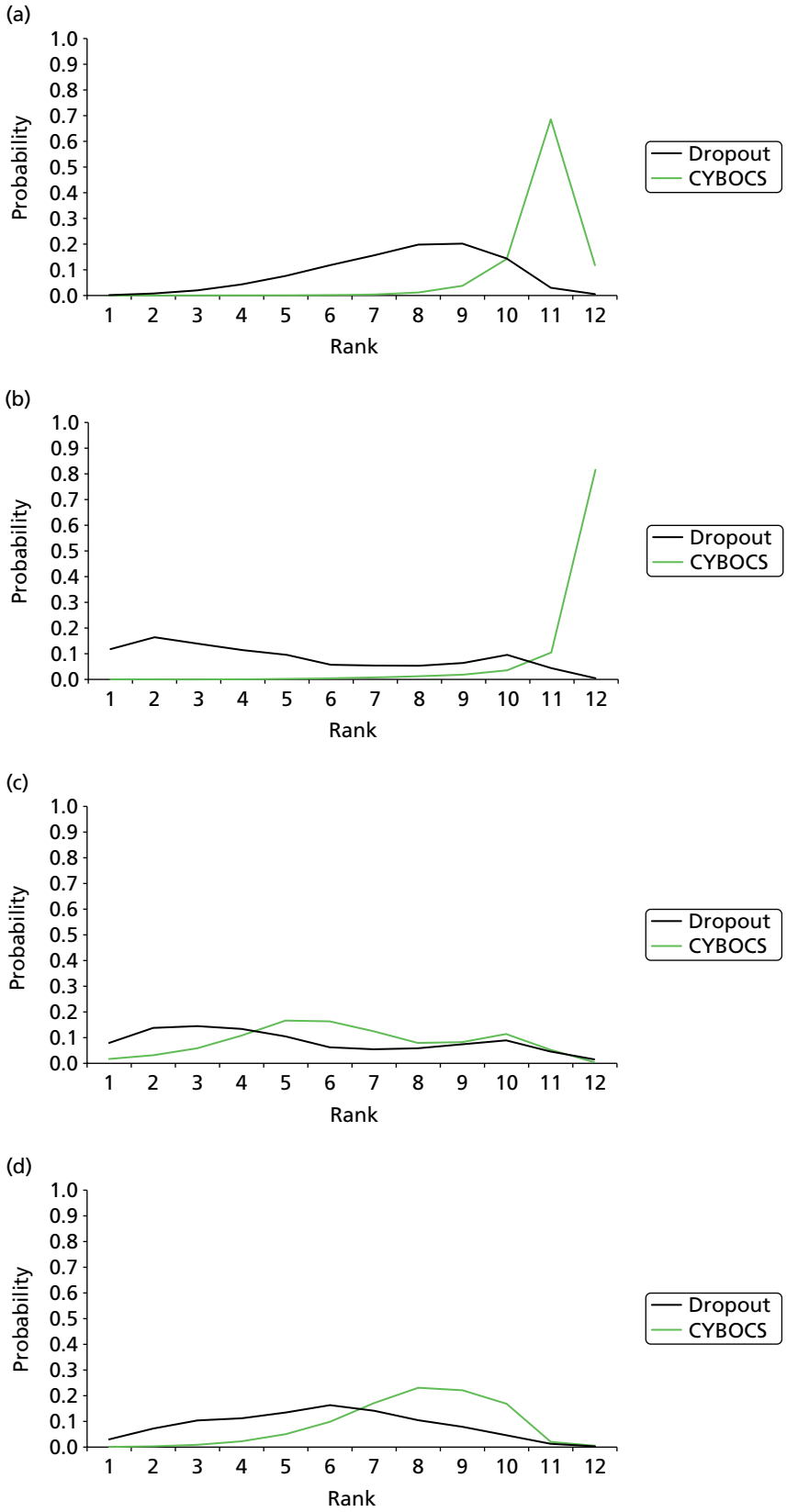


FIGURE 11 Rankograms for children and adolescents: dropout (black lines); CYBOCS (green lines). (a) Placebo; (b) waitlist; (c) psychological placebo; (d) fluoxetine; (e) fluvoxamine; (f) sertraline; (g) clomipramine; (h) BT; (i) CBT; (j) CBT + sertraline; (k) CBT + placebo; (l) BT + fluvoxamine; and (m) paroxetine. (*continued*)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

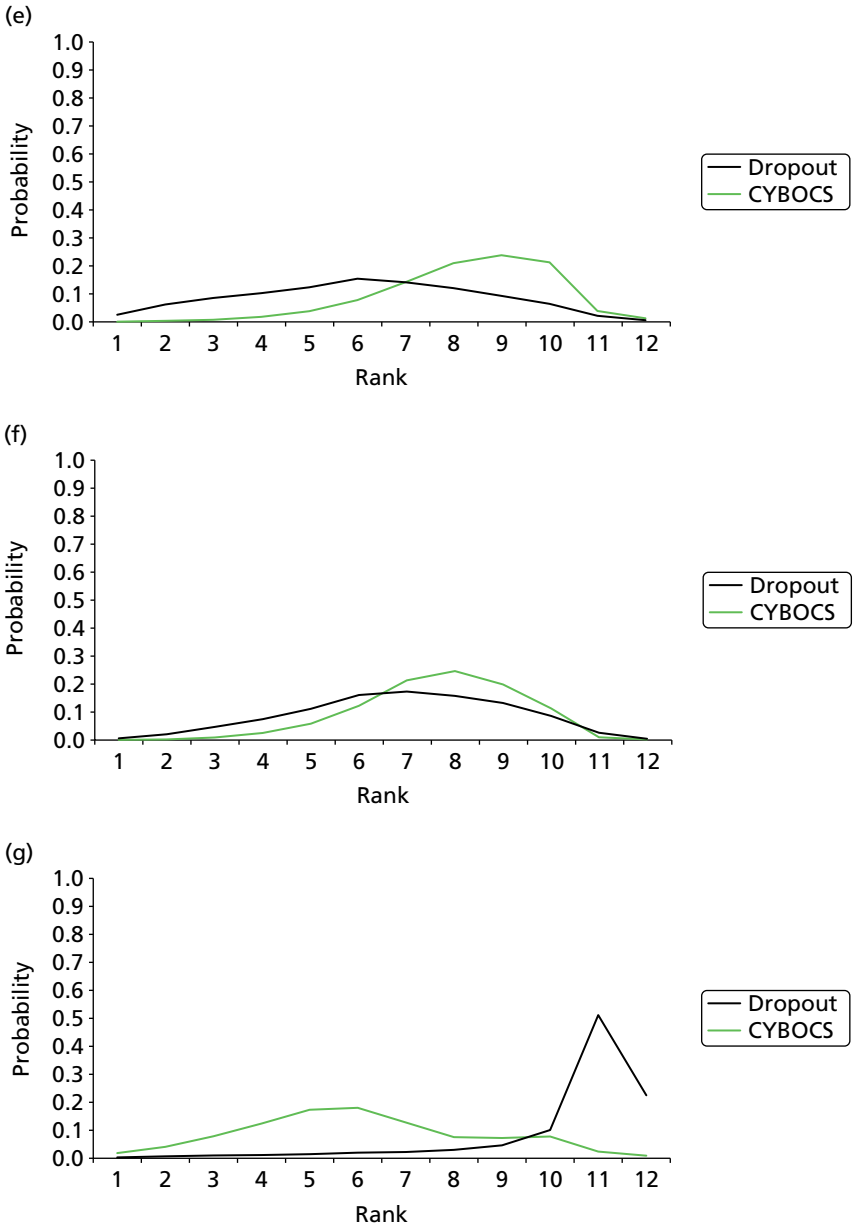


FIGURE 11 Rankograms for children and adolescents: dropout (black lines); CYBOCS (green lines). (a) Placebo; (b) waitlist; (c) psychological placebo; (d) fluoxetine; (e) fluvoxamine; (f) sertraline; (g) clomipramine; (h) BT; (i) CBT; (j) CBT + sertraline; (k) CBT + placebo; (l) BT + fluvoxamine; and (m) paroxetine. (*continued*)

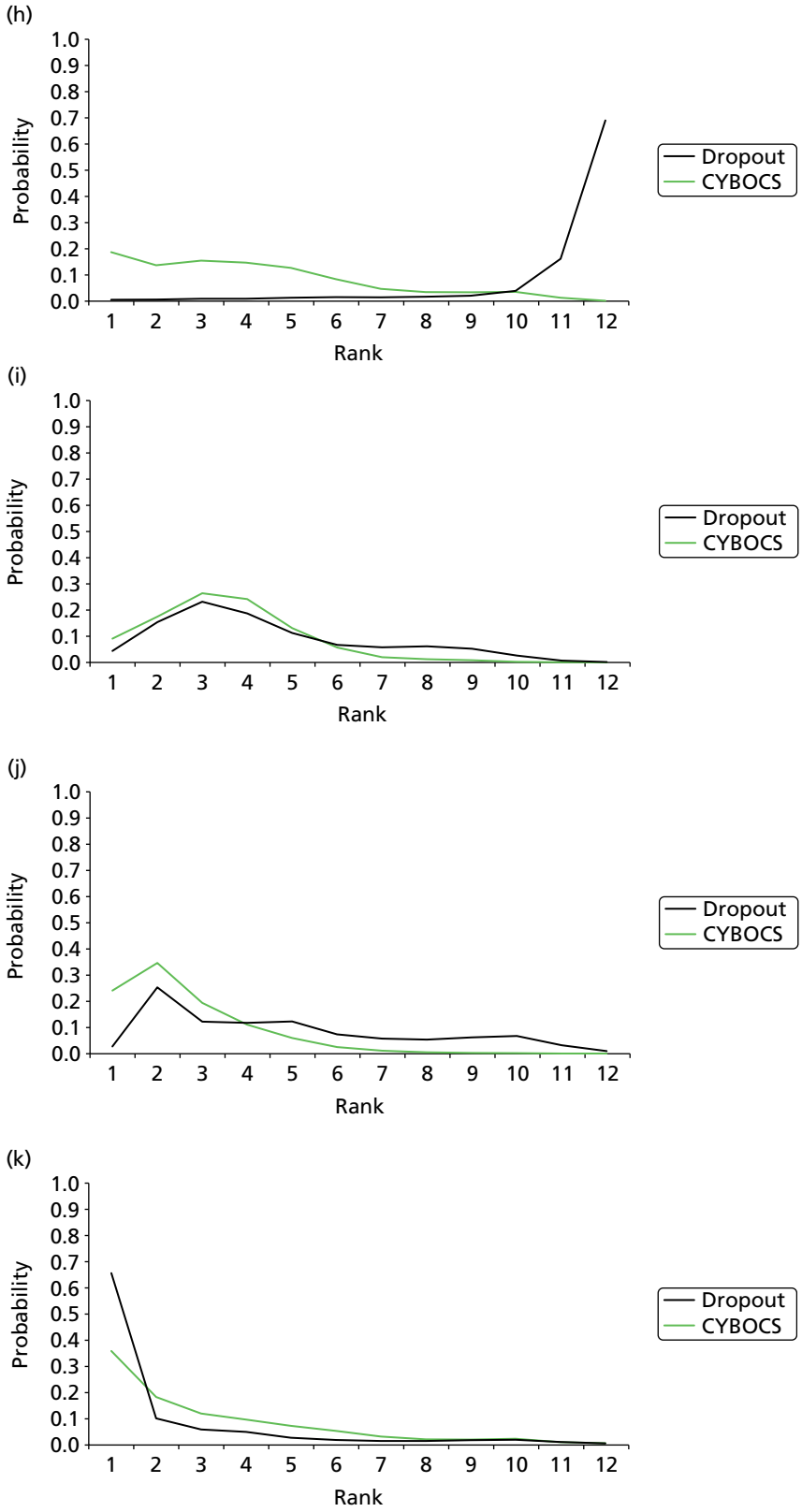


FIGURE 11 Rankograms for children and adolescents: dropout (black lines); CYBOCS (green lines). (a) Placebo; (b) waitlist; (c) psychological placebo; (d) fluoxetine; (e) fluvoxamine; (f) sertraline; (g) clomipramine; (h) BT; (i) CBT; (j) CBT + sertraline; (k) CBT + placebo; (l) BT + fluvoxamine; and (m) paroxetine. (*continued*)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

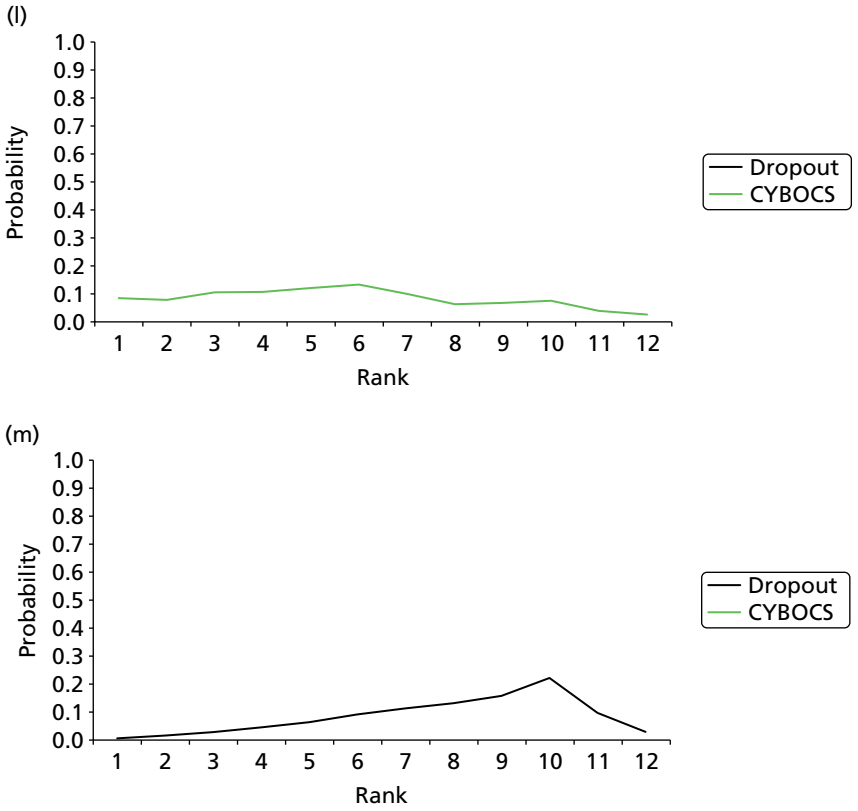


FIGURE 11 Rankograms for children and adolescents: dropout (black lines); CYBOCS (green lines). (a) Placebo; (b) waitlist; (c) psychological placebo; (d) fluoxetine; (e) fluvoxamine; (f) sertraline; (g) clomipramine; (h) BT; (i) CBT; (j) CBT + sertraline; (k) CBT + placebo; (l) BT + fluvoxamine; and (m) paroxetine.

Chapter 7 Assessment of cost-effectiveness

Background

The economic burden of obsessive–compulsive disorder

The total economic burden of OCD for the NHS and society in the UK is difficult to estimate and is not accurately known.[237] Work conducted in the USA during the 1990s suggests that the total costs of OCD equated to 5.7% of the estimated US$147.8B cost of all mental illness, and 18.0% of the costs of all anxiety disorders.[238] The direct costs to health services and patients of medical care represents only one aspect of the total burden. Indirect costs to patients and society as a result of lost productivity and wider impacts on informal care from friends and family members are also substantial.[239] Very few studies have estimated the per-patient health-care costs of OCD or the incremental costs compared with the general population or patients with other mental health problems.[240,241] The limited evidence available suggests that OCD has a similar health-care burden to depression, but with a relatively higher use of psychotropic medications.[240] The high cost of care for patients with OCD raises the possibility that therapies with a substantial and sustained effect on symptoms may reduce health-care costs in the long run.

Existing evidence on the cost-effectiveness of treatment for obsessive–compulsive disorder: primary studies

There are very few primary economic studies of interventions for patients with OCD, particularly economic evaluations conducted alongside RCTs likely to provide the most internally valid data. Tolin *et al.*[242] collected cost and outcome data alongside a trial comparing stepped with standard ERP therapy in 30 adults with moderate OCD symptoms (YBOCS score of ≥ 16) of at least 12 months' duration. This study reported no statistically significant differences in efficacy between interventions, measured by mean improvement in YBOCS scores or response rates (defined as YBOCS score of ≤ 12) at 3 months' follow-up. Total costs, including direct and indirect costs to patients, those who pay for health care (e.g. regional health-care authorities) and health-care providers (e.g. hospitals), were lower in the stepped care arm (US$2480 vs. US$4280; $p < 0.05$). An incremental cost-effectiveness ratio was not calculated and the small sample size limits interpretation. However, the authors conclude that their results suggest that stepped ERP care can significantly reduce treatment costs. McCrone *et al.*[243] report an economic evaluation of a three-arm RCT[178] comparing computer-guided BT, clinician-guided BT and a relaxation control therapy in 218 adults with DSM-IV-defined OCD. In incremental analyses, the authors report that the cost per one point improvement in YBOCS score of computer-guided therapy (£64, 95% CI £36 to £249) and clinician-guided therapy (£90, 95% CI £61 to £167) was modest compared with relaxation control.

A Cochrane review of psychological treatments for OCD, noting the lack of evidence on efficiency, called for future trials to include an economic evaluation.[244] Such trials are under way, including the Obsessive Compulsive Treatment Efficacy Trial,[245] which compares the cost-effectiveness of computerised CBT with guided self-help, and a Dutch trial comparing schema therapy versus clarification-oriented psychotherapy versus treatment as usual.[246] When published, these trials will improve the evidence base on cost-effective care for OCD. However, they will not answer many of the questions facing clinicians, policy-makers and health-care funders. A single trial cannot compare the large number of pharmacological and behavioural therapies available for OCD and typically will not have sufficient follow-up to determine whether or not initially expensive therapies are justified by better long-term outcomes.[247] A decision analysis based on a NMA of RCTs, estimating costs and outcomes beyond the end of trial follow-up is likely to provide the best evidence to inform this complex decision.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Existing evidence on the cost-effectiveness of treatment for obsessive–compulsive disorder: models

Previous work[248] has developed decision-analytic models to evaluate the cost-effectiveness of therapy for patients with OCD underpinning the NICE appraisal of computerised CBT. These authors developed a decision tree comparing three interventions (computer-guided BT, clinician-led BT or relaxation) based predominantly on one RCT in 218 adults with DSM-IV-defined OCD. The decision model tracked compliance with BT, response among compliers and relapse among responders during 6-month cycles over an 18-month time horizon. The authors concluded that, subject to substantial uncertainties, therapist-led CBT is cost-effective compared with relaxation and that computerised CBT has the potential to be cost-effective, depending on the licence fees for health-care commissioners.[248] The authors acknowledged significant limitations in their model, particularly relating to the indirect method of estimating quality-of-life (utility) scores for calculating quality-adjusted life-years (QALYs) because data on this parameter are scarce.

In developing their clinical guidelines for the treatment of OCD, NICE[118] also describe a crude model for comparing the cost-per-responder of usual care, SSRIs, CBT and combination therapy. Pooled effect sizes for each therapy were estimated based on separate pairwise meta-analyses. NICE concluded that CBT alone is dominated by SSRIs and combination therapy and, therefore, that CBT alone is unlikely to be cost-effective. However, this conclusion does not appear to be supported by the data (see table 3, p. 214[118]); furthermore, no probabilistic sensitivity analyses were conducted to estimate statistical uncertainty about this conclusion.

Our model addresses a broader question than the previous cost per QALY gained model[248] by comparing behavioural and pharmacological interventions. We used a more comprehensive range of evidence, based on a NMA of RCTs, to inform model estimates of effect size and allowing a full probabilistic assessment of the relative cost-effectiveness of treatment strategies.

Cost-effectiveness model methods

Overview

The model evaluates the cost-effectiveness (cost per QALY gained) of pharmacotherapies, psychological interventions and combinations of both from a NHS perspective. In the final section of this chapter, we discuss the likely implications of a broader societal perspective. The primary model time horizon is 5 years. The interventions evaluated in trials are relatively inexpensive, meaning that therapies with a sustained effect on OCD symptoms would be expected to become cost-effective over a relatively short time horizon. Furthermore, as longitudinal cohort studies of patients with OCD over protracted periods of time are rare, any extrapolation of trial results over the lifetime of patients would be very speculative. Therefore, we elected to evaluate cost-effectiveness over a 5-year time horizon. The model uses probabilistic analysis to quantify the stochastic uncertainty around estimates of cost-effectiveness. The importance of parameter and structural uncertainty is also tested through sensitivity analyses.

Patient populations and interventions compared

The model evaluates the cost-effectiveness of interventions in two patient populations; children and adolescents, and adults. This reflects our NMA, which is also stratified by age. The weighted average age of patients recruited to adult trials is approximately 36 years, compared with 12 years in trials conducted in children or adolescents. The model structure is identical for the two populations; however, the parameter values vary to reflect differing treatment effects and long-term probabilities of response and relapse in these patient populations. All active interventions that were included in the NMA for both outcomes (dropout and YBOCS/CYBOCS scores) were compared in the cost-effectiveness model. We did not evaluate pharmacological and psychological placebos and the herbal remedy hypericum, as they are not directly relevant to NHS decision-makers. In total, there were 13 interventions compared in adult trials, including six SSRIs (see *Table 20*), and seven interventions evaluated in trials of children and adolescents, including three SSRIs (see *Table 37*). As the NMA revealed no clear difference within SSRIs in effect on symptoms or dropout rates, we elected to evaluate SSRIs at the class level in the cost-effectiveness analysis. Therefore, the

cost-effectiveness of eight interventions in the adult model and five interventions in the child and adolescent model is compared. In sensitivity analyses, we reran the model restricting the evidence on treatment response and dropout rates to those RCTs considered to have (1) low attrition; (2) low risk of bias on 'incomplete outcome assessment'; or (3) low risk of bias on 'blinding of the outcome assessor', to evaluate the potential impact of RCT bias on our findings and mirror the NMA. In the adult model, we also conducted a sensitivity analysis excluding RCTs that used a waitlist control group for psychological therapies. Blinding of participants is not possible in these trials and, therefore, they may be more prone to bias.

Model structure

The model comprises a decision tree covering the initial response to treatment at 12 weeks and a Markov model to simulate the course, costs and outcomes (utilities) of OCD from 12 weeks to 5 years. The initial 12-week period is chosen, as this represents the median follow-up period used in the trials summarised in our meta-analysis. The structure of the decision tree is the same for all interventions in both adult and child and adolescent models (*Figure 12*). Patients are assigned to treatment and will either continue to receive the prescribed course of treatment during the 12-week period or prematurely discontinue treatment (drop out). In our primary analysis, we assumed that if a patient drops out of treatment they get no benefit from treatment ('no response'). Patients who continue treatment (comply) during the 12-week period are categorised in accordance with the degree to which their symptoms improve after treatment ('full response', 'partial response', 'no response'). The appropriateness of the assumption that patients who drop out of treatment have no response depends on the statistical methods used in RCTs when analysing CYBOCS/YBOCS scores. It would be appropriate in trials reporting 'per-protocol' analyses, where mean CYBOCS/YBOCS scores exclude those who drop out. However, in trials reporting 'intention-to-treat' analyses where dropouts are already included in the CYBOCS/YBOCS effect estimate, it would effectively double-weight poorer outcomes in patients who drop out. It was often difficult to ascertain whether trials had conducted a pure 'per-protocol' analysis or a pure 'intention-to-treat' analysis. Therefore, in sensitivity analysis, we test this structural assumption.

After the initial 12 weeks, the course of patients' OCD symptoms is tracked using a Markov model with four health states (*Figure 13*). The Markov model includes a 'dead' state; however, in a young cohort of patients with OCD over a 5-year time horizon this will be a very rare event. The remaining three health states are connected by bidirectional arrows, meaning that patients in the model can relapse to a more symptomatic state or achieve partial or full symptom response at any point during the 5 years. In order to estimate the pathway of a patient cohort through this Markov model, we need information on nine transition probabilities at each time point (cycle) of the model. The Markov model uses a 12-week (3-month) cycle length to track OCD symptom response at intervals from 12 weeks to 5 years.

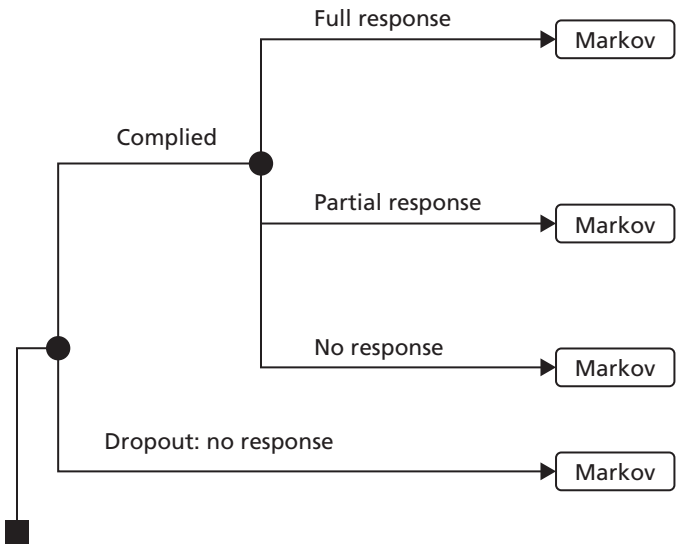


FIGURE 12 Decision tree structure over the first 12 weeks.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

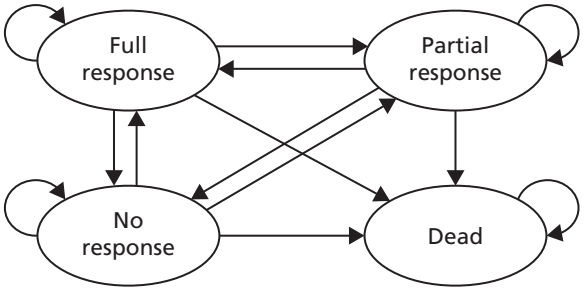


FIGURE 13 Markov model structure for disease course from 12 weeks to 5 years.

Model parameters: dropouts and responses during the initial 12 weeks

The results of the NMA are used to estimate the probability that patients will drop out of treatment before 12 weeks. In the meta-analysis, the ORs for dropout, compared with drug placebo, were typically close to 1 and, with the exception of clomipramine in adults, had wide CrIs spanning unity (see *Tables 27* and *44*). The equivalent probability of dropout and associated CrIs for each intervention are provided in *Table 49* (adults) and *Table 50* (children/adolescents).

We also used the results of the NMA to estimate the initial probability of full, partial and no response to therapy. One challenge in using this modelling approach is that there is no consistent definition in the literature of how response should be measured or categorised.[249] Response may be defined based on the CYBOCS/YBOCS, using absolute (e.g. YBOCS score of ≤ 12) or relative (e.g. YBOCS score improves by ≥ 25 or 30% or 35% from baseline) thresholds,[90,250,251] or using additional measures such as the Clinical Global

TABLE 49 Adult dropout probabilities

Intervention	Source	Probability	95% CrI	Probabilistic analysis
SSRIs	NMA	0.21	0.15 to 0.28	5000 MCMC posterior distribution
Venlafaxine	NMA	0.10	0.03 to 0.22	5000 MCMC posterior distribution
Clomipramine	NMA	0.27	0.20 to 0.36	5000 MCMC posterior distribution
BT	NMA	0.21	0.10 to 0.35	5000 MCMC posterior distribution
CBT	NMA	0.17	0.08 to 0.29	5000 MCMC posterior distribution
CT	NMA	0.21	0.09 to 0.37	5000 MCMC posterior distribution
Fluvoxamine + CBT	NMA	0.41	0.01 to 0.96	5000 MCMC posterior distribution
Clomipramine + BT	NMA	0.25	0.11 to 0.44	5000 MCMC posterior distribution

MCMC, Markov chain Monte Carlo.

TABLE 50 Children and adolescents dropout probabilities

Intervention	Source	Probability	95% CrI	Probabilistic analysis
SSRIs	NMA	0.20	0.04 to 0.48	5000 MCMC posterior distribution
Clomipramine	NMA	0.46	0.11 to 0.87	5000 MCMC posterior distribution
BT	NMA	0.62	0.09 to 0.99	5000 MCMC posterior distribution
CBT	NMA	0.14	0.02 to 0.42	5000 MCMC posterior distribution
CBT + sertraline	NMA	0.16	0.02 to 0.49	5000 MCMC posterior distribution

MCMC, Markov chain Monte Carlo.

Impressions[252] scale assessment of overall illness improvement or psychiatric status ratings (PSRs).[91,97] Not all RCTs in the NMA reported response rates, and definitions of response varied among those that did. Therefore, it is not possible to directly estimate response rates from the meta-analysis. Instead, we indirectly estimate the initial response based on CYBOCS/YBOCS scores. In our primary analysis, we used a CYBOCS/YBOCS score threshold of < 16 to define full response and a CYBOCS/YBOCS score of ≥ 16 and < 20 to define partial response. The < 20 threshold corresponds to an approximately 25% improvement or 1 SD improvement upon the mean baseline YBOCS scores observed in trials. We tested a range of other values in sensitivity analysis.

We estimate a normal distribution for individual CYBOCS/YBOCS scores on placebo (reference). The mean of this distribution is estimated by fitting a standard normal random-effects meta-analysis model to all reference (placebo) arms of trials (included in the NMA) that recorded a mean score and standard error at follow-up. The mean score was estimated using a standard meta-analysis model in which each study provides an estimate of the mean with associated standard error. The SD of the distribution is estimated by fitting a normal random-effects distribution to the SDs at follow-up for all treatments that report this. Note that this assumes that the spread of CYBOCS/YBOCS scores does not depend on treatment. A prediction from these two random-effects distributions (i.e. predictive distribution for mean and SD response) is used to describe our uncertainty in the estimated normal distribution parameters. Relative treatment effects obtained from the NMA were added to the mean reference (placebo) CYBOCS/YBOCS scores, to obtain a predicted mean CYBOCS/YBOCS score for each intervention, and the SD in absolute scores is assumed to be equal for all interventions [and equal to that predicted for the reference (placebo)]. This gives us a prediction for the distribution of absolute CYBOCS/YBOCS scores across individuals for each intervention at follow-up. Assuming these scores follow a normal distribution, the proportion of patients achieving a CYBOCS/YBOCS score of < 16 (full response), between 16 and 20 (partial response), and > 20 (no response) were estimated using appropriate evaluations of the cumulative distribution function for the normal distribution. All of the above is computed at each iteration of a Bayesian Markov chain Monte Carlo simulation, so that we fully reflect uncertainty and correlations in our estimates of the proportions in each category for each intervention. The resulting probabilities for response at 12 weeks, stratified by intervention class and age, are provided in *Tables 51* and *52*.

TABLE 51 Probability of full, partial and no response at 12 weeks, based on a NMA; adult population stratified by intervention

Intervention	Source	Probability of full response	95% CrI	Probability of partial response	95% CrI	Probabilistic analysis
SSRIs	NMA	0.32	0.02 to 0.71	0.22	0.09 to 0.42	5000 MCMC posterior distribution
Venlafaxine	NMA	0.32	0.01 to 0.78	0.20	0.05 to 0.40	5000 MCMC posterior distribution
Clomipramine	NMA	0.39	0.04 to 0.79	0.22	0.10 to 0.43	5000 MCMC posterior distribution
BT	NMA	0.84	0.50 to > 0.99	0.09	< 0.01 to 0.23	5000 MCMC posterior distribution
CBT	NMA	0.42	0.05 to 0.86	0.21	0.08 to 0.42	5000 MCMC posterior distribution
CT	NMA	0.80	0.39 to > 0.99	0.11	< 0.01 to 0.27	5000 MCMC posterior distribution
Fluvoxamine + CBT	NMA	0.54	0.07 to 0.97	0.19	0.02 to 0.38	5000 MCMC posterior distribution
Clomipramine + BT	NMA	0.78	0.33 to > 0.99	0.11	< 0.01 to 0.29	5000 MCMC posterior distribution

MCMC, Markov chain Monte Carlo.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 52 Probability of full, partial and no response at 12 weeks, based on a NMA; child and adolescent population stratified by intervention

Intervention	Source	Probability of full response	95% CrI	Probability of partial response	95% CrI	Probabilistic analysis
SSRIs	NMA	0.53	0.05 to 0.97	0.16	0.02 to 0.31	5000 MCMC posterior distribution
Clomipramine	NMA	0.62	0.08 to 0.99	0.14	0.01 to 0.29	5000 MCMC posterior distribution
BT	NMA	0.71	0.13 to > 0.99	0.12	< 0.01 to 0.26	5000 MCMC posterior distribution
CBT	NMA	0.73	0.19 to > 0.99	0.11	< 0.01 to 0.26	5000 MCMC posterior distribution
CBT + sertraline	NMA	0.78	0.25 to > 0.99	0.10	< 0.01 to 0.24	5000 MCMC posterior distribution

MCMC, Markov chain Monte Carlo.

Model parameters: initial pharmacological and psychological therapy costs

The mean daily dose of pharmacological interventions varied between and within trials (see *Appendix 6*). In order to estimate the initial costs of pharmacotherapy, we selected a daily dose close to the mean of the mean daily doses reported in RCTs, stratified by adults and children and adolescents populations (*Table 53*). This dose was rounded to the nearest multiple of a tablet/capsule size available. We also used data on mean daily dose reported in RCTs to define the plausible maximum and minimum daily dose, and tested the impact of these daily doses on incremental costs and cost-effectiveness in deterministic sensitivity analyses.

TABLE 53 Mean daily dose, cost and minimum and maximum value of pharmacotherapy stratified by drug and age group

Intervention	Mean dose across arms, daily (mg)[a]	Minimum dose during the study (mg)	Maximum dose during the study (mg)	Daily dose in model (mg)	12-week cost in model (£)	Cost of pack (for dropouts) (£)
Adults						
SSRIs					31.43	9.25
Fluoxetine	49.46	20	80	60	8.48	1.01
Fluvoxamine	252.32	50	300	250	117.81	33.66
Paroxetine	45.95	20	60	50	9.21	3.29
Sertraline	154.25	50	200	150	12.48	4.16
Citalopram	42.73	20	60	40	3.51	1.17
Escitalopram	15	10	20	15	71.10	23.70
Venlafaxine	282.5	225	350	300	14.46	2.41
Clomipramine	196.48	50	300	200	25.80	2.15
Children/adolescents						
SSRIs					22.92	9.56
Fluoxetine	32.35	20	80	40	5.66	1.01
Fluvoxamine	165	50	200	150	70.69	33.66
Sertraline	154.36	25	200	150	12.48	4.16
Clomipramine	190	75	200	200	25.80	2.15

a Mean of the mean dose in RCT arms where reported.

The unit costs for pharmaceuticals were based on the *British National Formulary* estimates.[253] The cheapest combination of pack sizes was used to derive the cost of pharmacotherapy for 12 weeks (*Table 54*). The cost of the SSRI class was estimated by taking an average cost of the SSRIs used in the RCTs, weighted by the number of participants randomised to each SSRI. We assumed that patients who complied with therapy would incur pharmaceutical costs throughout the initial 12-week period. We assumed that patients who dropped out of pharmacotherapy incurred only the cost of one prescription (see *Table 53*).

The number of psychological therapy sessions showed little consistency within or between BT, CT and CBT trials (see *Appendix 6*), ranging from a maximum of 40 to fewer than 10 sessions. Session duration, where reported, ranged from < 1 hour to 2.5 hours per session. We estimated typical therapist contact hours of psychological therapy, stratified by therapy type (BT, CT and CBT) and patient group (adults, children/adolescents) based on the mean number of contact hours estimated from trial reports (*Table 55*). We used the contact hours reported in RCTs to define the plausible maximum and minimum contact hours for use in sensitivity analyses. We used Personal Social Services Research Unit (PSSRU)[254] unit costs to value initial psychological therapy. The estimated hourly face-to-face cost of conducting all types of psychological therapy (BT, CT and CBT) was assumed to be equal to the CBT hourly cost (£99; 2013 prices) estimated by the PSSRU. We assumed that patients who dropped out of psychological therapy did so after attending, on average, one-quarter of sessions, thereby incurring one-quarter of therapy costs. The cost of combinations of pharmacological and psychological therapies were estimated to be the sum of the components.

TABLE 54 *British National Formulary* drug costs stratified by pack size and dose

Intervention	Units I	Unit dose I (mg)	Cost I, £	Units II	Unit dose II (mg)	Cost II (£)	Units III	Unit dose III (mg)	Cost III (£)
SSRIs									
Fluoxetine	30	20	1.01	30	60	28.79			
Fluvoxamine	60	50	16.83	30	100	16.83			
Paroxetine	30	20	1.52	30	30	1.77			
Sertraline	28	50	1.92	28	100	2.24			
Citalopram	28	10	0.91	28	20	1.00	28	40	1.17
Escitalopram	28	5	8.97	28	10	14.73	28	20	25.20
Venlafaxine	56	37.5	2.15	56	75	2.41			
Clomipramine	28	10	1.30	28	25	1.71	28	50	2.15

TABLE 55 Mean contact hours, cost and minimum and maximum value of psychological therapy, stratified by therapy type and age group

Intervention	Mean hours across arms	Minimum hours	Maximum hours	Cost per therapy (£)	Cost for patients dropping out (£)
Adult					
BT	17.17	10	46.5	1699.83	424.96
CBT	20.78	10	60	2057.22	514.31
CT	15.25	8	30	1509.75	377.44
Children/adolescents					
BT	22.5	15	30	2227.50	556.88
CBT	15	10	21	1485.00	371.25

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Model parameters: mortality, symptoms, costs and utilities in the longer term

Mortality

Epidemiological evidence[255] suggests that mortality rates are not higher in individuals with OCD; indeed, observed mortality rates may be lower than the expected rates. Therefore, we used the Office for National Statistics all-cause mortality life tables[256] to estimate mortality, independent of OCD symptom severity. Mortality was estimated based on the mean age of patients recruited to the adult and child and adolescent RCTs, and mortality estimates were weighted to reflect their gender profile (see *Appendix 10*).

Symptoms

Most trials included in the NMA had relatively short periods of follow-up; there is little evidence from RCTs on how differences between interventions evident in the short term (e.g. 12 weeks) might be sustained in the longer term.[122] In our primary economic analysis, we assumed that, after the first 12-week period, the initial choice of therapy did not affect the probability of further remission or relapse. In other words, initial therapy affected the probability of being in each of the three health states in the Markov model (full, partial or no response) at 12 weeks, but did not affect transition probabilities thereafter. We tested other assumptions in sensitivity analyses.

In order to identify evidence on transition probabilities for OCD symptom severity, we conducted a rapid literature review. We used an adapted version of the Scottish Intercollegiate Guidelines Network MEDLINE filter for observational studies[257] supplemented with text words for OCD and the YBOCS to identify studies reporting on the long-term course of OCD remission and relapse in adults and in children and adolescents (see *Appendix 10*). Of 561 articles initially identified, we selected 24 for full-text review, based on the title and abstract. On review of the full text, we selected two publications, Mancebo *et al.*[97] and Eisen *et al.*,[91] based on the Brown Longitudinal Obsessive–Compulsive Study (BLOCS) cohort study as containing the most relevant information on remission and relapse transition probabilities. The BLOCS recruited treatment-seeking subjects (325 adults and 70 children) with OCD from multiple psychiatric treatment settings in the USA (71% outpatient OCD clinic, 4% inpatient units, 25% community mental health centres). Subjects had annual assessments using a semistructured interview. Each assessment recorded a weekly PSR, which was used to define partial or full remission and any subsequent relapse. PSR is a rating of 6 points based on OCD symptom severity and functional impairment. A rating of 6 points indicates the most severe symptoms and impairment, and one indicates no OCD symptoms or impairment. BLOCS defined full remission as a PSR score of ≤ 2 (minimal or no symptoms and no impairment) for 8 consecutive weeks, partial remission as a score of 3 (symptoms present for less than 1 hour daily, but not impairing) for 8 consecutive weeks and relapse as a score of 4 or more for 4 consecutive weeks after achieving a full or partial response.

Eisen *et al.*[91] report the 5-year course of symptoms for 213 adults enrolled in the BLOCS who had at least 3 years of follow-up data. Over 5 years, 36 (16.9%) patients in the sample had full remission and a further 47 (22.1%) had partial remission. However, subsequent relapse was common in those who achieved partial remission (70%) or full remission (45%). Mancebo *et al.*[97] report the 3-year course of symptoms for 46 children and adolescents, aged 6–18 years, participating in the BLOCS who met the DSM-IV criteria for OCD at enrolment and completed at least 2 years of follow-up. Of these, 12 (27%) had achieved full remission by 3 years and a further 12 (27%) were in partial remission; five (21%) of these 24 individuals subsequently relapsed.

Data used to estimate 'no response' to 'partial response' and 'no response' to 'full response' time-varying transition probabilities in both adult and child and adolescent populations over the first 36 months post treatment were obtained from Mancebo *et al.*[97] From 36 to 60 months, in the absence of direct evidence from the BLOCS, the transition probabilities were assumed to remain constant (i.e. equal to the 31–36 month transition probabilities). Six-monthly probabilities were converted to 3-monthly probabilities to match the model cycle length.

A plot in Eisen *et al.*[91] displayed the probability of relapse after initial response, stratified by partial and full response, over 4 years in an adult population. Three-monthly transition probabilities were extracted from this plot using Digitizeit version 2.0 (Bormisoft, Braunschweig, Germany; www.digitizeit.de/) software that extracts numerical data from images. The 3-monthly transition probabilities between 48 and 60 months were assumed to remain constant (i.e. equal to the 46- to 48-month probabilities). In children and adolescents, Mancebo *et al.*[97] report that 5 of 24 subjects (21%) who had partial or full response subsequently relapsed over a study period of, on average, 88 weeks. However, this study did not provide further detail on relapse rates over time. Therefore, we assumed that the relapse probability was constant over the 5-year period and that the relative proportion of relapse from full or partial response was the same as that observed in the adult population.

These two articles provide evidence on the bidirectional time-varying transition probabilities between full response and no response (i.e. relapse) and between partial response and no response. However, they do not provide evidence on the transition probabilities between full and partial response. In our primary analysis, we arbitrarily assumed no transition between full and partial response, which is equivalent to assuming the proportion of patients moving from partial to full response is counterbalanced in each cycle by the proportion of patients moving from full to partial response. We tested other assumptions in sensitivity analyses. The time-varying transition probabilities for adults and children and adolescents are presented in *Tables 56* and *57*, respectively.

TABLE 56 Adult symptom transition probabilities (from 12 weeks to 5 years) among patients surviving in each cycle

Time period for Markov model (months)	Source	Rate	A[a]	B[a]	Probabilistic distribution
No response to partial or full response					
0–6	Mancebo *et al.*, 2014[97]	0.109	24	221	Beta
7–12	Mancebo *et al.*, 2014[97]	0.091	18	197	Beta
13–18	Mancebo *et al.*, 2014[97]	0.039	7	179	Beta
19–24	Mancebo *et al.*, 2014[97]	0.070	12	172	Beta
25–30	Mancebo *et al.*, 2014[97]	0.038	6	160	Beta
31–36	Mancebo *et al.*, 2014[97]	0.052	8	154	Beta
37+[b]	Mancebo *et al.*, 2014[97]	0.052	8	154	Beta
Proportion of responders who have full response					
0–6	Mancebo *et al.*, 2014[97]	0.208	5	24	Beta
7–12	Mancebo *et al.*, 2014[97]	0.278	5	18	Beta
13–18	Mancebo *et al.*, 2014[97]	0.571	4	7	Beta
19–24	Mancebo *et al.*, 2014[97]	0.500	6	12	Beta
25–30	Mancebo *et al.*, 2014[97]	0.667	4	6	Beta
31–36	Mancebo *et al.*, 2014[97]	0.500	4	8	Beta
37+[b]	Mancebo *et al.*, 2014[97]	0.500	4	8	Beta
Partial response to no response (relapse)					
0–3	Eisen *et al.*, 2013[91]	0.013	0.59	46.41	Beta
4–6	Eisen *et al.*, 2013[91]	0.170	6.83	40.17	Beta
7–9	Eisen *et al.*, 2013[91]	0.098	4.18	42.82	Beta
10–12	Eisen *et al.*, 2013[91]	0.057	2.54	44.46	Beta

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 56 Adult symptom transition probabilities (from 12 weeks to 5 years) among patients surviving in each cycle (*continued*)

Time period for Markov model (months)	Source	Rate	A[a]	B[a]	Probabilistic distribution
13–15	Eisen *et al.*, 2013[91]	0.046	2.07	44.93	Beta
16–18	Eisen *et al.*, 2013[91]	0.000	0.00	47.00	Beta
19–21	Eisen *et al.*, 2013[91]	0.035	1.60	45.40	Beta
22–24	Eisen *et al.*, 2013[91]	0.065	2.87	44.13	Beta
25–27	Eisen *et al.*, 2013[91]	0.000	0.00	47.00	Beta
28–30	Eisen *et al.*, 2013[91]	0.000	0.00	47.00	Beta
31–33	Eisen *et al.*, 2013[91]	0.074	3.24	43.76	Beta
34–36	Eisen *et al.*, 2013[91]	0.074	3.24	43.76	Beta
37–39	Eisen *et al.*, 2013[91]	0.034	1.55	45.45	Beta
40–42	Eisen *et al.*, 2013[91]	0.020	0.94	46.06	Beta
43–45	Eisen *et al.*, 2013[91]	0.031	1.41	45.59	Beta
46–48	Eisen *et al.*, 2013[91]	0.029	1.32	45.68	Beta
49+[c]	Eisen *et al.*, 2013[91]	0.029	1.32	45.68	Beta
Full response to no response (relapse)					
0–3	Eisen *et al.*, 2013[91]	0.011	0.38	35.62	Beta
4–6	Eisen *et al.*, 2013[91]	0.107	3.47	32.53	Beta
7–9	Eisen *et al.*, 2013[91]	0.026	0.90	35.10	Beta
10–12	Eisen *et al.*, 2013[91]	0.035	1.22	34.78	Beta
13–15	Eisen *et al.*, 2013[91]	0.068	2.30	33.70	Beta
16–18	Eisen *et al.*, 2013[91]	0.022	0.79	35.21	Beta
19–21	Eisen *et al.*, 2013[91]	0.001	0.04	35.96	Beta
22–24	Eisen *et al.*, 2013[91]	0.000	0.00	36.00	Beta
25–27	Eisen *et al.*, 2013[91]	0.030	1.04	34.96	Beta
28–30	Eisen *et al.*, 2013[91]	0.030	1.04	34.96	Beta
31–33	Eisen *et al.*, 2013[91]	0.048	1.66	34.34	Beta
34–36	Eisen *et al.*, 2013[91]	0.047	1.62	34.38	Beta
37–39	Eisen *et al.*, 2013[91]	0.014	0.50	35.50	Beta
40–42	Eisen *et al.*, 2013[91]	0.010	0.36	35.64	Beta
43–45	Eisen *et al.*, 2013[91]	0.011	0.40	35.60	Beta
46–48	Eisen *et al.*, 2013[91]	0.010	0.36	35.64	Beta
49+[c]	Eisen *et al.*, 2013[91]	0.010	0.36	35.64	Beta

a A and B represent the shape parameters in the beta distribution.
b Transition rates are assumed to be constant from 37 months to 5 years.
c Transition rates are assumed to be constant from 49 months to 5 years.

TABLE 57 Children and adolescents symptom transition rates (from 12 weeks to 5 years) among patients surviving in each cycle

Time period for Markov model (months)	Source	Rate	A[a]	B[a]	Probabilistic distribution
No response to partial or full remission					
0–6	Mancebo *et al.*, 2014[97]	0.087	4	46	Beta
7–12	Mancebo *et al.*, 2014[97]	0.143	6	42	Beta
13–18	Mancebo *et al.*, 2014[97]	0.111	4	36	Beta
19–24	Mancebo *et al.*, 2014[97]	0.156	5	32	Beta
25–30	Mancebo *et al.*, 2014[97]	0.111	3	27	Beta
31–36	Mancebo *et al.*, 2014[97]	0.083	2	24	Beta
37+[b]	Mancebo *et al.* 2014[97]	0.091	2	22	Beta
Proportion of responders who have full response					
0–6	Mancebo *et al.*, 2014[97]	0.500	2	4	Beta
7–12	Mancebo *et al.*, 2014[97]	0.333	2	6	Beta
13–18	Mancebo *et al.*, 2014[97]	0.500	2	4	Beta
19–24	Mancebo *et al.*, 2014[97]	0.600	3	5	Beta
25–30	Mancebo *et al.*, 2014[97]	0.667	2	3	Beta
31–36	Mancebo *et al.*, 2014[97]	0.500	1	2	Beta
37+[b]	Mancebo *et al.*, 2014[97]	0.500	1	2	Beta
Partial response to no response					
88.2-week interval[c]	Mancebo *et al.*, 2014[97] and Eisen *et al.*, 2013[91]	0.333	3	9	Beta
Full response to no response					
88.2-week interval[c]	Mancebo *et al.*, 2014[97] and Eisen *et al.*, 2013[91]	0.200	2	10	Beta

a A and B represent the shape parameters in the beta distribution.
b Transition rates are assumed to be constant from 37 months to 5 years.
c Transition rate is constant over time.

Utilities

A rapid literature review was conducted to identify quality-of-life studies in OCD. The review identified 447 abstracts; after initial screening, 12 abstracts were selected for full-text review (see *Appendix 10*). Most studies did not use a generic preference-based outcome measure, such as the European Quality of Life-5 Dimensions (EQ-5D™) or Short Form questionnaire-6 Dimensions (SF-6D),[258] both of which allow calculation of QALYs. Of those studies that did use these measures, several did not report results for the health states (full, partial, no response) that correspond to the Markov model. We did not find any studies reporting utility values in children and adolescents with OCD; therefore, we assume that the impact of OCD on health-related quality of life in adults is generalisable to children and adolescents and use one set of utility values for both age groups.

Hollander *et al.*[114] used data from two double-blind, placebo-controlled RCTs with similar eligibility criteria in adults with OCD.[124,128] Stein *et al.*[124] recruited 466 patients with a mean age of 23 years and a mean YBOCS score of 27, and Fineberg *et al.*[128] recruited 468 patients with a mean age of 23 years and a mean YBOCS score of 26.4. In this study, response was defined as a decrease in YBOCS score of $\geq 25\%$ relative to baseline. In responders, relapse was defined as a subsequent increase in YBOCS score of 5 points or more, or an unsatisfactory treatment effect as judged by the investigators. Both studies collected Short

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Form questionnaire-36 Items data from which SF-6D utility scores were derived. The study estimates SF-6D utility values for adult patients at baseline (pre-randomisation) and for patients with response; no response; response and relapse; and response and no relapse at 16 weeks from the start of treatment. The definitions of response used by Hollander *et al.*[114] in measuring utility values do not correspond exactly with the definitions of response used by the BLOCS in defining symptom course. Therefore, we had to make assumptions about the most appropriate utility values to use in our Markov model. The utility values applied in our primary economic analysis are described in *Table 58*.

Long-term costs of health care

Patients who fail to respond fully to initial therapy are likely to be prescribed a number of other pharmacological or psychological therapies with their attendant costs and benefits. Our cost-effectiveness model aims to predict the impact of initial therapy on longer-term costs and outcomes, but there is insufficient information to track all treatment switching or therapy combinations likely to occur in practice. We therefore assumed that the incremental differences in treatment cost after 12 weeks are driven solely by symptom severity. As previously discussed, the literature on the health-care costs of OCD is very sparse. The only study in the peer-reviewed literature that we are aware of which has estimated the per-patient costs of OCD used retrospective claims data from Medicaid enrolees in Florida.[248] Hankin *et al.*[240] used the ICD Ninth Edition diagnosis codes to identify 85 newly diagnosed patients with 'pure OCD' and 14,906 patients with newly diagnosed 'pure depression' in order to compare health-care costs over a 2-year period. The median 2-year cost of inpatient, outpatient and pharmacy health-care claims were similar in patients with OCD and depression (US$6588 for OCD vs. US$5347 for depression; Wilcoxon's signed-rank *p*-value 0.27). However, the composition of costs differed; patients with OCD had higher use of psychotropic medications, whereas patients with depression had higher use of non-psychiatric outpatient care. The authors note that the long-term costs of OCD may be higher than those of depression because OCD is a chronic disorder requiring ongoing therapy, whereas depression is episodic in most cases. This study has limited value in informing our cost-effectiveness model, because it is based on findings from a selected subset of patients (i.e. eligible for Medicaid) in a US health-care setting in which unit costs are higher than in the NHS and the analysis does not stratify costs by symptom response to therapy.

In order to estimate a proxy NHS cost in our model for long-term OCD care, we assumed costs to be similar to patients treated for depression. In a study of 88,935 patients aged > 18 years, diagnosed with depression, Byford *et al.*[259] found that the mean 12-month NHS costs, including medications, primary care, psychological therapies and secondary care, were 33% lower among patients who achieved remission from depressive symptoms than in those who did not [£656 vs. £973 (2005/6 values) or £945 vs. £1402 at 2014 values; $p < 0.001$]. Therefore, we assumed that the annual NHS costs in patients with OCD who have no response to therapy were equivalent to patients with depression who do not achieve remission. Furthermore, in our primary analysis, we assumed that patients with OCD who have a full response to therapy will have 33% lower NHS costs, and we selected an arbitrary value (17% reduction) for patients with partial response to therapy. Owing to the weak and indirect evidence on costs, we tested these assumptions using a wide range of alternative values in our sensitivity analysis (*Table 59*).

TABLE 58 Utility values

Markov health state	Label used	Source	Mean utility value	SD	Probabilistic distribution
Pre-treatment	Baseline value	Hollander *et al.*, 2010[114]	0.648	0.103	1 – gamma
Partial response	Response	Hollander *et al.*, 2010[114]	0.725	0.108	1 – gamma
No response	No response	Hollander *et al.*, 2010[114]	0.664	0.106	1 – gamma
Not used in Markov model	Relapse	Hollander *et al.*, 2010[114]	0.684	0.116	1 – gamma
Full response	No relapse	Hollander *et al.*, 2010[114]	0.776	0.113	1 – gamma

TABLE 59 Costs per health state (3 months)

Health state	Source	Cost (£)	SE (£)[a]	Distribution
Full response	Byford *et al.*, 2011[259]	236		
Partial response	Byford *et al.*, 2011[259]	291		
No response	Byford *et al.*, 2011[259]	351	88	Log-normal
Dead		0		

SE, standard error.
a Owing to the high uncertainty around the costs, we have assumed a SE of 25% of the cost of no response. The costs from the other health states are then derived from this cost.

Methods of analysis

The model was constructed in Microsoft Excel 2010. A half-cycle correction was applied to estimate costs and utilities for patients who move between health states during each cycle of the Markov model. Costs and utilities were discounted at 3.5%, in line with NICE guidelines.[260] Verification of the model's internal validity was tested using extreme value analysis. The cost-effectiveness of each intervention is summarised using the net benefit statistic at thresholds of £20,000 and £30,000 (i.e. the amount the NHS is prepared to pay in order to produce a QALY).[260] Parametric uncertainty surrounding the point estimate is estimated using 95th-percentile intervals from a probabilistic analysis, generated using second-order Monte Carlo simulation taking 3000 random draws from parameter distributions. The probability that each intervention is the most cost-effective at a range of willingness-to-pay thresholds (£0–50,000 per QALY) is summarised using cost-effectiveness acceptability curves (CEACs).[261]

Sensitivity analyses

We used a series of sensitivity analyses to evaluate the robustness of the cost-effectiveness results to several of the assumptions made within the model.

1. **Risk of bias:** we reran the model using the subset of studies that met the NMA criteria of low risk of bias in (1) overall attrition; (2) incomplete outcome assessment; or (3) blinding of outcome assessor to assess the potential impact of RCT bias on cost-effectiveness results. In the adult model, we also reran the model excluding RCTs that used a waitlist control for psychotherapy interventions.
2. **Effectiveness in patients who drop out:** we reran the model assuming that patients who dropped out of treatment had lower costs, but identical outcomes to those who completed treatment.
3. **Definition of full response:** we lowered the threshold for defining full response (≤ 12).
4. **Cost of initial therapy:** we used minimum and maximum dose and contact hours to assess the impact of initial therapy costs on cost-effectiveness estimates.
5. **Sustained effect of initial therapy:** we reduced the time horizon of the model to assess the impact on cost-effectiveness if treatment effects were sustained for fewer than 5 years.
6. **Transition from full to partial response:** we varied the net flow of patients from full to partial response in the Markov model to assess the impact on cost-effectiveness results.
7. **Change cost of long-term care:** we assessed the impact of assuming higher incremental long-term costs of care for patients with no response (compared with those with full and partial response).
8. **SSRI costs:** in both the adult and child and adolescent models we reran the model assuming that SSRI medication costs were equivalent to the cheapest SSRI, rather than the class average cost. Medication costs vary considerably among SSRIs and, therefore, if effectiveness is equivalent within the class, cheaper SSRIs will be more cost-effective.
9. **Venlafaxine:** in the adult model, we reran analyses excluding venlafaxine, which is not licensed for OCD despite being evaluated in a small number of RCTs for off-label use.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Cost-effectiveness results: adults

Primary cost-effectiveness analysis

The estimated NHS costs, QALYs and cost-effectiveness of each of the eight interventions in adults are reported in *Table 60*. Over a 5-year time period, the high upfront costs of psychological therapies are not completely offset by lower NHS costs in subsequent years. The three drug groups (SSRIs, clomipramine and venlafaxine) have the lowest NHS costs (range £5727–5788), strategies including CT and BT have higher costs (range £6590–6778), and strategies including CBT had the highest estimated costs (range £7206–7428). The difference in cost between CBT and the other two psychological therapies is partly attributable to the higher number of contact hours used in adult CBT trials (see *Table 55*) and partly attributable to the lower effect size of CBT estimated in the NMA (see *Table 51*).

Psychological therapies, particularly CT and BT, are estimated to result in the highest QALYs over the 5-year period. The absolute difference in QALYs is quite small [range from 3.208 (SSRIs) to 3.320 (BT)]. However, this range is approximately equivalent to an additional 365 days in 'full response' rather than 'no response' over the 5-year period. The net monetary benefit (NMB) (£20,000) column summarises cost-effectiveness if the NHS is willing to pay £20,000 for each QALY gained by patients, which is at the lower end of NICE's stated threshold. *Table 60* is ordered by this column, with interventions with the lowest estimated NMB (i.e. least cost-effective) at the top and interventions with the highest estimated NMB (i.e. most cost-effective) at the bottom. The interventions fall into three clusters based on NMB (£20,000). Strategies involving CT or BT are most cost-effective (NMB range £59,208–59,695). The additional upfront costs of the CT and BT strategies, compared with the pharmacological monotherapies are justified by better outcomes (QALYs). The pharmacological monotherapies have a similar range of cost-effectiveness [NMB range from £58,373 (SSRIs) to £58,664 (venlafaxine)]. Differences between the pharmacological monotherapies are driven by the slightly higher costs of SSRIs (see *Table 53*) and the low probability of dropout from venlafaxine estimated from two relatively small RCTs (see *Table 49*). The strategies including CBT have the poorest cost-effectiveness [NMB range from £57,174 (fluvoxamine + CBT) to £57,337 (CBT)]. The higher upfront costs of CBT, compared with pharmacotherapy, are not justified by the marginal improvement in symptom response (see *Table 51*). The 95th percentile intervals around the NMBs (£20,000) estimated by the probabilistic analysis overlap, indicate that there is no strong evidence that any single therapy is more cost-effective than the other therapies. The findings are not materially altered if the NHS is willing to pay more (NMB £30,000) for each QALY gained (*Table 60*).

TABLE 60 Cost-effectiveness of therapy: adults

Intervention	Total costs (£)	Total QALYs	NMB (£20,000) (£)	Lower 95th percentile (£)	Upper 95th percentile (£)	NMB (£30,000) (£)
Fluvoxamine + CBT	7206	3.219	57,174	53,043	61,108	89,364
CBT	7428	3.238	57,337	53,189	61,367	89,719
SSRIs	5788	3.208	58,373	54,498	62,047	90,453
Clomipramine	5751	3.215	58,549	54,768	62,061	90,699
Venlafaxine	5727	3.220	58,664	54,442	62,675	90,860
Clomipramine + BT	6778	3.299	59,208	55,120	62,692	92,201
CT	6590	3.313	59,668	55,571	63,112	92,797
BT	6715	3.320	59,695	55,718	63,168	92,899

The CEAC (*Figure 14*) depicts the probability that each intervention is the most cost-effective, on the vertical axis, as a function of increasing NHS willingness to pay for a QALY, on the horizontal axis. The CEAC demonstrates that at lower willingness-to-pay thresholds (i.e. < £10,000 per QALY), the cheaper pharmacotherapies (venlafaxine and clomipramine and, to a lesser extent, SSRIs) have higher probabilities of being most cost-effective. Once the willingness to pay exceeds NICE's stated threshold (£20,000 per QALY), strategies involving CT and BT become the most likely to be cost-effective. The CEAC suggests that there is no clear 'winner' in terms of cost-effectiveness, with the difference in probability of being most cost-effective between the therapies ranked first and second rarely exceeding 0.1 across all willingness-to-pay values. Therapies including CBT had a very low probability of being most cost-effective across the range of willingness-to-pay values. These findings are supported by the cost-effectiveness acceptability frontier (*Figure 15*), which identifies, with a low degree of certainty, venlafaxine as the most cost-effective (optimal) therapy at low willingness-to-pay thresholds and BT as the optimal therapy at the thresholds (£20,000–30,000 per QALY) used by NICE.

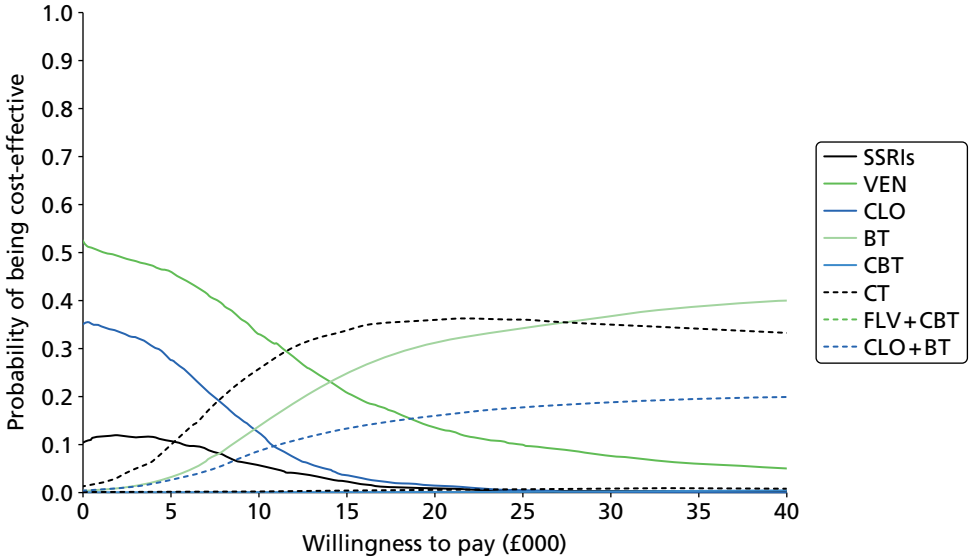


FIGURE 14 Cost-effectiveness acceptability curve: adults, primary analysis. CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

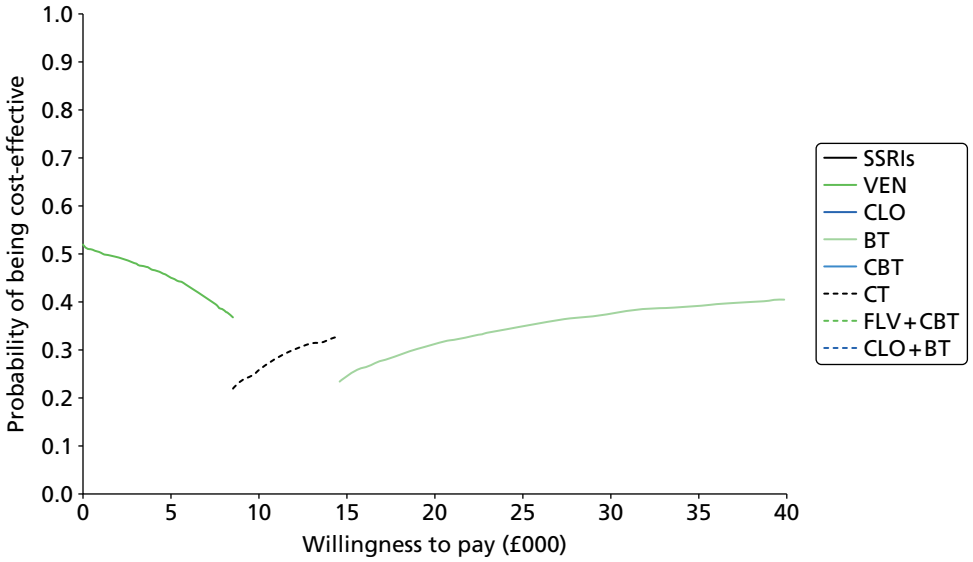


FIGURE 15 Cost-effectiveness acceptability frontier: adults, primary analysis. CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Sensitivity analyses

Full results of all sensitivity analyses are provided in *Appendix 10*. Here, we focus on the five sensitivity analyses that had most impact on the interpretation of the cost-effectiveness model.

The exclusion of evidence from RCTs that used waitlist controls decreased the probability that BT and CT strategies were most cost-effective at the thresholds (£20,000–30,000 per QALY) used by NICE (*Figure 16*). The difference in effectiveness between different types of psychological therapy was very small in this sensitivity analysis (*Table 61*). However, the higher estimated cost of CBT, owing to the higher number of contact hours used in adult CBT trials, meant that CBT strategies were less likely to be cost-effective. Clomipramine and BT had the highest probability of being cost-effective, although this did not exceed 0.4 (*Figure 16*).

The most cost-effective pharmacotherapy was strongly dependent on assumptions about outcomes in patients who drop out. If we assume that the outcomes in patients who drop out are fully reflected in analyses of YBOCS scores in the meta-analysis (i.e. analyses were predominantly intention to treat), then clomipramine, rather than venlafaxine, is much more likely to be the most cost-effective pharmacotherapy at lower willingness-to-pay thresholds (*Figure 17*). The finding that strategies involving CT and BT become more cost-effective at higher willingness-to-pay thresholds is not affected by this assumption.

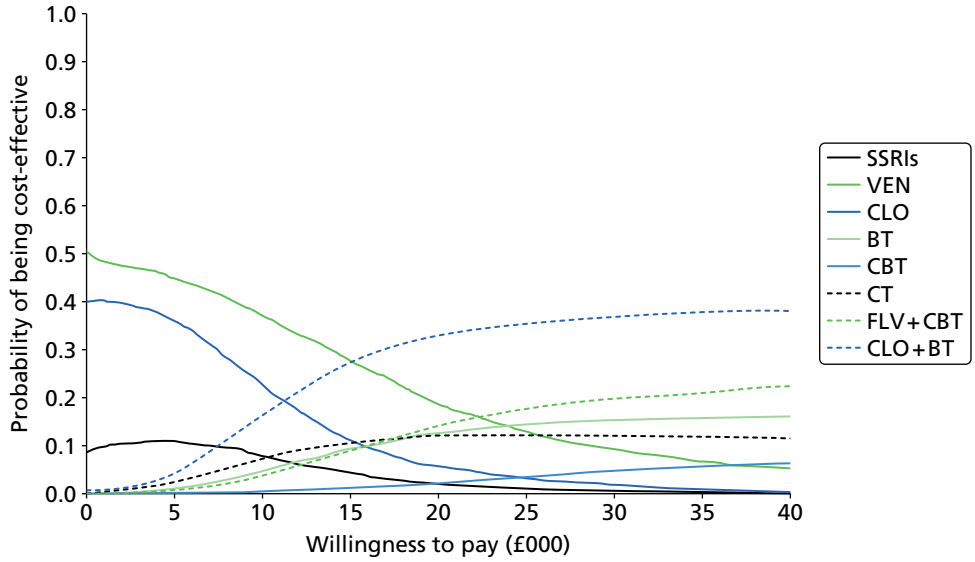


FIGURE 16 Cost-effectiveness acceptability curve: adults – excluding RCTs with waitlist controls. CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

TABLE 61 Cost-effectiveness of therapy: adults – excluding RCTs with waitlist controls

Intervention	Total costs (£)	Total QALYs	NMB (£20,000) (£)	Lower 95th percentile (£)	Upper 95th percentile (£)	NMB (£30,000) (£)
CBT	7385	3.256	57,743	53,805	61,290	90,307
Fluvoxamine + CBT	7438	3.266	57,883	53,879	61,846	90,543
SSRIs	5865	3.190	57,930	54,314	61,020	89,827
Clomipramine	5834	3.195	58,065	54,516	61,146	90,015
Venlafaxine	5822	3.197	58,115	54,344	61,527	90,084
CT	6818	3.256	58,296	54,354	61,773	90,853
BT	6920	3.265	58,380	54,612	61,851	91,030
Clomipramine + BT	6867	3.274	58,605	54,811	62,119	91,341

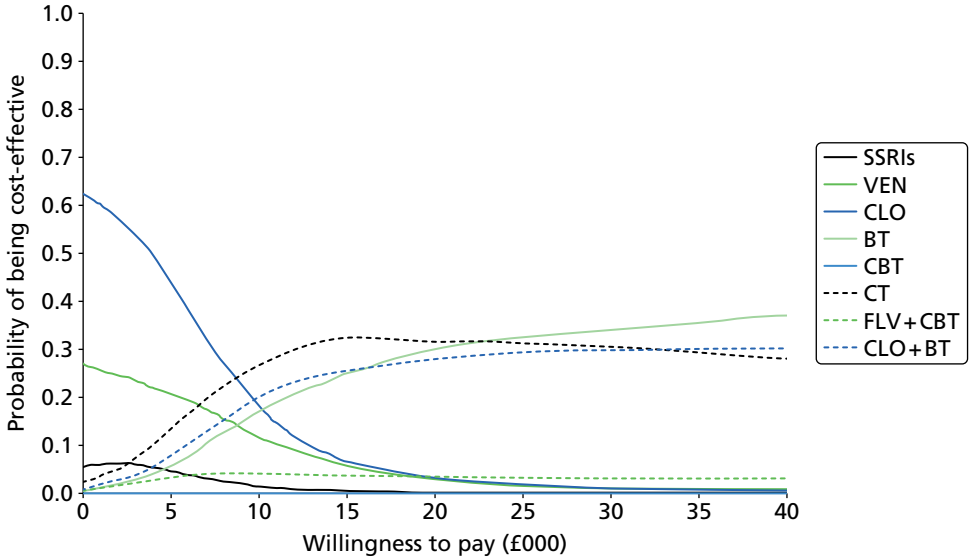


FIGURE 17 Cost-effectiveness acceptability curve: adults – effectiveness in patients who drop out. CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

The initial cost of therapy, particularly psychological therapies, was also influential. The number of contact hours of BT, CT and CBT differed greatly across RCTs (see *Table 55*). The impact of this on NHS costs of initial therapy was much greater than the range of daily doses used in pharmacotherapy trials. Therefore, if we assume that all psychological and pharmacological therapies have a cost at the upper end of the range evaluated in RCTs, pharmacotherapies become relatively cheaper and more cost-effective (*Figure 18*). Although psychological therapy (specifically CT) was still estimated to be cost-effective at higher willingness-to-pay thresholds, cheaper pharmacotherapies (e.g. venlafaxine and clomipramine) remain relatively cost-effective options at the £20,000-per-QALY threshold.

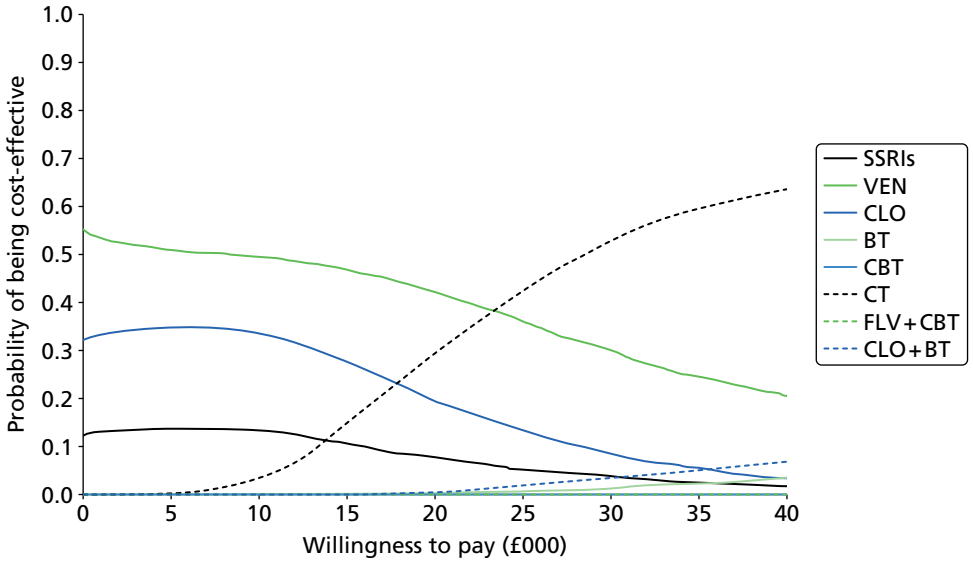


FIGURE 18 Cost-effectiveness acceptability curve: adults – maximum cost of initial therapy. CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Assumptions about the sustainability of treatment effects observed in RCTs with short follow-up periods (e.g. 12 weeks) are influential on the cost-effectiveness results. Our primary analysis assumes that some of the benefits of more effective therapies (i.e. the psychological therapies, particularly CT and BT) are sustained beyond the end of the trial, although they gradually diminish as patients who had an initial response relapse. If we were to assume that all differences in intervention costs and benefits are limited to the within-trial period, then the initially cheaper pharmacotherapies (venlafaxine and clomipramine) are predominantly likely to be most cost-effective (*Figure 19*).

Excluding venlafaxine, which does not have a licensed indication in OCD, affected the choice of optimal intervention at lower willingness-to-pay thresholds (*Figure 20*). Under this scenario, clomipramine and, to a certain extent, SSRIs, become more likely to be cost-effective, but psychological therapies remain most likely to be cost-effective at the £20,000-per-QALY threshold.

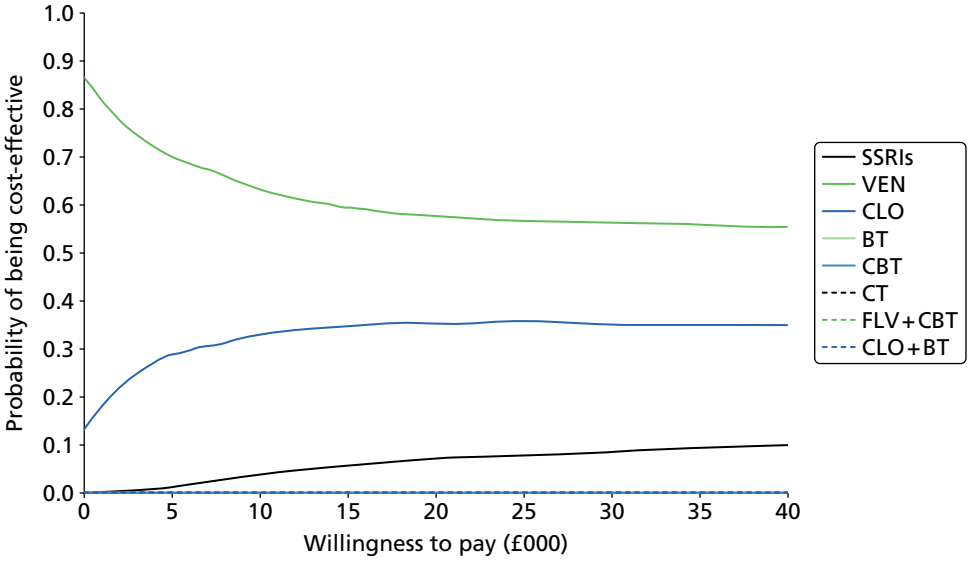


FIGURE 19 Cost-effectiveness acceptability curve: adults – costs and benefits limited to the within-trial period. CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

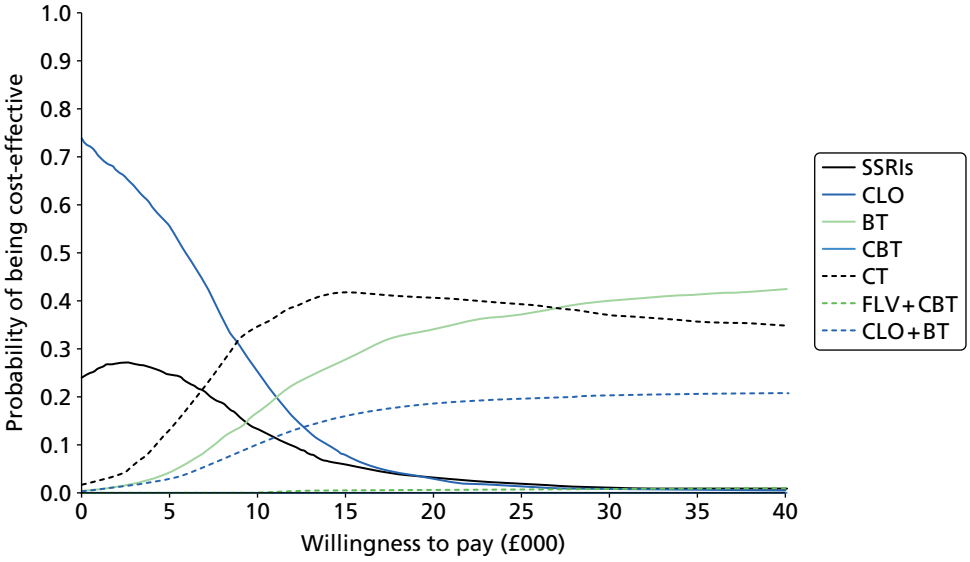


FIGURE 20 Cost-effectiveness acceptability curve: adults – excluding venlafaxine. CLO, clomipramine; FLV, fluvoxamine.

Cost-effectiveness results: children and adolescents

Primary cost-effectiveness analysis

The estimated NHS costs, QALYs and cost-effectiveness of each of the five interventions in children and adolescents are reported in *Table 62*. As with the adult population, over a 5-year time period, the high upfront costs of psychological therapies are not completely counterbalanced by lower NHS costs in subsequent years. The two pharmacotherapies (SSRIs and clomipramine) have the lowest NHS costs (range £5398–5515), and strategies including BT or CBT have higher costs (range £6418–6762). The cost of CBT was similar to BT, because RCTs in children and adolescents, unlike those in adults, used a similar number of contact hours to deliver CBT and BT (see *Table 55*).

In children and adolescents, strategies including CBT were estimated to result in the highest QALYs over the 5-year period. The absolute difference in QALYs is again relatively small [range from 3.254 (BT) to 3.376 (sertraline and CBT)]. However, this range is approximately equivalent to an additional 397 days in 'full response' rather than 'no response' over the 5-year period. The NMB (£20,000) column summarises cost-effectiveness if the NHS is willing to pay £20,000 for each QALY gained by patients, which is at the lower end of NICE's stated threshold. *Table 61* is ordered by this column, with interventions with the lowest estimated NMB (i.e. least cost-effective) at the top and interventions with the highest estimated NMB (i.e. most cost-effective) at the bottom. In contrast to findings in the adult population, BT was estimated to be least cost-effective (NMB £58,325). The additional upfront costs of BT, compared with the pharmacological monotherapies, were not justified by better outcomes (QALYs). In fact, the high dropout rate from BT among children and adolescents (see *Table 50*), albeit imprecisely estimated from two very small trials,[218,220] led to BT being both more expensive and less effective than SSRIs and clomipramine. The pharmacological monotherapies have a similar range of cost-effectiveness [NMB range from £60,087 (clomipramine) to £60,828 (SSRIs)]. Differences between the pharmacological monotherapies are driven by higher dropout rates estimated for clomipramine than SSRIs (see *Table 50*). The cost-effectiveness of strategies including CBT was similar to pharmacotherapies [NMB range from £60,905 (CBT) to £61,107 (sertraline and CBT)]. The 95th percentile intervals around the NMBs (£20,000) estimated by the probabilistic analysis overlap, which indicates that there is no strong evidence that any single therapy is more cost-effective than any other therapy. Strategies including CBT became relatively more cost-effective if the NHS is willing to pay more (NMB £30,000) for each QALY gained (*Table 62*).

The CEAC (*Figure 21*) depicts the probability that each intervention is the most cost-effective, on the vertical axis, as a function of increasing NHS willingness to pay for a QALY, on the horizontal axis. The CEAC demonstrates that at lower willingness-to-pay thresholds (i.e. < £15,000 per QALY), the pharmacotherapies (particularly SSRIs) are more likely to be most cost-effective. Once the willingness-to-pay threshold exceeds £20,000 per QALY, the combined strategy of CBT and sertraline becomes the most likely to be cost-effective, with a probability exceeding 0.5. BT had a very low probability of being most cost-effective across the range of willingness-to-pay values. These findings are supported by the cost-effectiveness acceptability frontier (*Figure 22*), which identifies SSRIs as probably the most cost-effective (optimal) therapy at low (< £15,000 per QALY) willingness-to-pay thresholds. At the thresholds (£20,000–30,000 per QALY) used by NICE, combined CBT and sertraline is the optimal therapy.

TABLE 62 Cost-effectiveness of therapy: children and adolescents

Intervention	Total costs (£)	Total QALYs	NMB (£20,000) (£)	Lower 95th percentile (£)	Upper 95th percentile (£)	NMB (£30,000) (£)
BT	6762	3.254	58,325	54,212	62,524	90,868
Clomipramine	5515	3.280	60,087	55,775	64,407	92,888
SSRIs	5394	3.311	60,828	56,298	65,162	93,934
CBT	6459	3.368	60,905	56,188	64,974	94,586
Sertraline + CBT	6418	3.376	61,107	56,510	65,215	94,869

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

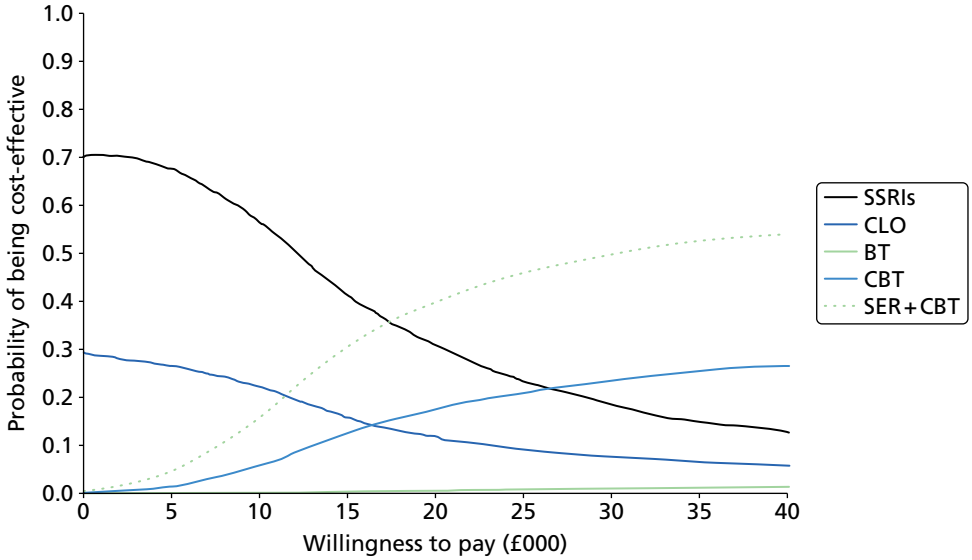


FIGURE 21 Cost-effectiveness acceptability curve: children and adolescents – primary analysis. CLO, clomipramine; SER, sertraline.

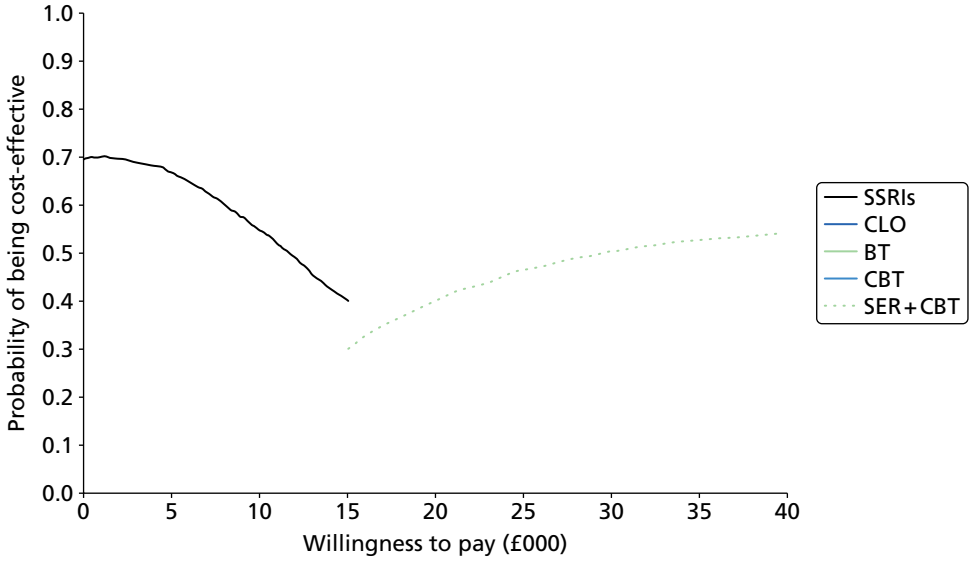


FIGURE 22 Cost-effectiveness acceptability frontier: children and adolescents – primary analysis. CLO, clomipramine; SER, sertraline.

Sensitivity analyses

Full results of all sensitivity analyses are provided in *Appendix 10*. Here, we focus on the three sensitivity analyses that had most impact on the findings of the cost-effectiveness model.

The most cost-effective pharmacotherapy was again strongly dependent on assumptions about outcomes in patients who drop out. If we assume that the outcomes in patients who drop out are fully reflected in analyses of CYBOCS scores in the meta-analysis (i.e. analyses were predominantly intention to treat), then clomipramine, rather than SSRIs, is more likely to be the most cost-effective pharmacotherapy at lower willingness-to pay-thresholds (*Figure 23*) and continues to be more cost-effective than strategies including CBT even at higher willingness-to-pay thresholds.

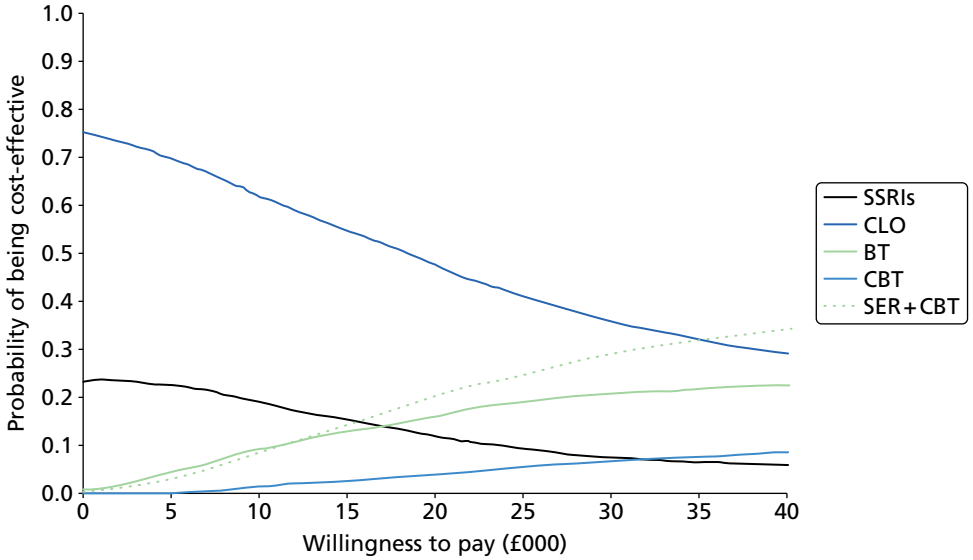


FIGURE 23 Cost-effectiveness acceptability curve: children and adolescents. Effectiveness in patients who drop out. CLO, clomipramine; SER, sertraline.

As with the adult RCTs, the initial cost of psychological therapies is difficult to estimate because the number of contact hours differed greatly across RCTs (see *Table 55*). The impact of this on NHS costs of initial therapy was much greater than the range of daily doses used in pharmacotherapy trials. Therefore, if we assume that all psychological and pharmacological therapies have a cost at the upper end of the range evaluated in RCTs, pharmacotherapies become relatively cheaper and more cost-effective (*Figure 24*). Although psychological therapy (specifically CBT and sertraline) was still estimated to be cost-effective at higher willingness-to-pay thresholds, SSRIs remain the most cost-effective option at the £20,000-per-QALY threshold.

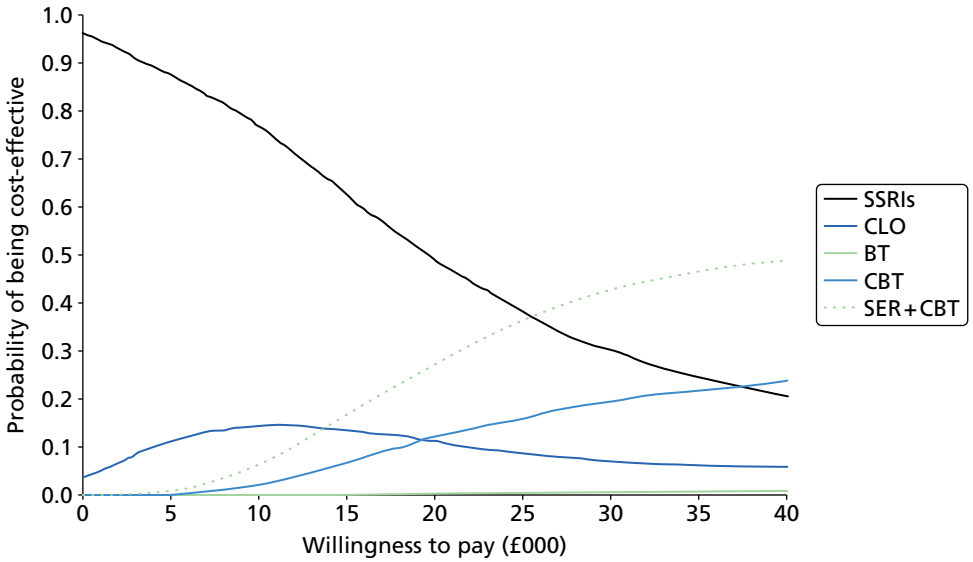


FIGURE 24 Cost-effectiveness acceptability curve: children and adolescents. Maximum cost of initial therapy. CLO, clomipramine; SER, sertraline.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Assumptions about the sustainability of treatment effects observed in RCTs with short follow-up periods (e.g. 12 weeks) are influential on the cost-effectiveness results. Our primary analysis assumes that some of the benefits of more effective therapies (i.e. the psychological therapies, particularly CBT) are sustained beyond the end of the trial, although they gradually diminish as patients who had an initial response relapse. If we were to assume that all differences in intervention costs and benefits are limited to the within-trial period, then SSRIs are predominantly likely to be most cost-effective (*Figure 25*).

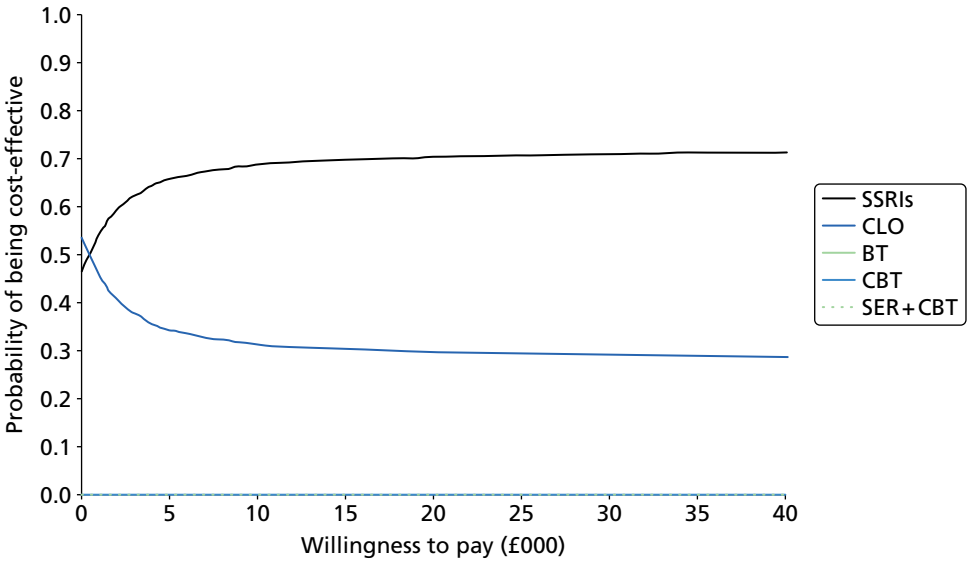


FIGURE 25 Cost-effectiveness acceptability curve: children and adolescents. Costs and benefits limited to the within-trial period. CLO, clomipramine; SER, sertraline.

Chapter 8 Discussion

Principal findings

In this NMA, we compared the effect of pharmacological and psychological interventions for the management of OCD in all age groups. As far as we know, this is the first time that all available interventions for OCD have been compared in a single analysis using mixed evidence (direct and indirect). Previous meta-analyses on this issue had examined only the direct evidence between different interventions and most are now outdated.[120,262–264] More recent meta-analyses comparing the full range of treatment options in depression and anxiety disorders did not focus specifically on OCD and also used the direct comparisons.[265,266] Overall, we included 86 studies reported in 85 papers (64 in adults and 22 in children and adolescents) involving 8611 randomised patients (7306 adults and 1305 children and adolescents). In the total sample, 23 different interventions were tested in 194 arms. Interventions with the most studies were, in adults, clomipramine ($n = 17$), fluvoxamine ($n = 16$) and BT ($n = 15$) and, in children and adolescents, CBT ($n = 9$), fluoxetine ($n = 4$); clomipramine ($n = 4$) and sertraline ($n = 4$).

Clinical effectiveness findings

Results in adults

In total, 54 studies were included in this analysis, involving 6652 randomised patients. All active interventions, apart from venlafaxine and hypericum, had a greater effect than drug placebo on OCD symptom reduction. It should be noted that venlafaxine has not been directly compared with placebo, and the result is based on indirect evidence only.

Regarding the pharmacological interventions, SSRIs as a class had greater effects than placebo (class effect MD –3.49, 95% CrI –5.12 to –1.81) with small differences between them confirming previous meta-analyses using pairwise comparisons only.[263] There was a trend for clomipramine to have a greater effect than SSRIs, but the 95% CrI included the null value. Previous meta-analyses have pointed to a possible superior effect of clomipramine over SSRIs.[120,263] Using the full data set we confirmed this trend, although this was not formally significant. Clomipramine studies, however, were more likely to report per-protocol and not intention-to-treat analyses (see *Table 14*). In our sensitivity analysis, including studies with low risk of bias in the domain 'incomplete outcome assessment', the effect of clomipramine was no longer different from those of other SSRIs (see *Table 22*). Therefore, our analysis cannot confirm the supposed superiority of clomipramine over other SSRIs.

Regarding the psychological interventions, all active psychotherapies had larger effects than drug placebo, with BT and CT having the largest effects, with small differences between them. However, CBT had a smaller effect than both BT and CT (MD –9.11, 95% CrI –13.18 to –4.97 and MD –7.99, 95% CrI –12.97 to –3.01, respectively). Regarding the comparison between psychological interventions and psychological placebo, both BT and CT had greater effects (MD –10.33, 95% CrI–13.38 to –7.29 and MD –9.21, 95% CrI –13.1 to –5.34, respectively) but the effect of CBT was not significantly different from psychological placebo (MD –1.22, 95% CrI –5.54 to 3.03).

It is difficult to explain why patients randomised to BT or CT fared better than those receiving CBT. It is worth noting that in the sensitivity analyses, excluding the studies with high overall attrition, all three psychotherapies had similar effects. In addition, CT has mainly been compared with BT, whereas CBT has been compared with other interventions in a more extensive network of trials. CBT has also been compared directly with several drugs in the same trial. Therefore, the differential effect found for CBT in the full data set should be interpreted with caution.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Regarding the comparison between psychological and pharmacological interventions, both BT and CT had larger effects than SSRIs and clomipramine. The difference in effect between drugs and CBT was smaller and the 95% CrI included the null value for both SSRIs and clomipramine. In a recent meta-analysis using direct data only, Cuijpers *et al.*[265] examined the differential effect of pharmacotherapy and psychotherapy in major depression, dysthymia, panic disorder, social anxiety disorder and OCD. A positive effect for psychotherapy over medications was reported for OCD only. The same finding was reported in a recent meta-analysis of head-to-head comparisons of behavioural psychotherapy versus medications.[267] Our NMA confirms this trend for BT and CT but not for CBT (which is a combination of the two therapies). However, there are two points that need to be taken into account. First, as mentioned, CT has been compared mainly with BT, and in the data used for the analysis, BT had very limited connections with drugs (one direct comparison with clomipramine and one with fluvoxamine). CBT, however, has several direct links with other drugs. Second, a major limitation of psychotherapy trials is that most patients in these trials were on a stable dose of a medication, usually a SSRI. Very few trials excluded patients on medications and these were mainly trials that compared psychological interventions with pharmacological interventions in the same trial (most often these were trials including CBT arms). Therefore, trials that have compared psychological interventions only (e.g. CT vs. BT) have essentially examined the effectiveness of these therapies in patients taking stable doses of antidepressant medications. Although patients were symptomatic and fulfilled the criteria for inclusion in the trials (for example a YBOCS score of ≥ 16), it is not known whether or not the concurrent use of medications could have influenced the results at the end of the study. There is some evidence that continuous use of medications beyond the 12 weeks of the short-term trials may reduce symptoms further.[268] It is also unknown whether or not the effect of a therapy would be different if patients were off medications, because such trials have not been performed. However, placebo-controlled studies that used antipsychotic augmentation of SSRIs in treatment-refractory patients have shown very small effects for 'SSRIs + placebo'; this is against the hypothesis of a delayed effect of SSRIs in symptomatic patients in particular. In any case, the generalisability of these results in patients not taking a stable dose of medication should be made with caution.

Combinations of medications and psychotherapy showed greater effects than drug placebo. The combination of clomipramine with BT was also better than psychological placebo and clomipramine as monotherapy (although this evidence is based on a small number of patients). However, there was no evidence that the combinations were better than psychotherapy as monotherapy. In this respect, we did not confirm the results of a previous direct meta-analysis that the effects of psychotherapy and pharmacotherapy are largely independent and have additive effects.[266]

One of the aims of the NMA is to rank the treatments relative to each other. We have produced ranking tables and rankograms. We would like to emphasise, however, that ranks are based on the calculated MDs and, in that sense, they are considered a supplementary analysis regarding treatment effectiveness. The rankograms in *Figure 8* show the substantial uncertainty surrounding our estimates. In general, we did not achieve more than a 50% probability that any of the treatments were best (and this refers to BT). A more conservative interpretation is that there is a 50% probability that BT is the best treatment but this also means that there is a 50% probability that it is not. Detailed tables in *Appendix 8* present all the rank probabilities.

Results in children

A total of 17 studies were included in the analysis, involving 991 randomised patients. CBT and BT had greater effects than drug placebo. Compared with psychological placebo, both psychotherapies, and in particular CBT, showed a trend for a greater effect, but the 95% CrIs included the null value. These results are in line with those reported in a recent direct meta-analysis for the effectiveness of CBT in paediatric OCD.[269]

Selective serotonin reuptake inhibitors as a class showed a trend for a greater effect than drug placebo, but the 95% CrIs included the null value. Individual SSRIs (fluoxetine and sertraline, but in particular the latter), however, reached marginal statistical significance. Regarding clomipramine, taking into account both the direct and indirect evidence (i.e. the results of the NMA), the 95% CrIs included the null value.

The results of the pairwise analysis were formally statistically significant, whereas the results of one of the sensitivity analyses (excluding studies with completers analyses) showed a greater effect than drug placebo. Taken together, these results confirm that there is a trend for clomipramine to have a greater effect than drug placebo. There is one previous meta-analysis of SSRIs and clomipramine conducted in 2003,[264] but since then most recent trials have included psychological therapies, with the exception of one recent trial that compared CBT both alone and in combination with sertraline.[234] Considering all the evidence, both direct and indirect, our findings point to a possible advantage of some SSRIs and possibly clomipramine in children and adolescents compared with drug placebo, although we do not confirm any superiority for clomipramine as previously reported.[264]

Compared with SSRIs as a class, both psychological therapies (BT and CBT) showed a trend for a greater effect, although the 95% CrIs included the null value. Similar results were found for clomipramine. The combination of sertraline with CBT was associated with the largest effect compared with drug placebo and showed marginal statistical significance compared with sertraline alone, but compared with CBT as monotherapy, the combination had similar effects.

Regarding ranking of treatments, taking into account the limitations mentioned in the discussion of the adult subset, CBT either as monotherapy or combined with sertraline were the best treatments, followed by BT. All sensitivity analyses gave results with similar trends.

Tolerability findings

There is less uncertainty regarding the results of tolerability in all age groups. In adults, clomipramine was clearly less well tolerated. All other drugs and therapies were not significantly different from placebo. There was no evidence that combination treatments fared worse than monotherapies, although the data are limited for these comparisons. In children and adolescents, clomipramine also showed a trend for worse tolerability. The same was observed for BT, although this result is based on a very limited number of patients and should be interpreted with caution. SSRIs in children and adolescents showed very good tolerability compared with placebo, and CBT had excellent acceptability either alone or in combination with sertraline.

Cost-effectiveness findings

Main findings

The selection of the most cost-effective therapy for adults or children and adolescents with OCD is not clear-cut. In both populations, the most effective therapies were also among the more expensive therapies; there is a trade-off between the higher upfront costs of psychological therapies and the potential for them to improve outcomes and reduce long-term costs of care.

In the primary economic evaluation in adults, psychological therapies, specifically CT and BT, had the highest probability of being most cost-effective at the conventional NICE thresholds (£20,000 to £30,000 per QALY) and above. Perhaps surprisingly, CBT had a low probability of being cost-effective in adults at all cost-effectiveness thresholds. This was predominantly a result of the substantially lower estimated effect size of CBT, compared with CT and BT, and the higher intensity and, therefore, higher cost of CBT evaluated in RCTs. However, the difference in estimated effectiveness between CBT and other psychotherapies was very sensitive to the inclusion of RCTs that used waitlist controls and in which, therefore, participants were unblinded. At lower willingness-to-pay thresholds (< £10,000 per QALY), pharmacotherapy, particularly clomipramine and venlafaxine, had a relatively high probability of being cost-effective. The cost-effectiveness of venlafaxine is particularly sensitive to the low dropout rate estimated from just two trials, which might be viewed as an anomaly. It should be noted that the dropout rate in these two trials (< 10%) is well below the average dropout rate of venlafaxine trials in depression or other anxiety disorders (usually > 20%). The finding

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

that clomipramine is more likely to be more cost-effective than SSRIs should be considered in conjunction with the known toxicity and side-effect profile of clomipramine.

There is substantially less trial evidence in children and adolescents. Of the five interventions compared, SSRIs had the highest probability of being most cost-effective at lower willingness-to-pay thresholds (< £15,000 per QALY). At the conventional NICE thresholds (£20,000 to £30,000 per QALY) and above, CBT or CBT combined with a SSRI were more likely to be cost-effective.

The results of the economic evaluation reflect considerable uncertainty from many different sources. Although several thousand patients with OCD have participated in RCTs, the numbers randomised to each intervention varied considerably and were often small. The economic model is dependent on the validity of the NMA, which itself depends on the transitivity of interventions and methods between RCTs. Furthermore, we have demonstrated that cost-effectiveness results are sensitive to assumptions about the sustainability of treatment effects beyond the initial treatment period. Clinicians and policy-makers should bear this uncertainty in mind when developing treatment guidelines and prioritising future research.

Comparisons with previous studies

It is not possible to directly compare our results with those of the previous cost-effectiveness models. In developing NICE clinical guidelines for the treatment of OCD,[118] researchers developed a crude model for comparing the cost-per-responder of SSRIs, CBT and combination therapy. They concluded that CBT alone is dominated by SSRIs and combination (CBT and SSRI) therapy and that combination therapy is likely to be a cost-effective option. Other work underpinning the NICE appraisal of computerised CBT compared three interventions (computer-guided BT, clinician-led BT or relaxation) and concluded that, subject to substantial uncertainties, therapist-led CBT is cost-effective compared with relaxation, and that computerised CBT has the potential to be cost-effective, depending on the licence fees for health-care commissioners.[248] Our work is different in that it draws on a network of evidence, stratifies analysis by adults and children and adolescents and provides a probabilistic analysis of treatment class options at various thresholds of willingness to pay for a QALY.

Main limitations

Main limitations: clinical effectiveness

(a) In our NMA, we excluded studies that had not used the YBOCS to avoid using standardised MDs instead of the MDs. There were only a small number of older trials with small sample sizes that had not used the YBOCS. This decision was made in light of the well-documented methodological[270] and interpretational difficulties[142] associated with the standardised MD.
(b) There were few studies ($n = 5$) that had used different fixed doses of the same drug in order to investigate the possibility of a dose–response association. Owing to the limited data in the NMA, we were unable to treat these dosing schemes as different nodes in the network and, therefore, we merged these treatment groups into one.
(c) There is meta-epidemiological evidence that suggests that blinding is crucial to avoid bias for subjective and semi-objective outcome measures.[271] Blinding in psychotherapy trials is difficult owing to the nature of intervention, but in the case of waitlist controls, it is impossible. Therefore, trials that have used waitlist controls (e.g. most of the CBT trials in children and adolescent) are more prone to bias owing to a lack of blinding and this may have resulted in overestimation of the effect of psychotherapies.[272]
(d) We did not run additional tests, such as loop-specific examinations of inconsistency or a node-splitting approach, to examine inconsistency, as suggested by some authors.[149] However, given the good fit we have observed in all our analyses we think that this was not necessary.
(e) Given that most trials were of a short-term duration rarely exceeding 12 weeks, generalisation of the results beyond this point should be made with caution.

Main limitations: cost-effectiveness

There has been very little research on the cost-effectiveness of therapy for OCD. Our work addresses a broader question than two previous cost-effectiveness models by estimating cost per QALY gained and by comparing behavioural therapies and pharmacotherapies. We use a more comprehensive range of evidence, based on a systematic review and a NMA of RCTs, to inform model estimates of effect size and allowing a full probabilistic assessment of the relative cost-effectiveness of treatment strategies. We also used rapid literature reviews to identify recent evidence on the life course of OCD symptoms[91,97] and utility scores.[114]

Any cost-effectiveness model is only as valid as the structural assumptions and evidence that underlie it.[273] We conducted the analysis from a NHS perspective, although it would be preferable to broaden it to also include Personal Social Services costs (the perspective recommended by NICE) and broader societal costs to patients, carers, employers and others. We could not identify any relevant data on the NHS costs of routine care of patients with OCD, and including costs to other sectors of society would have been even more speculative. However, it seems likely that if these costs had been available, the therapies that are initially expensive, but also effective (i.e. psychological therapies), would become more cost-effective, as reducing symptoms will reduce the impacts of OCD on wider society. Our model assesses the cost-effectiveness of initial therapy only in patients with moderate or severe OCD symptoms, whereas clinical guidelines need to consider appropriate treatment options for milder symptoms and where initial therapy has failed. Without individual patient data from RCTs, it is difficult to judge how the (cost-)effectiveness of therapy varies by initial symptom severity or to appropriately account for potential correlations between parameters, such as effectiveness and dropout rates, in probabilistic sensitivity analyses. Furthermore, RCTs often collect little detail on previous or concurrent treatment used by trial participants. Therefore, for example, an intervention described in a RCT as 'CBT' may in fact include patients who have failed or are still being prescribed various types of pharmacotherapies. In fact, our review showed that most of the patients who were included in RCTs of psychological interventions were also taking stable doses of medications.

We conducted our economic evaluation at the class level, combining different SSRIs and different intensities of psychological therapies. In part, this decision reflects the similarity of effect sizes within drug classes and also the scarcity of data for conducting sub-class analysis. However, there are important economic implications at the sub-class level. For example, although the average cost of SSRIs used in the model was higher than clomipramine, a number of SSRIs (e.g. fluoxetine, paroxetine, sertraline or citalopram) are cheaper and potentially more cost-effective. However, this was not confirmed from our sensitivity analysis, assuming that SSRI medication costs were equivalent to the cheapest SSRI rather than the class average cost. Likewise, psychological therapy might be delivered with different intensity (e.g. brief or stepped care) and in different formats (group/individual, face to face/telephone/computer) tailored to individual patients which may have important implications for cost-effectiveness.

Our model is based on relatively weak evidence on costs and outcomes in several areas, particularly for children and adolescents. The sustainability of treatment effects beyond the typical 12-week follow-up period observed in trials is particularly important. We relied on longitudinal data on response and relapse from cohort studies following relatively small numbers of patients over a 3- to 5-year period.[91,97] Long-term follow-up of trial participants, particularly those in trials comparing pharmacotherapy and psychological therapy, are essential to inform the cost-effectiveness of treatment options. We linked symptoms scores (YBOCS) to response rates (full, partial or none) in order to estimate utilities via a Markov model. This indirect approach would not have been necessary if utility scores, for instance the EQ-5D,[274] were collected in RCTs or if robust mapping functions had been developed between the YBOCS and EQ-5D.[275] The estimation of patient outcomes was further complicated by the absence of information on utilities in children and adolescents and the widely differing definitions of full and partial response used in the OCD literature.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Our conclusions are sensitive to structural assumptions about patients who drop out of therapy. One example of this is the cost-effectiveness of venlafaxine at low willingness-to-pay thresholds in adults. The prominence of venlafaxine in our results is surprising, given the low effect size estimated in the NMA and the fact that venlafaxine is explicitly not recommended in NICE OCD clinical guidelines[118] and is caused by the low apparent dropout rate for venlafaxine estimated in two trials. If the majority of RCTs report 'intention to treat' analyses where dropouts are already included in the CYBOCS/YBOCS effect size estimate, then our primary analysis effectively 'double-weights' poorer outcomes in patients who drop out, thereby unfairly favouring interventions such as venlafaxine with low dropout rates. This underlines the importance of considering the cost-effectiveness findings alongside other evidence on the toxicity and side effects of interventions.

Chapter 9 Conclusions

Conclusions: clinical effectiveness

The results of this review support a range of effective options, both pharmacological and psychological, for the management of OCD in all age groups. Regarding the relative effectiveness of treatments, our review highlighted the great uncertainty surrounding the published randomised evidence. Although specific psychological interventions were found to have greater effects than medications, there are important methodological limitations that need to be taken into account in future research before a final decision can be made.

Relevance of the findings to national guidelines: clinical effectiveness

The NICE guideline[118] recommends a 'stepped care' approach towards managing OCD in both adults and young people. They recommend that those with mild symptoms should be offered low-intensity (< 10 sessions or group treatment) CBT including ERP. The evidence we found did not stratify the analyses in accordance with the severity of the illness so we could not justify this approach from the empirical data, although it might appear sensible from a clinical perspective.

For adults with moderate symptoms, the NICE guideline recommends either SSRIs or high-intensity CBT (including ERP). Our review finds evidence to support both these interventions. As discussed above, there was some indication that behavioural approaches were more effective than SSRIs but we cannot be certain of this conclusion. However, the combination of SSRIs and BT or CBT seemed an acceptable treatment, although we do not have sufficient evidence to suggest that the combination of medication and psychotherapy is better than psychotherapy alone. This is also relevant to the recommendation that for those with severe illness, the combination of SSRI and BT is used.

Our review supports the NICE decision to recommend SSRIs rather than clomipramine as the first-line antidepressant. Although clomipramine had a slightly larger effect size, we did not have any convincing statistical evidence to suggest that clomipramine is more effective. Given the increased tolerability of SSRIs, our review supports the recommendation that these should be used as a first-line treatment.

In conclusion, the evidence broadly supports the approach of the NICE guideline. At present, the trial evidence on effectiveness does not justify a stepped approach towards the recommendations, although, of course, other considerations would also have informed the NICE guideline group. The evidence suggested that behavioural interventions could be more effective than SSRI medication, but there is a great deal of uncertainty and we cannot confidently make that recommendation on the basis of the current evidence of clinical effectiveness.

Research implications: clinical effectiveness

- More RCTs are needed comparing medications with psychotherapies in a single trial.
- Issues of blinding in psychotherapy trials should be taken into account. The possibility of comparing combinations of mixed arms of the following types: 'drug + psychological placebo' and 'drug placebo + psychotherapy' should be better explored. In the reviewed literature, there was just one study that combined CBT with drug placebo. More studies of this design are needed.
- The use of the waitlist as a control in psychotherapy trials should be re-examined and perhaps replaced with psychological placebo.
- Psychotherapy trials should exclude patients taking concurrent medications during the period of the trial.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Conclusions: cost-effectiveness

Relevance of the findings to national guidelines: cost-effectiveness

In adults with OCD with moderate functional impairment, current NICE guidance recommends either a course of a SSRI or more intensive CBT (including ERP) with > 10 therapist hours per patient, noting that these treatments appear to be comparably efficacious. The findings of our cost-effectiveness model have important implications for guidance.

(a) There is considerable uncertainty in the economic model; at current NICE thresholds (£20,000–30,000 per QALY), CrIs of all therapies overlap and, therefore, clinical guidance is necessarily a difficult judgement based on the balance of probabilities of costs, outcomes and risks of side effects and withdrawal.
(b) The choice of the most cost-effective psychological therapy depends, to a large extent, on the subset of RCTs informing effect size estimates. If all RCTs are included, the considerably larger effect sizes of CT and BT (compared with CBT) make them most likely to be cost-effective options at current NICE thresholds. If trials with high risk of bias owing to 'incomplete outcome assessment' are excluded, no CT trials remain and the difference in effect size between BT and CBT is much smaller (see *Appendix 10*). Excluding trials that use waitlist controls also reduces the differences in effect size between these psychological therapies.
(c) The choice of the most cost-effective pharmacological therapy also depends, to a large extent, on the subset of RCTs informing effect size estimates. In our primary analysis, clomipramine and venlafaxine are slightly more cost-effective than SSRIs because of somewhat greater effectiveness (clomipramine) or a lower dropout rate (venlafaxine). In sensitivity analyses, excluding trials with high risk of bias owing to 'incomplete outcome assessment' and assuming patients who drop out are incorporated in the intention-to-treat effect size estimates, SSRIs become relatively more cost-effective.
(d) Therefore, current NICE recommendations [SSRI or intensive CBT (including ERP)] are not inconsistent with the evidence synthesised in this report, particularly if the focus is placed on trials with complete outcome assessment. Our analysis suggests that CBT might be slightly more efficacious that SSRIs but is initially more expensive. There is a fine balance between the relative costs and effects of SSRIs and CBT. Tailoring the format and intensity of CBT might make it more cost-effective.
(e) If a SSRI is used, the choice of drug has important economic implications. Our analysis suggests that the within-class treatment effect is similar, but current prices vary substantially. NICE guidance does not currently distinguish between higher and lower cost SSRIs, but given that prescribing is recommended for extended periods (12 months and beyond), a focus on the cheaper SSRIs (e.g. fluoxetine, paroxetine, sertraline and citalopram) seems prudent.

In children and adolescents with OCD with moderate to severe functional impairment, NICE guidance recommends CBT (including ERP), involving family or carers and adapted to suit the developmental age of the child. Group or individual CBT should be offered based on patient and family preferences.

(a) Based on the limited evidence available, our findings suggest that this is a reasonable initial treatment strategy. Again, there is considerable uncertainty in the economic model, which makes it impossible to definitively identify a single most cost-effective treatment strategy.
(b) CBT is among the most effective treatment options, and the higher initial costs of CBT compared with SSRIs are counterbalanced by better outcomes and lower long-term costs of care at current NICE willingness-to-pay thresholds. Given the risk of withdrawal and side effects in this young population, a strategy of reserving SSRI and combined SSRI and CBT therapy to children and adolescents who have not responded to a full trial of CBT and who have had a multidisciplinary review seems appropriate.
(c) As with adult patients, considering ways to tailor the format and intensity of CBT and, if SSRIs are used, selecting less expensive drugs licensed in children (e.g. sertraline) may improve the cost-effectiveness of care.

Research implications: cost-effectiveness

There are a number of areas of further research that would help policy-makers draw firmer conclusions about the most cost-effective interventions for OCD:

(a) Observational research, most feasibly retrospective cohort studies based on routinely collected and electronically collated primary care records, could provide evidence, currently absent, on the costs of NHS care for patients with a diagnosis of OCD, stratified by symptom severity.
(b) Cross-sectional surveys of patients with OCD and their families should be conducted to provide new information on the wider societal cost of OCD and might also be used to provide additional evidence on the quality-of-life (utility) impact of OCD. These studies are particularly needed in children and adolescents, where there is no strong evidence currently.
(c) Existing RCT evidence could be further used in individual patient data meta-analyses to provide a fuller picture about any association between symptom severity and (cost) effectiveness of pharmacological and psychological therapies.
(d) Long-term follow-up (i.e. at 12, 24 and 36 months) of published and ongoing high-quality RCTs, particularly those directly comparing psychological and pharmacological therapies, would be very valuable in establishing whether or not the initial high cost of psychological therapies is justified by sustained treatment effects.
(e) New RCTs are needed to evaluate different formats and intensities of psychological therapies in direct comparison with pharmacotherapy and should include data on costs and quality of life (utilities) of patients over the course of the trial follow-up.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Acknowledgements

We would like to thank the following people for their assistance in the production of this report:

- Petros Skapinakis would like to acknowledge his main affiliation with the Department of Psychiatry, University of Ioannina School of Medicine.
- Lazaros Belbasis and Vanesa Bellou, School of Medicine, University of Ioannina, Ioannina, Greece, for their assistance in data extraction.
- Sarah Dawson and the team at the CCDAN, University of Bristol, Bristol, UK, for their help in the search for files.
- Joel Rose, OCD Action UK, for his comments on the final draft.

Contributions of authors

Petros Skapinakis led the review, was responsible for managing the project and drafted the report.

Deborah Caldwell provided statistical support, undertook the network meta-analyses with **Peter Bryden** and reviewed the final report.

William Hollingworth oversaw the economic modelling, drafted the economic synthesis and reviewed the final report.

Peter Bryden conducted the economic modelling, helped in the drafting of the economic synthesis, and undertook the NMA with Deborah Caldwell.

Naomi Fineberg provided expert clinical advice (psychopharmacology), made critical comments that helped in the interpretation of results, helped in writing sections of the report and reviewed the final report.

Paul Salkovskis provided expert clinical advice (psychotherapy) and reviewed the final report.

Nicky Welton provided statistical advice and helped with the statistical modelling.

Helen Baxter contributed to the data extraction and the systematic review.

David Kessler provided clinical advice, helped to write sections of the report and reviewed the final report.

Rachel Churchill provided advice for the systematic review and methodology, and reviewed the final report.

Glyn Lewis provided advice on the methodology and systematic review, made critical comments that helped in the interpretation of the results, helped in writing sections of the report and reviewed the final report.

All authors read and commented on draft versions of the report.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Publications

Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, *et al*. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis [published online ahead of print June 15 2016]. *Lancet Psychiatry* 2016. http://dx.doi.org/10.1016/S2215-0366(16)30069-4.

Data sharing statement

All data used for the analysis are included in tables in the main report (see *Chapters 5* and *6*) and detailed data extraction can be found in the Appendices.

References

1. Berrios GE. Our knowledge of anancasm (psychic compulsive states). *Hist Psychiatry* 2003;**14**:113–28. http://dx.doi.org/10.1177/0957154X03014001007
2. Berrios GE. *The History of Mental Symptoms: Descriptive Psychopathology Since the Nineteenth Century*. Cambridge: Cambridge University Press; 1995.
3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 1st edn. Washington, DC: American Psychiatric Association; 1952.
4. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 2nd edn. Washington, DC: American Psychiatric Association; 1968.
5. World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research*. Geneva: World Health Organization; 1993.
6. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th edn. Washington, DC: American Psychiatric Association; 2000.
7. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th edn. Washington DC: American Psychiatric Association; 2013.
8. Leckman JF, Denys D, Simpson HB, Mataix-Cols D, Hollander E, Saxena S, *et al.* Obsessive–compulsive disorder: a review of the diagnostic criteria and possible subtypes and dimensional specifiers for DSM-V. *Depress Anxiety* 2010;**27**:507–27. http://dx.doi.org/10.1002/da.20669
9. Khanna S, Kaliaperumal VG, Channabasavanna SM. Clusters of obsessive–compulsive phenomena in obsessive–compulsive disorder. *Br J Psychiatry* 1990;**156**:51–4. http://dx.doi.org/10.1192/bjp.156.1.51
10. Rasmussen SA, Eisen JL. Epidemiology of obsessive compulsive disorder. *J Clin Psychiatry* 1990;**51**:10–13.
11. Foa EB, Kozak MJ, Goodman WK, Hollander E, Jenike MA, Rasmussen SA. DSM-IV field trial: obsessive–compulsive disorder. *Am J Psychiatry* 1995;**152**:90–6.
12. Bloch MH, Landeros-Weisenberger A, Rosario MC, Pittenger C, Leckman JF. Meta-analysis of the symptom structure of obsessive–compulsive disorder. *Am J Psychiatry* 2008;**165**:1532–42. http://dx.doi.org/10.1176/appi.ajp.2008.08020320
13. Mataix-Cols D, Rauch SL, Baer L, Eisen JL, Shera DM, Goodman WK, *et al.* Symptom stability in adult obsessive–compulsive disorder: data from a naturalistic 2-year follow-up study. *Am J Psychiatry* 2002;**159**:263–8. http://dx.doi.org/10.1176/appi.ajp.159.2.263
14. de Mathis MA, Alvarenga PD, Funaro G, Torresan RC, Moraes I, Torres AR, *et al.* Gender differences in obsessive–compulsive disorder: a literature review. *Rev Bras Psiquiatr* 2011;**33**:390–9. http://dx.doi.org/10.1590/S1516-44462011000400014
15. Lensi P, Cassano GB, Correddu G, Ravagli S, Kunovac JL, Akiskal HS. Obsessive–compulsive disorder. Familial-developmental history, symptomatology, comorbidity and course with special reference to gender-related differences. *Br J Psychiatry* 1996;**169**:101–17. http://dx.doi.org/10.1192/bjp.169.1.101
16. Labad J, Menchon JM, Alonso P, Segalas C, Jimenez S, Jaurrieta N, *et al.* Gender differences in obsessive–compulsive symptom dimensions. *Depress Anxiety* 2008;**25**:832–8. http://dx.doi.org/10.1002/da.20332

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

17. Masi G, Millepiedi S, Perugi G, Pfanner C, Berloffa S, Pari C, *et al.* A naturalistic exploratory study of the impact of demographic, phenotypic and comorbid features in pediatric obsessive–compulsive disorder. *Psychopathology* 2010;**43**:69–78. http://dx.doi.org/10.1159/000274175

18. Torresan RC, Ramos-Cerqueira AT, Shavitt RG, do Rosário MC, de Mathis MA, Miguel EC, *et al.* Symptom dimensions, clinical course and comorbidity in men and women with obsessive–compulsive disorder. *Psychiatry Res* 2013;**209**:186–95. http://dx.doi.org/10.1016/j.psychres.2012.12.006

19. Fontenelle LF, Mendlowicz MV, Versiani M. The descriptive epidemiology of obsessive–compulsive disorder. *Prog Neuropsychopharmacol Biol Psychiatry* 2006;**30**:327–37. http://dx.doi.org/10.1016/j.pnpbp.2005.11.001

20. Geller DA, Biederman J, Faraone S, Agranat A, Cradock K, Hagermoser L, *et al.* Developmental aspects of obsessive compulsive disorder: findings in children, adolescents, and adults. *J Nerv Ment Dis* 2001;**189**:471–7. http://dx.doi.org/10.1097/00005053-200107000-00009

21. Rasmussen S, Eisen J. The Epidemiology and Clinical Features of Obsessive–Compulsive Disorder. In Jenike MA, Baer L, Minichiello WE, editors. *Obsessive–Compulsive Disorders: Practical Management*. New York, NY: Mosby; 1998. pp. 12–43.

22. Swedo SE, Rapoport JL, Leonard H, Lenane M, Cheslow D. Obsessive–compulsive disorder in children and adolescents. Clinical phenomenology of 70 consecutive cases. *Arch Gen Psychiatry* 1989;**46**:335–41. http://dx.doi.org/10.1001/archpsyc.1989.01810040041007

23. March JS, Leonard HL. Obsessive–compulsive disorder in children and adolescents: a review of the past 10 years. *J Am Acad Child Adolesc Psychiatry* 1996;**35**:1265–73. http://dx.doi.org/10.1097/00004583-199610000-00012

24. Grabill K, Merlo L, Duke D, Harford KL, Keeley ML, Geffken GR, *et al.* Assessment of obsessive–compulsive disorder: a review. *J Anxiety Disord* 2008;**22**:1–17. http://dx.doi.org/10.1016/j.janxdis.2007.01.012

25. Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann RL, Hill CL, *et al.* The Yale–Brown Obsessive Compulsive Scale. I. Development, use, and reliability. *Arch Gen Psychiatry* 1989;**46**:1006–11. http://dx.doi.org/10.1001/archpsyc.1989.01810110048007

26. Steketee G, Frost R, Bogart K. The Yale–Brown Obsessive–Compulsive Scale: interview versus self-report. *Behav Res Ther* 1996;**34**:675–84. http://dx.doi.org/10.1016/0005-7967(96)00036-8

27. Storch EA, Rasmussen SA, Price LH, Larson MJ, Murphy TK, Goodman WK. Development and psychometric evaluation of the Yale–Brown Obsessive–Compulsive Scale, 2nd edn. *Psychol Assess* 2010;**22**:223–32. http://dx.doi.org/10.1037/a0018492

28. Scahill L, Riddle MA, McSwiggin-Hardin M, Ort SI, King RA, Goodman WK, *et al.* Children's Yale–Brown Obsessive–Compulsive Scale: reliability and validity. *J Am Acad Child Adolesc Psychiatry* 1997;**36**:844–52. http://dx.doi.org/10.1097/00004583-199706000-00023

29. Anholt GE, van Oppen P, Cath DC, Smit JH, den Boer JA, Verbraak MJ, *et al.* The Yale–Brown obsessive–compulsive scale: factor structure of a large sample. *Front Psychiatry* 2010;**1**:18. http://dx.doi.org/10.3389/fpsyt.2010.00018

30. Fineberg NA, Chamberlain SR, Hollander E, Boulougouris V, Robbins TW. Translational approaches to obsessive–compulsive disorder: from animal models to clinical treatment. *Br J Pharmacol* 2011;**164**:1044–61. http://dx.doi.org/10.1111/j.1476-5381.2011.01422.x

31. Pauls DL, Alsobrook JP, Goodman W, Rasmussen S, Leckman JF. A family study of obsessive–compulsive disorder. *Am J Psychiatry* 1995;**152**:76–84. http://dx.doi.org/10.1176/ajp.152.1.76

32. Nestadt G, Samuels J, Riddle M, Bienvenu OJ, Liang KY, LaBuda M, *et al.* A family study of obsessive–compulsive disorder. *Arch Gen Psychiatry* 2000;**57**:358–63. http://dx.doi.org/10.1001/archpsyc.57.4.358

33. Pauls DL, Abramovitch A, Rauch SL, Geller DA. Obsessive–compulsive disorder: an integrative genetic and neurobiological perspective. *Nat Rev Neurosci* 2014;**15**:410–24. http://dx.doi.org/10.1038/nrn3746

34. Hanna GL, Himle JA, Curtis GC, Gillespie BW. A family study of obsessive–compulsive disorder with pediatric probands. *Am J Med Genet B Neuropsychiatr Genet* 2005;**134B**:13–19. http://dx.doi.org/10.1002/ajmg.b.30138

35. do Rosario-Campos MC, Leckman JF, Curi M, Quatrano S, Katsovitch L, Miguel EC, *et al.* A family study of early-onset obsessive–compulsive disorder. *Am J Med Genet B Neuropsychiatr Genet* 2005;**136B**:92–7. http://dx.doi.org/10.1002/ajmg.b.30149

36. van Grootheest DS, Cath DC, Beekman AT, Boomsma DI. Twin studies on obsessive–compulsive disorder: a review. *Twin Res Hum Genet* 2005;**8**:450–8. http://dx.doi.org/10.1375/twin.8.5.450

37. Taylor S. Etiology of obsessions and compulsions: a meta-analysis and narrative review of twin studies. *Clin Psychol Rev* 2011;**31**:1361–72. http://dx.doi.org/10.1016/j.cpr.2011.09.008

38. Milad MR, Rauch SL. Obsessive–compulsive disorder: beyond segregated cortico-striatal pathways. *Trends Cogn Sci* 2012;**16**:43–51. http://dx.doi.org/10.1016/j.tics.2011.11.003

39. Ahmari SE, Spellman T, Douglass NL, Kheirbek MA, Simpson HB, Deisseroth K, *et al.* Repeated cortico-striatal stimulation generates persistent OCD-like behavior. *Science* 2013;**340**:1234–9. http://dx.doi.org/10.1126/science.1234733

40. Salkovskis PM. Obsessional-compulsive problems: a cognitive–behavioural analysis. *Behav Res Ther* 1985;**23**:571–83. http://dx.doi.org/10.1016/0005-7967(85)90105-6

41. Rachman S. A cognitive theory of obsessions. *Behav Res Ther* 1997;**35**:793–802. http://dx.doi.org/10.1016/S0005-7967(97)00040-5

42. Torres AR, Lima MCP. Epidemiology of obsessive–compulsive disorder: a review. *Rev Bras Psiquiatr* 2005;**27**:237–42. http://dx.doi.org/10.1590/S1516-44462005000300015

43. Rudin E. Beitrag zur frage der zwangskrankheit insbesondere ihrere editaren beziechungen. *Arch Psychiatr Nervenkr* 1953;**191**:14–54. http://dx.doi.org/10.1007/BF00345572

44. Brunetti PM. A prevalence survey of mental disorders in a rural commune in Vaucluse. *Acta Psychiatr Scand* 1964;**40**:323–58. http://dx.doi.org/10.1111/j.1600-0447.1964.tb05758.x

45. Robins LN, Helzer JE, Weissman MM, Orvaschel H, Gruenberg E, Burke JD, *et al.* Lifetime prevalence of specific psychiatric disorders in three sites. *Arch Gen Psychiatry* 1984;**41**:949–58. http://dx.doi.org/10.1001/archpsyc.1984.01790210031005

46. Karno M, Golding JM, Sorenson SB, Burnam MA. The epidemiology of obsessive–compulsive disorder in five US communities. *Arch Gen Psychiatry* 1988;**45**:1094–9. http://dx.doi.org/10.1001/archpsyc.1988.01800360042006

47. Anthony JC, Folstein M, Romanoski AJ, Von Korff MR, Nestadt GR, Chahal R, *et al.* Comparison of the lay Diagnostic Interview Schedule and a standardized psychiatric diagnosis. Experience in eastern Baltimore. *Arch Gen Psychiatry* 1985;**42**:667–75. http://dx.doi.org/10.1001/archpsyc.1985.01790300029004

48. Nelson E, Rice J. Stability of diagnosis of obsessive–compulsive disorder in the Epidemiologic Catchment Area study. *Am J Psychiatry* 1997;**154**:826–31. http://dx.doi.org/10.1176/ajp.154.6.826

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

49. Wittchen HU, Essau CA, von Zerssen D, Krieg JC, Zaudig M. Lifetime and 6-month prevalence of mental disorders in the Munich Follow-Up Study. *Eur Arch Psychiatry Clin Neurosci* 1992;**241**:247–58. http://dx.doi.org/10.1007/BF02190261

50. Bijl RV, Ravelli A, van Zessen G. Prevalence of psychiatric disorder in the general population: results of The Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Soc Psychiatry Psychiatr Epidemiol* 1998;**33**:587–95. http://dx.doi.org/10.1007/s001270050098

51. Stein MB, Forde DR, Anderson G, Walker JR. Obsessive–compulsive disorder in the community: an epidemiologic survey with clinical reappraisal. *Am J Psychiatry* 1997;**154**:1120–6. http://dx.doi.org/10.1176/ajp.154.8.1120

52. Torres AR, Prince MJ, Bebbington PE, Bhugra D, Brugha TS, Farrell M, *et al.* Obsessive–compulsive disorder: prevalence, comorbidity, impact, and help-seeking in the British National Psychiatric Morbidity Survey of 2000. *Am J Psychiatry* 2006;**163**:1978–85. http://dx.doi.org/10.1176/ajp.2006.163.11.1978

53. Faravelli C, Abrardi L, Bartolozzi D, Cecchi C, Cosci F, D'Adamo D, *et al.* The Sesto Fiorentino study: background, methods and preliminary results. Lifetime prevalence of psychiatric disorders in an Italian community sample using clinical interviewers. *Psychother Psychosom* 2004;**73**:216–25. http://dx.doi.org/10.1159/000077740

54. Skapinakis P, Bellos S, Koupidis S, Grammatikopoulos I, Theodorakis PN, Mavreas V. Prevalence and sociodemographic associations of common mental disorders in a nationally representative sample of the general population of Greece. *BMC Psychiatry* 2013;**13**:163. http://dx.doi.org/10.1186/1471-244X-13-163

55. Heyman I, Fombonne E, Simmons H, Ford T, Meltzer H, Goodman R. Prevalence of obsessive–compulsive disorder in the British nationwide survey of child mental health. *Br J Psychiatry* 2001;**179**:324–9. http://dx.doi.org/10.1192/bjp.179.4.324

56. Costello EJ, Angold A, Burns BJ, Stangl DK, Tweed DL, Erkanli A, *et al.* The Great Smoky Mountains Study of Youth. Goals, design, methods, and the prevalence of DSM-III-R disorders. *Arch Gen Psychiatry* 1996;**53**:1129–36. http://dx.doi.org/10.1001/archpsyc.1996.01830120067012

57. Verhulst FC, van der Ende J, Ferdinand RF, Kasius MC. The prevalence of DSM-III-R diagnoses in a national sample of Dutch adolescents. *Arch Gen Psychiatry* 1997;**54**:329–36. http://dx.doi.org/10.1001/archpsyc.1997.01830160049008

58. Rapoport JL, Inoff-Germain G, Weissman MM, Greenwald S, Narrow WE, Jensen PS, *et al.* Childhood obsessive–compulsive disorder in the NIMH MECA study: parent versus child identification of cases. Methods for the Epidemiology of Child and Adolescent Mental Disorders. *J Anxiety Disord* 2000;**14**:535–48. http://dx.doi.org/10.1016/S0887-6185(00)00048-7

59. Nestadt G, Bienvenu OJ, Cai G, Samuels J, Eaton WW. A family study of obsessive–compulsive disorder. *Arch Gen Psychiatry* 2000;**57**:358–63. http://dx.doi.org/10.1001/archpsyc.57.4.358

60. De Graaf R, Bijl RV, Ravelli A, Smit F, Vollebergh WA. Predictors of first incidence of DSM-III-R psychiatric disorders in the general population: findings from the Netherlands Mental Health Survey and Incidence Study. *Acta Psychiatr Scand* 2002;**106**:303–13. http://dx.doi.org/10.1034/j.1600-0447.2002.01397.x

61. Valleni-Basile LA, Garrison CZ, Waller JL, Addy CL, McKeown RE, Jackson KL, *et al.* Incidence of obsessive–compulsive disorder in a community sample of young adolescents. *J Am Acad Child Adolesc Psychiatry* 1996;**35**:898–906. http://dx.doi.org/10.1097/00004583-199607000-00015

62. Fontenelle LF, Hasler G. The analytical epidemiology of obsessive–compulsive disorder: risk factors and correlates. *Prog Neuropsychopharmacol Biol Psychiatry* 2008;**32**:1–15. http://dx.doi.org/10.1016/j.pnpbp.2007.06.024

63. Flament MF, Whitaker A, Rapoport JL, Davies M, Berg CZ, Kalikow K, *et al.* Obsessive compulsive disorder in adolescence: an epidemiological study. *J Am Acad Child Adolesc Psychiatry* 1988;**27**:764–71. http://dx.doi.org/10.1097/00004583-198811000-00018

64. Canals J, Domenech E, Carbajo G, Blade J. Prevalence of DSM-III-R and ICD-10 psychiatric disorders in a Spanish population of 18-year-olds. *Acta Psychiatr Scand* 1997;**96**:287–94. http://dx.doi.org/10.1111/j.1600-0447.1997.tb10165.x

65. Zohar AH, Ratzoni G, Pauls DL, Apter A, Bleich A, Kron S, *et al.* An epidemiological study of obsessive–compulsive disorder and related disorders in Israeli adolescents. *J Am Acad Child Adolesc Psychiatry* 1992;**31**:1057–61. http://dx.doi.org/10.1097/00004583-199211000-00010

66. LaSalle VH, Cromer KR, Nelson KN, Kazuba D, Justement L, Murphy DL. Diagnostic interview assessed neuropsychiatric disorder comorbidity in 334 individuals with obsessive–compulsive disorder. *Depress Anxiety* 2004;**19**:163–73. http://dx.doi.org/10.1002/da.20009

67. Denys D, Tenney N, van Megen HJ, de Geus F, Westenberg HG. Axis I and II comorbidity in a large sample of patients with obsessive–compulsive disorder. *J Affect Disord* 2004;**80**:155–62. http://dx.doi.org/10.1016/S0165-0327(03)00056-9

68. Pinto A, Mancebo MC, Eisen JL, Pagano ME, Rasmussen SA. The Brown Longitudinal Obsessive Compulsive Study: clinical features and symptoms of the sample at intake. *J Clin Psychiatry* 2006;**67**:703–11. http://dx.doi.org/10.4088/JCP.v67n0503

69. Ruscio AM, Stein DJ, Chiu WT, Kessler RC. The epidemiology of obsessive–compulsive disorder in the National Comorbidity Survey Replication. *Mol Psychiatry* 2010;**15**:53–63. http://dx.doi.org/10.1038/mp.2008.94

70. Perugi G, Akiskal HS, Pfanner C, Presta S, Gemignani A, Milanfranchi A, *et al.* The clinical impact of bipolar and unipolar affective comorbidity on obsessive–compulsive disorder. *J Affect Disord* 1997;**46**:15–23. http://dx.doi.org/10.1016/S0165-0327(97)00075-X

71. Krüger S, Cooke RG, Hasey GM, Jorna T, Persad E. Comorbidity of obsessive compulsive disorder in bipolar disorder. *J Affect Disord* 1995;**34**:117–20. http://dx.doi.org/10.1016/0165-0327(95)00008-B

72. Pallanti S, Grassi G, Sarrecchia ED, Cantisani A, Pellegrini M. Obsessive–compulsive disorder comorbidity: clinical assessment and therapeutic implications. *Front Psychiatry* 2011;**2**:70. http://dx.doi.org/10.3389/fpsyt.2011.00070

73. Henry C, Van den Bulke D, Bellivier F, Etain B, Rouillon F, Leboyer M. Anxiety disorders in 318 bipolar patients: prevalence and impact on illness severity and response to mood stabilizer. *J Clin Psychiatry* 2003;**64**:331–5. http://dx.doi.org/10.4088/JCP.v64n0316

74. Achim AM, Maziade M, Raymond E, Olivier D, Mérette C, Roy MA. How prevalent are anxiety disorders in schizophrenia? A meta-analysis and critical review on a significant association. *Schizophr Bull* 2011;**37**:811–21. http://dx.doi.org/10.1093/schbul/sbp148

75. Sterk B, Lankreijer K, Linszen DH, de Haan L. Obsessive–compulsive symptoms in first episode psychosis and in subjects at ultra high risk for developing psychosis; onset and relationship to psychotic symptoms. *Aust N Z J Psychiatry* 2011;**45**:400–6. http://dx.doi.org/10.3109/00048674.2010.533363

76. Swets M, Dekker J, van Emmerik-van Oortmerssen K, Smid GE, Smit F, de Haan L, *et al.* The obsessive compulsive spectrum in schizophrenia, a meta-analysis and meta-regression exploring prevalence rates. *Schizophr Res* 2014;**152**:458–68. http://dx.doi.org/10.1016/j.schres.2013.10.033

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

77. Eisen JL, Beer DA, Pato MT, Venditto TA, Rasmussen SA. Obsessive–compulsive disorder in patients with schizophrenia or schizoaffective disorder. *Am J Psychiatry* 1997;**154**:271–3. http://dx.doi.org/10.1176/ajp.154.2.271

78. Eisen JL, Rasmussen SA. Obsessive compulsive disorder with psychotic features. *J Clin Psychiatry* 1993;**54**:373–9.

79. Van Dael F, van Os J, de Graaf R, ten Have M, Krabbendam L, Myin-Germeys I. Can obsessions drive you mad? Longitudinal evidence that obsessive–compulsive symptoms worsen the outcome of early psychotic experiences. *Acta Psychiatr Scand* 2011;**123**:136. http://dx.doi.org/10.1111/j.1600-0447.2010.01609.x

80. Coryell W. Obsessive–compulsive disorder and primary unipolar depression. Comparisons of background, family history, course, and mortality. *J Nerv Ment Dis* 1981;**169**:220–4. http://dx.doi.org/10.1097/00005053-198104000-00003

81. Torres AR, Ramos-Cerqueira AT, Ferrão YA, Fontenelle LF, do Rosário MC, Miguel EC. Suicidality in obsessive–compulsive disorder: prevalence and relation to symptom dimensions and comorbid conditions. *J Clin Psychiatry* 2011;**72**:17–26. http://dx.doi.org/10.4088/JCP.09m05651blu

82. Alonso P, Segalàs C, Real E, Pertusa A, Labad J, Jiménez-Murcia S, *et al.* Suicide in patients treated for obsessive–compulsive disorder: a prospective follow-up study. *J Affect Disord* 2010;**124**:300–8. http://dx.doi.org/10.1016/j.jad.2009.12.001

83. ten Have M, de Graaf R, van Dorsselaer S, Verdurmen J, van't Land H, Vollebergh W, *et al.* Incidence and course of suicidal ideation and suicide attempts in the general population. *Can J Psychiatry* 2009;**54**:824–33.

84. Khan A, Leventhal RM, Khan S, Brown WA. Suicide risk in patients with anxiety disorders: a meta-analysis of the FDA database. *J Affect Disord* 2002;**68**:183–90. http://dx.doi.org/10.1016/S0165-0327(01)00354-8

85. Khan A, Warner HA, Brown WA. Symptom reduction and suicide risk in patients treated with placebo in antidepressant clinical trials: an analysis of the Food and Drug Administration database. *Arch Gen Psychiatry* 2000;**57**:311–17. http://dx.doi.org/10.1001/archpsyc.57.4.311

86. Sareen J, Cox BJ, Afifi TO, de Graaf R, Asmundson GJ, ten Have M, *et al.* Anxiety disorders and risk for suicidal ideation and suicide attempts: a population-based longitudinal study of adults. *Arch Gen Psychiatry* 2005;**62**:1249–57. http://dx.doi.org/10.1001/archpsyc.62.11.1249

87. Storch EA, Bussing R, Jacob ML, Nadeau JM, Crawford E, Mutch PJ, *et al.* Frequency and correlates of suicidal ideation in pediatric obsessive–compulsive disorder. *Child Psychiatry Hum Dev* 2015;**46**:75–83. http://dx.doi.org/10.1007/s10578-014-0453-7

88. Pollitt J. Natural history of obsessional states; a study of 150 cases. *Br Med J* 1957;**1**:194–8. http://dx.doi.org/10.1136/bmj.1.5012.194

89. Skoog G, Skoog I. A 40-year follow-up of patients with obsessive–compulsive disorder. *Arch Gen Psychiatry* 1999;**56**:121–7. http://dx.doi.org/10.1001/archpsyc.56.2.121

90. Bloch MH, Green C, Kichuk SA, Dombrowski PA, Wasylink S, Billingslea E, *et al.* Long-term outcome in adults with obsessive–compulsive disorder. *Depress Anxiety* 2013;**30**:716–22. http://dx.doi.org/10.1002/da.22103

91. Eisen JL, Sibrava NJ, Boisseau CL, Mancebo MC, Stout RL, Pinto A, *et al.* Five-year course of obsessive–compulsive disorder: predictors of remission and relapse. *J Clin Psychiatry* 2013;**74**:233–9. http://dx.doi.org/10.4088/JCP.12m07657

92. Catapano F, Perris F, Masella M, Rossano F, Cigliano M, Magliano L, *et al.* Obsessive compulsive disorder: a 3-year prospective follow-up study of patients treated with serotonin reuptake inhibitors OCD follow-up study. *J Psychiatr Res* 2006;**40**:502–10. http://dx.doi.org/10.1016/j.jpsychires.2005.04.010

93. Jakubovski E, Diniz JB, Valerio C, Fossaluza V, Belotto-Silva C, Gorenstein C, *et al.* Clinical predictors of long-term outcome in obsessive–compulsive disorder. *Depress Anxiety* 2013;**30**:763–72. http://dx.doi.org/10.1002/da.22013

94. Dell'Osso B, Benatti B, Buoli M, Altamura AC, Marazziti D, Hollander E, *et al.* The influence of age at onset and duration of illness on long-term outcome in patients with obsessive compulsive disorder: a report from the International College of Obsessive–compulsive Spectrum Disorders. *Eur Neuropsychopharmacol* 2013;**23**:865–71. http://dx.doi.org/10.1016/j.euroneuro.2013.05.004

95. Marcks BA, Weisberg RB, Dyck I, Keller MB. Longitudinal course of obsessive–compulsive disorder in patients with anxiety disorders: a 15-year prospective follow-up study. *Compr Psychiatry* 2011;**52**:670–7. http://dx.doi.org/10.1016/j.comppsych.2011.01.001

96. Stewart SE, Geller DA, Jenike M, Pauls D, Shaw D, Mullin B, *et al.* Long-term outcome of pediatric obsessive–compulsive disorder: a meta-analysis and qualitative review of the literature. *Acta Psychiatr Scand* 2004;**110**:4–13. http://dx.doi.org/10.1111/j.1600-0447.2004.00302.x

97. Mancebo MC, Boisseau CL, Garnaat SL, Eisen JL, Greenberg BD, Sibrava NJ, *et al.* Long-term course of pediatric obsessive–compulsive disorder: 3 years of prospective follow-up. *Compr Psychiatry* 2014;**55**:1498–504. http://dx.doi.org/10.1016/j.comppsych.2014.04.010

98. Bloch MH, Craiglow BG, Landeros-Weisenberger A, Dombrowski PA, Panza KE, Peterson BS, *et al.* Predictors of early adult outcomes in pediatric onset obsessive–compulsive disorder. *Pediatrics* 2009;**124**:1085–93. http://dx.doi.org/10.1542/peds.2009-0015

99. Micali N, Heyman I, Perez M, Hilton K, Nakatani E, Turner C, *et al.* Long-term outcomes of obsessive–compulsive disorder: follow-up of 142 children and adolescents. *Br J Psychiatry* 2010;**197**:128–34. http://dx.doi.org/10.1192/bjp.bp.109.075317

100. Macy AS, Theo JN, Kaufmann SC, Ghazzaoui RB, Pawlowski PA, Fakhry HI, *et al.* Quality of life in obsessive compulsive disorder. *CNS Spectr* 2013;**18**:21–33. http://dx.doi.org/10.1017/S1092852912000697

101. Subramaniam M, Soh P, Vaingankar JA, Picco L, Chong SA. Quality of life in obsessive–compulsive disorder: impact of the disorder and of treatment. *CNS Drugs* 2013;**27**:367–83. http://dx.doi.org/10.1007/s40263-013-0056-z

102. Roberts J, Lenton P, Keetharuth AD, Brazier J. Quality of life impact of mental health conditions in England: results from the adult psychiatric morbidity surveys. *Health Qual Life Outcomes* 2014;**12**:6. http://dx.doi.org/10.1186/1477-7525-12-6

103. Subramaniam M, Abdin E, Vaingankar JA, Chong SA. Obsessive–compulsive disorder: prevalence, correlates, help-seeking and quality of life in a multiracial Asian population. *Soc Psychiatry Psychiatr Epidemiol* 2012;**47**:2035–43. http://dx.doi.org/10.1007/s00127-012-0507-8

104. Cramer V, Torgersen S, Kringlen E. Quality of life and anxiety disorders: a population study. *J Nerv Ment Dis* 2005;**193**:196–202. http://dx.doi.org/10.1097/01.nmd.0000154836.22687.13

105. Rapaport MH, Clary C, Fayyad R, Endicott J. Quality-of-life impairment in depressive and anxiety disorders. *Am J Psychiatry* 2005;**162**:1171–8. http://dx.doi.org/10.1176/appi.ajp.162.6.1171

106. Olatunji BO, Cisler JM, Tolin DF. Quality of life in the anxiety disorders: a meta-analytic review. *Clin Psychol Rev* 2007;**27**:572–81. http://dx.doi.org/10.1016/j.cpr.2007.01.015

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

107. Koran LM, Bromberg D, Hornfeldt CS, Shepski JC, Wang S, Hollander E. Extended-release fluvoxamine and improvements in quality of life in patients with obsessive–compulsive disorder. *Compr Psychiatry* 2010;**51**:373–9. http://dx.doi.org/10.1016/j.comppsych.2009.10.001

108. Lack CW, Storch EA, Keeley ML, Geffken GR, Ricketts ED, Murphy TK, *et al.* Quality of life in children and adolescents with obsessive–compulsive disorder: base rates, parent-child agreement, and clinical correlates. *Soc Psychiatry Psychiatr Epidemiol* 2009;**44**:935–42. http://dx.doi.org/10.1007/s00127-009-0013-9

109. Vivan Ade S, Rodrigues L, Wendt G, Bicca MG, Cordioli AV. Quality of life in adolescents with obsessive–compulsive disorder. *Rev Bras Psiquiatr* 2013;**35**:369–74. http://dx.doi.org/10.1590/1516-4446-2013-1135

110. Bebbington PE, Brugha TS, Meltzer H, Jenkins R, Ceresa C, Farrell M, *et al.* Neurotic disorders and the receipt of psychiatric treatment. *Psychol Med* 2000;**30**:1369–76. http://dx.doi.org/10.1017/S0033291799002974

111. Baldwin DS, Anderson IM, Nutt DJ, Allgulander C, Bandelow B, den Boer JA, *et al.* Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive–compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. *J Psychopharmacol* 2014;**28**:403–33. http://dx.doi.org/10.1177/0269881114525674

112. Stein DJ, Koen N, Fineberg N, Fontenelle LF, Matsunaga H, Osser D, *et al.* A 2012 evidence-based algorithm for the pharmacotherapy for obsessive–compulsive disorder. *Curr Psychiatry Rep* 2012;**14**:211–19. http://dx.doi.org/10.1007/s11920-012-0268-9

113. Skapinakis P, Papatheodorou T, Mavreas V. Antipsychotic augmentation of serotonergic antidepressants in treatment-resistant obsessive–compulsive disorder: a meta-analysis of the randomized controlled trials. *Eur Neuropsychopharmacol* 2007;**17**:79–93. http://dx.doi.org/10.1016/j.euroneuro.2006.07.002

114. Hollander E, Stein DJ, Fineberg NA, Marteau F, Legault M. Quality of life outcomes in patients with obsessive–compulsive disorder: relationship to treatment response and symptom relapse. *J Clin Psychiatry* 2010;**71**:784–92. http://dx.doi.org/10.4088/JCP.09m05911blu

115. Katzman MA, Bleau P, Blier P, Chokka P, Kjernisted K, Van Ameringen M. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive–compulsive disorders. *BMC Psychiatry* 2014;**14**(Suppl. 1):1. http://dx.doi.org/10.1186/1471-244X-14-S1-S1

116. Koran LM, Hanna GL, Hollander E, Nestadt G, Simpson HB. Practice guideline for the treatment of patients with obsessive–compulsive disorder. *Am J Psychiatry* 2007;**164**(Suppl. 7):5–53.

117. Bandelow B, Zohar J, Hollander E, Kasper S, Möller HJ. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive–compulsive and post-traumatic stress disorders – first revision. *World J Biol Psychiatry* 2008;**9**:248–312. http://dx.doi.org/10.1080/15622970802465807

118. National Institute for Health and Care Excellence. *Obsessive–Compulsive Disorder: Core Interventions in the Treatment of Obsessive–Compulsive Disorder and Body Dysmorphic Disorder CG31*. London: NICE; 2005.

119. Fineberg NA, Brown A, Reghunandanan S, Pampaloni I. Evidence-based pharmacotherapy of obsessive–compulsive disorder. *Int J Neuropsychopharmacol* 2012;**15**:1173–91. http://dx.doi.org/10.1017/S1461145711001829

120. Ackerman DL, Greenland S. Multivariate meta-analysis of controlled drug studies for obsessive–compulsive disorder. *J Clin Psychopharmacol* 2002;**22**:309–17. http://dx.doi.org/10.1097/00004714-200206000-00012

121. Soomro GM, Altman D, Rajagopal S, Oakley-Browne M. Selective serotonin re-uptake inhibitors (SSRIs) versus placebo for obsessive compulsive disorder (OCD). *Cochrane Database Syst Rev* 2008;**1**:CD001765. http://dx.doi.org/10.1002/14651858.cd001765.pub3

122. Mancebo MC, Eisen JL, Pinto A, Greenberg BD, Dyck IR, Rasmussen SA. The Brown longitudinal obsessive compulsive study: treatments received and patient impressions of improvement. *J Clin Psychiatry* 2006;**67**:1713–20. http://dx.doi.org/10.4088/JCP.v67n1107

123. Reddy YC, Alur AM, Manjunath S, Kandavel T, Math SB. Long-term follow-up study of patients with serotonin reuptake inhibitor-nonresponsive obsessive–compulsive disorder. *J Clin Psychopharmacol* 2010;**30**:267–72. http://dx.doi.org/10.1097/JCP.0b013e3181dbfb53

124. Stein DJ, Andersen EW, Tonnoir B, Fineberg N. Escitalopram in obsessive–compulsive disorder: a randomized, placebo-controlled, paroxetine-referenced, fixed-dose, 24-week study. *Curr Med Res Opin* 2007;**23**:701–11. http://dx.doi.org/10.1185/030079907X178838

125. Stein DJ, Carey PD, Lochner C, Seedat S, Fineberg N, Andersen EW. Escitalopram in obsessive–compulsive disorder: response of symptom dimensions to pharmacotherapy. *CNS Spectr* 2008;**13**:492–8.

126. Greist JH, Jefferson JW, Kobak KA, Chouinard G, DuBoff E, Halaris A, *et al.* A 1 year double-blind placebo-controlled fixed dose study of sertraline in the treatment of obsessive–compulsive disorder. *Int Clin Psychopharmacol* 1995;**10**:57–65. http://dx.doi.org/10.1097/00004850-199506000-00001

127. Tollefson GD, Birkett M, Koran L, Genduso L. Continuation treatment of OCD: double-blind and open-label experience with fluoxetine. *J Clin Psychiatry* 1994;**55**:69–76.

128. Fineberg NA, Tonnoir B, Lemming O, Stein DJ. Escitalopram prevents relapse of obsessive–compulsive disorder. *Eur Neuropsychopharmacol* 2007;**17**:430–9. http://dx.doi.org/10.1016/j.euroneuro.2006.11.005

129. Donovan MR, Glue P, Kolluri S, Emir B. Comparative efficacy of antidepressants in preventing relapse in anxiety disorders – a meta-analysis. *J Affect Disord* 2010;**123**:9–16. http://dx.doi.org/10.1016/j.jad.2009.06.021

130. Grant JE. Clinical practice: obsessive–compulsive disorder. *N Engl J Med* 2014;**371**:646–53. http://dx.doi.org/10.1056/NEJMcp1402176

131. Monteiro WO, Noshirvani HF, Marks IM, Lelliott PT. Anorgasmia from clomipramine in obsessive–compulsive disorder. A controlled trial. *Br J Psychiatry* 1987;**151**:107–12. http://dx.doi.org/10.1192/bjp.151.1.107

132. Bairy KL, Madhyastha S, Ashok KP, Bairy I, Malini S. Developmental and behavioral consequences of prenatal fluoxetine. *Pharmacology* 2007;**79**:1–11. http://dx.doi.org/10.1159/000096645

133. Zivin K, Pfeiffer PN, Bohnert AS, Ganoczy D, Blow FC, Nallamothu BK, *et al.* Evaluation of the FDA warning against prescribing citalopram at doses exceeding 40 mg. *Am J Psychiatry* 2013;**170**:642–50. http://dx.doi.org/10.1176/appi.ajp.2013.12030408

134. Maina G, Albert U, Salvi V, Bogetto F. Weight gain during long-term treatment of obsessive–compulsive disorder: a prospective comparison between serotonin reuptake inhibitors. *J Clin Psychiatry* 2004;**65**:1365–71. http://dx.doi.org/10.4088/JCP.v65n1011

135. March JS, Klee BJ, Kremer CM. Treatment benefit and the risk of suicidality in multicenter, randomized, controlled trials of sertraline in children and adolescents. *J Child Adolesc Psychopharmacol* 2006;**16**:91–102. http://dx.doi.org/10.1089/cap.2006.16.91

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

136. Bridge JA, Iyengar S, Salary CB, Barbe RP, Birmaher B, Pincus HA, *et al.* Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. *JAMA* 2007;**297**:1683–96. http://dx.doi.org/10.1001/jama.297.15.1683

137. Abramowitz JS. The psychological treatment of obsessive–compulsive disorder. *Can J Psychiatry* 2006;**51**:407–16

138. Meyer V. Modification of expectations in cases with obsessional rituals. *Behav Res Ther* 1966;**4**:273–80. http://dx.doi.org/10.1016/0005-7967(66)90023-4

139. Rachman S, de Silva P. Abnormal and normal obsessions. *Behav Res Ther* 1978;**16**:233–48. http://dx.doi.org/10.1016/0005-7967(78)90022-0

140. Obsessive Compulsive Cognitions Working Group. Cognitive assessment of obsessive–compulsive disorder. Obsessive Compulsive Cognitions Working Group. *Behav Res Ther* 1997;**35**:667–81. http://dx.doi.org/10.1016/S0005-7967(97)00017-X

141. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLOS Med* 2009;**6**:7. http://dx.doi.org/10.1371/journal.pmed.1000097

142. Higgins J, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.0.0. Chichester, UK: Cochrane Collaboration; 2008. http://dx.doi.org/10.1002/9780470712184

143. Lu G, Ades AE. Combination of direct and indirect evidence in mixed treatment comparisons. *Stat Med* 2004;**23**:3105–24. http://dx.doi.org/10.1002/sim.1875

144. Caldwell DM, Ades AE, Higgins JPT. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ* 2005;**331**:897–900. http://dx.doi.org/10.1136/bmj.331.7521.897

145. Dias S, Sutton AJ, Ades AE, Welton NJ. Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. *Med Decis Making* 2013;**33**:607–17. http://dx.doi.org/10.1177/0272989X12458724

146. Caldwell DM. An overview of conducting systematic reviews with network meta-analysis. *Syst Rev* 2014;**3**:109. http://dx.doi.org/10.1186/2046-4053-3-109

147. Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. *Res Synth Method* 2012;**3**:80–97. http://dx.doi.org/10.1002/jrsm.1037

148. Jansen J, Naci H. Is network meta-analysis as valid as standard pairwise meta-analysis? It all depends on the distribution of effect modifiers. *BMC Med* 2013;**11**:159. http://dx.doi.org/10.1186/1741-7015-11-159

149. Chaimani A, Higgins JPT, Mavridis D, Spyridonos P, Salanti G. Graphical tools for network meta-analysis in STATA. *PLOS ONE* 2013;**8**:e76654. http://dx.doi.org/10.1371/journal.pone.0076654

150. Dias S, Welton NJ, Sutton AJ, Ades AE. Evidence synthesis for decision making 1: introduction. *Med Decis Making* 2013;**33**:597–606. http://dx.doi.org/10.1177/0272989X13487604

151. Haas DM, Caldwell DM, Kirkpatrick P, McIntosh JJ, Welton NJ. Tocolytic therapy for preterm delivery: systematic review and network meta-analysis. *BMJ* 2012;**345**:e6226. http://dx.doi.org/10.1136/bmj.e6226

152. Spiegelhalter DJ, Best NG, Carlin BP, van der Linde A. Bayesian measures of model complexity and fit. *J Roy Stat Soc B* 2002;**64**:583–616. http://dx.doi.org/10.1111/1467-9868.00353

153. Dias S, Welton NJ, Sutton AJ, Caldwell DM, Lu G, Ades AE. Evidence synthesis for decision making 4: inconsistency in networks of evidence based on randomized controlled trials. *Med Decis Making* 2013;**33**:641–56. http://dx.doi.org/10.1177/0272989X12455847

154. Clomipramine Collaborative Study Group. Clomipramine in the treatment of patients with obsessive–compulsive disorder. *Arch Gen Psychiatry* 1991;**48**:730–8. http://dx.doi.org/10.1001/archpsyc.1991.01810320054008

155. Albert U, Aguglia E, Maina G, Bogetto F. Venlafaxine versus clomipramine in the treatment of obsessive–compulsive disorder: a preliminary single-blind, 12-week, controlled study. *J Clin Psychiatry* 2002;**63**:1004–9. http://dx.doi.org/10.4088/JCP.v63n1108

156. Ananth J, Pecknold JC, van den Steen N, Engelsmann F. Double-blind comparative study of clomipramine and amitriptyline in obsessive neurosis. *Prog Neuropsychopharmacol* 1981;**5**:257–62. http://dx.doi.org/10.1016/0364-7722(81)90077-1

157. Anderson RA, Rees CS. Group versus individual cognitive–behavioural treatment for obsessive–compulsive disorder: a controlled trial. *Behav Res Ther* 2007;**45**:123–37. http://dx.doi.org/10.1016/j.brat.2006.01.016

158. Andersson E, Enander J, Andrén P, Hedman E, Ljótsson B, Hursti T, *et al.* Internet-based cognitive behaviour therapy for obsessive–compulsive disorder: a randomized controlled trial. *Psychol Med* 2012;**42**:219. http://dx.doi.org/10.1017/S0033291712000244

159. Belloch A, Cabedo E, Carrio C. Cognitive versus behaviour therapy in the individual treatment of OCD: changes in cognitions and clinically significant outcomes at post-treatment and one-year follow-up. *Behav Cogn Psychother* 2008;**36**:521–40. http://dx.doi.org/10.1017/S1352465808004451

160. Belotto-Silva C, Diniz JB, Malavazzi DM, Valério C, Fossaluza V, Borcato S, *et al.* Group cognitive–behavioural therapy versus selective serotonin reuptake inhibitors for obsessive–compulsive disorder: a practical clinical trial *J Anxiety Disord* 2012;**26**:25–31. http://dx.doi.org/10.1016/j.janxdis.2011.08.008

161. Bergeron R, Ravindran AV, Chaput Y, Goldner E, Swinson R, van Ameringen MA, *et al.* Sertraline and fluoxetine treatment of obsessive–compulsive disorder: results of a double-blind, 6-month treatment study. *J Clin Psychopharmacol* 2002;**22**:148–54. http://dx.doi.org/10.1097/00004714-200204000-00007

162. Bisserbe JC, Lane RM, Flament MF. A double-blind comparison of sertraline and clomipramine in outpatients with obsessive–compulsive disorder. *Eur Psychiatry* 1997;**12**:82–93. http://dx.doi.org/10.1016/S0924-9338(97)89646-0

163. Chouinard G, Goodman W, Greist J, Jenike M, Rasmussen S, White K, *et al.* Results of a double-blind placebo controlled trial of a new serotonin uptake inhibitor, sertraline, in the treatment of obsessive–compulsive disorder. *Psychopharmacology Bull* 1990;**26**:279–84.

164. Cordioli AV, Heldt E, Braga Bochi D, Margis R, Basso de Sousa M, Fonseca Tonello J, *et al.* Cognitive–behavioural group therapy in obsessive–compulsive disorder: a randomized clinical trial. *Psychother Psychosom* 2003;**72**:211–16. http://dx.doi.org/10.1159/000070785

165. Cottraux J, Mollard E, Bouvard M, Marks I. Exposure therapy, fluvoxamine, or combination treatment in obsessive–compulsive disorder: 1-year follow up. *Psychiatry Res* 1993;**49**:63–75. http://dx.doi.org/10.1016/0165-1781(93)90030-K

166. Cottraux J, Note I, Yao SN, Lafont S, Note B, Mollard E, *et al.* A randomized controlled trial of cognitive therapy versus intensive behavior therapy in obsessive compulsive disorder. *Psychother Psychosom* 2001;**70**:288–97. http://dx.doi.org/10.1159/000056269

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

167. Denys D, van der Wee N, van Megen HJ, Westenberg HG. A double blind comparison of venlafaxine and paroxetine in obsessive–compulsive disorder. *J Clin Psychopharmacol* 2003;**23**:568–75. http://dx.doi.org/10.1097/01.jcp.0000095342.32154.54

168. Emmelkamp PM, Beens H. Cognitive therapy with obsessive–compulsive disorder: a comparative evaluation. *Behav Res Ther* 1991;**29**:293–300. http://dx.doi.org/10.1016/0005-7967(91)90120-R

169. Emmelkamp PM, Visser S, Hoekstra RJ. Cognitive therapy vs exposure in vivo in the treatment of obsessive–compulsives. *Cognit Ther Res* 1988;**12**:103–14. http://dx.doi.org/10.1007/BF01172784

170. Fals-Stewart W, Marks AP, Schafer J. A comparison of behavioral group therapy and individual behavior therapy in treating obsessive–compulsive disorder. *J Nerv Ment Dis* 1993;**181**:189–93. http://dx.doi.org/10.1097/00005053-199303000-00007

171. Foa EB, Liebowitz MR, Kozak MJ, Davies S, Campeas R, Franklin ME, *et al.* Randomized, placebo-controlled trial of exposure and ritual prevention, clomipramine, and their combination in the treatment of obsessive–compulsive disorder. *Am J Psychiatry* 2005;**162**:151–61. http://dx.doi.org/10.1176/appi.ajp.162.1.151

172. Freeman CP, Trimble MR, Deakin JF, Stokes TM, Ashford JJ. Fluvoxamine versus clomipramine in the treatment of obsessive compulsive disorder: a multicenter, randomized, double-blind, parallel group comparison. *J Clin Psychiatry* 1994;**55**:301–5.

173. Freeston MH, Ladouceur R, Gagnon F, Thibodeau N, Rhéaume J, Letarte H, *et al.* Cognitive–behavioural treatment of obsessive thoughts: a controlled study. *J Consult Clin Psychol* 1997;**65**:405–13. http://dx.doi.org/10.1037/0022-006X.65.3.405

174. GlaxoSmithKline. *Paroxetine versus Clomipramine and Placebo in the Treatment of Obsessive–Compulsive Disorder*. Study number: MY-1028/BRL–029060/1/CPMS–118 (date updated: 4 April 2005).

175. GlaxoSmithKline. *A Double Blind, Multicenter, Randomized, Drug-Controlled Study to Assess the Efficacy and Tolerance of Paroxetine Compared with Clomipramine in Treatment of Obsessive Compulsive Disorder*. Study number: 29060/526 (date updated: 16 November 2005).

176. Goodman WK, Price LH, Rasmussen SA, Delgado PL, Heninger GR, Charney DS. Efficacy of fluvoxamine in obsessive–compulsive disorder. A double-blind comparison with placebo. *Arch Gen Psychiatry* 1989;**46**:36–44. http://dx.doi.org/10.1001/archpsyc.1989.01810010038006

177. Goodman WK, Kozak MJ, Liebowitz M, White KL. Treatment of obsessive–compulsive disorder with fluvoxamine: a multicentre, double-blind, placebo-controlled trial. *Int Clin Psychopharmacol* 1996;**11**:21–9. http://dx.doi.org/10.1097/00004850-199603000-00003

178. Greist JH, Marks IM, Baer L, Kobak KA, Wenzel KW, Hirsch MJ, *et al.* Behavior therapy for obsessive–compulsive disorder guided by a computer or by a clinician compared with relaxation as a control. *J Clin Psychiatry* 2002;**63**:138–45. http://dx.doi.org/10.4088/JCP.v63n0209

179. Hohagen F, Winkelmann G, Rasche-Rüchle H, Hand I, König A, Münchau N, *et al.* Combination of behaviour therapy with fluvoxamine in comparison with behaviour therapy and placebo. Results of a multicentre study. *Br J Psychiatry Suppl* 1998;**35**:71–8.

180. Hollander E, Allen A, Steiner M, Wheadon DE, Oakes R, Burnham DB, *et al.* Acute and long-term treatment and prevention of relapse of obsessive–compulsive disorder with paroxetine. *J Clin Psychiatry* 2003;**64**:1113–21. http://dx.doi.org/10.4088/JCP.v64n0919

181. Hollander E, Koran LM, Goodman WK, Greist JH, Ninan PT, Yang H, *et al.* A double-blind, placebo-controlled study of the efficacy and safety of controlled-release fluvoxamine in patients with obsessive–compulsive disorder. *J Clin Psychiatry* 2003;**64**:640–7. http://dx.doi.org/10.4088/JCP.v64n0604

182. Jaurrieta N, Jimenez-Murcia S, Menchón JM, Del Pino Alonso M, Segalas C, Alvarez-Moya EM, *et al.* Individual versus group cognitive–behavioural treatment for obsessive–compulsive disorder: a controlled pilot study. *Psychother Res* 2008;**18**:604–14. http://dx.doi.org/10.1080/10503300802192141

183. Jenike MA, Baer L, Summergrad P, Minichiello WE, Holland A, Seymour R. Sertraline in obsessive–compulsive disorder: a double-blind comparison with placebo. *Am J Psychiatry* 1990;**147**:923–8.

184. Jenike MA, Hyman S, Baer L, Holland A, Minichiello WE, Buttolph L, *et al.* A controlled trial of fluvoxamine in obsessive–compulsive disorder: implications for a serotonergic theory. *Am J Psychiatry* 1990;**147**:1209–15. http://dx.doi.org/10.1176/ajp.147.9.1209

185. Jenike MA, Baer L, Minichiello WE, Rauch SL, Buttolph ML. Placebo-controlled trial of fluoxetine and phenelzine for obsessive–compulsive disorder. *Am J Psychiatry* 1997;**154**:1261–4. http://dx.doi.org/10.1176/ajp.154.9.1261

186. Jones MK, Menzies RG. Danger ideation reduction therapy (DIRT) for obsessive–compulsive washers. A controlled trial. *Behav Res Ther* 1998;**36**:959–70. http://dx.doi.org/10.1016/S0005-7967(98)00057-6

187. Kamijima K, Murasaki M, Asai M, Higuchi T, Nakajima T, Taga C, *et al.* Paroxetine in the treatment of obsessive–compulsive disorder: randomized, double-blind, placebo-controlled study in Japanese patients. *Psychiatry Clin Neurosci* 2004;**58**:427–33. http://dx.doi.org/10.1111/j.1440-1819.2004.01278.x

188. Khodarahimi S. Satiation therapy and exposure response prevention in the treatment of obsessive compulsive disorder. *J Contemp Psychother* 2009;**39**:203–7. http://dx.doi.org/10.1007/s10879-009-9110-z

189. Kobak KA, Taylor LV, Bystritsky A, Kohlenberg CJ, Greist JH, Tucker P, *et al.* St John's wort versus placebo in obsessive–compulsive disorder: results from a double-blind study. *Int Clin Psychopharmacol* 2005;**20**:299–304. http://dx.doi.org/10.1097/00004850-200511000-00003

190. Koran LM, McElroy SL, Davidson JR, Rasmussen SA, Hollander E, Jenike MA. Fluvoxamine versus clomipramine for obsessive–compulsive disorder: a double-blind comparison. *J Clin Psychopharmacol* 1996;**16**:121–9. http://dx.doi.org/10.1097/00004714-199604000-00004

191. Kronig MH, Apter J, Asnis G, Bystritsky A, Curtis G, Ferguson J, *et al.* Placebo-controlled, multicenter study of sertraline treatment for obsessive–compulsive disorder. *J Clin Psychopharmacol* 1999;**19**:172–6. http://dx.doi.org/10.1097/00004714-199904000-00013

192. Lindsay M, Crino R, Andrews G. Controlled trial of exposure and response prevention in obsessive–compulsive disorder. *Br J Psychiatry* 1997;**171**:135–9. http://dx.doi.org/10.1192/bjp.171.2.135

193. López-Ibor JJ Jr, Saiz J, Cottraux J, Note I, Viñas R, Bourgeois M, *et al.* Double-blind comparison of fluoxetine versus clomipramine in the treatment of obsessive compulsive disorder. *Eur Neuropsychopharmacol* 1996;**6**:111–18. http://dx.doi.org/10.1016/0924-977X(95)00071-V

194. Mavissakalian M, Turner SM, Michelson L, Jacob R. Tricyclic antidepressants in obsessive–compulsive disorder: antiobsessional or antidepressant agents? II. *Am J Psychiatry* 1985;**142**:572–6. http://dx.doi.org/10.1176/ajp.142.5.572

195. McLean PD, Whittal ML, Thordarson DS, Taylor S, Söchting I, Koch WJ, *et al.* Cognitive versus behavior therapy in the group treatment of obsessive–compulsive disorder. *J Consult Clin Psychol* 2001;**69**:205–14. http://dx.doi.org/10.1037/0022-006X.69.2.205

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

196. Milanfranchi A, Ravagli S, Lensi P, Marazziti D, Cassano GB. A double-blind study of fluvoxamine and clomipramine in the treatment of obsessive–compulsive disorder. *Int Clin Psychopharmacol* 1997;**12**:131–6. http://dx.doi.org/10.1097/00004850-199705000-00002

197. Montgomery SA, McIntyre A, Osterheider M, Sarteschi P, Zitterl W, Zohar J, *et al.* A double-blind, placebo-controlled study of fluoxetine in patients with DSM-III-R obsessive–compulsive disorder. *Eur Neuropsychopharmacol* 1993;**3**:143–52. http://dx.doi.org/10.1016/0924-977X(93)90266-O

198. Montgomery SA, Kasper S, Stein DJ, Bang Hedegaard K, Lemming OM. Citalopram 20 mg, 40 mg and 60 mg are all effective and well tolerated compared with placebo in obsessive–compulsive disorder. *Int Clin Psychopharmacol* 2001;**16**:75–86. http://dx.doi.org/10.1097/00004850-200103000-00002

199. Mundo E, Bianchi L, Bellodi L. Efficacy of fluvoxamine, paroxetine, and citalopram in the treatment of obsessive–compulsive disorder: a single-blind study. *J Clin Psychopharmacol* 1997;**17**:267–71. http://dx.doi.org/10.1097/00004714-199708000-00005

200. Mundo E, Rouillon F, Figuera ML, Stigler M. Fluvoxamine in obsessive–compulsive disorder: similar efficacy but superior tolerability in comparison with clomipramine. *Hum Psychopharmacol* 2001;**16**:461–8. http://dx.doi.org/10.1002/hup.317

201. Nakajima T, Kudo Y, Yamashita I. Clinical usefulness of fluvoxamine maleate (SME3110), a selective serotonin reuptake inhibitor, in the treatment of obsessive compulsive disorder: a double blind, placebo controlled study. *J Clin Ther Med* 1996;**12**:409–37.

202. Nakatani E, Nakagawa A, Nakao T, Yoshizato C, Nabeyama M, Kudo A, *et al.* A randomized controlled trial of Japanese patients with obsessive–compulsive disorder – effectiveness of behavior therapy and fluvoxamine. *Psychother Psychosom* 2005;**74**:269–76. http://dx.doi.org/10.1159/000086317

203. O'Connor K, Todorov C, Robillard S, Borgeat F, Brault M. Cognitive–behavour therapy and medication in the treatment of obsessive–compulsive disorder: a controlled study. *Can J Psychiatry* 1999;**44**:64–71.

204. O'Connor KP, Aardema F, Robillard S, Guay S, Pélissier MC, Todorov C, *et al.* Cognitive behaviour therapy and medication in the treatment of obsessive–compulsive disorder. *Acta Psychiatr Scand* 2006;**113**:408–19. http://dx.doi.org/10.1111/j.1600-0447.2006.00767.x

205. Perse TL, Greist JH, Jefferson JW, Rosenfeld R, Dar R. Fluvoxamine treatment of obsessive–compulsive disorder. *Am J Psychiatry* 1987;**144**:1543–8. http://dx.doi.org/10.1176/ajp.144.12.1543

206. Shareh H, Gharraee B, Atef-Vahid M, Eftekhar M. Metacognitive Therapy (MCT), fluvoxamine, and combined treatment in improving obsessive–compulsive, depressive and anxiety symptoms in patients with obsessive–compulsive disorder (OCD). *IJPBS* 2010;**4**:17–25.

207. Sousa MB, Isolan LR, Oliveira RR, Manfro GG, Cordioli AV. A randomized clinical trial of cognitive–behavioural group therapy and sertraline in the treatment of obsessive–compulsive disorder. *J Clin Psychiatry* 2006;**67**:1133–9. http://dx.doi.org/10.4088/JCP.v67n0717

208. Thoren P, Asberg M, Cronholm B, Jornestedt L, Traskman L. Clomipramine treatment of obsessive–compulsive disorder. I. A controlled clinical trial. *Arch Gen Psychiatry* 1980;**37**:1281–5. http://dx.doi.org/10.1001/archpsyc.1980.01780240079009

209. Van Oppen P, de Haan E, van Balkom AJ, Spinhoven P, Hoogduin K, van Dyck R. Cognitive therapy and exposure in vivo in the treatment of obsessive compulsive disorder. *Behav Res Ther* 1995;**33**:379–90. http://dx.doi.org/10.1016/0005-7967(94)00052-L

210. Volavka J, Neziroglu F, Yaryura-Tobias JA. Clomipramine and imipramine in obsessive–compulsive disorder. *Psychiatry Res* 1985;**14**:85–93. http://dx.doi.org/10.1016/0165-1781(85)90092-7

211. Whittal ML, Thordarson DS, McLean PD. Treatment of obsessive–compulsive disorder: cognitive behavior therapy vs. exposure and response prevention. *Behav Res Ther* 2005;**43**:1559–76. http://dx.doi.org/10.1016/j.brat.2004.11.012

212. Whittal ML, Woody SR, McLean PD, Rachman SJ, Robichaud M. Treatment of obsessions: a randomized controlled trial. *Behav Res Ther* 2010;**48**:295–303. http://dx.doi.org/10.1016/j.brat.2009.11.010

213. Zohar J, Judge R. Paroxetine versus clomipramine in the treatment of obsessive–compulsive disorder. OCD Paroxetine Study Investigators. *Br J Psychiatry* 1996;**169**:468–74. http://dx.doi.org/10.1192/bjp.169.4.468

214. Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, *et al.* Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis [published online ahead of print June 15 2016]. *Lancet Psychiatry* 2016. http://dx.doi.org/10.1016/S2215-0366(16)30069-4

215. Alaghband-Rad J, Hakimshooshtary M. A randomized controlled clinical trial of citalopram versus fluoxetine in children and adolescents with obsessive–compulsive disorder (OCD). *Eur Child Adolesc Psychiatry* 2009;**18**:131–5. http://dx.doi.org/10.1007/s00787-007-0634-z

216. Asbahr FR, Castillo AR, Ito LM, Latorre MR, Moreira MN, Lotufo-Neto F. Group cognitive–behavioural therapy versus sertraline for the treatment of children and adolescents with obsessive–compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 2005;**44**:1128–36. http://dx.doi.org/10.1097/01.chi.0000177324.40005.6f

217. Barrett P, Healy-Farrell L, March JS. Cognitive–behavioural family treatment of childhood obsessive–compulsive disorder: a controlled trial. *J Am Acad Child Adolesc Psychiatry* 2004;**43**:46–62. http://dx.doi.org/10.1097/00004583-200401000-00014

218. Bolton D, Perrin S. Evaluation of exposure with response-prevention for obsessive compulsive disorder in childhood and adolescence. *J Behav Ther Exp Psychiatry* 2008;**39**:11–22. http://dx.doi.org/10.1016/j.jbtep.2006.11.002

219. Bolton D, Williams T, Perrin S, Atkinson L, Gallop C, Waite P, *et al.* Randomized controlled trial of full and brief cognitive–behaviour therapy and wait-list for paediatric obsessive–compulsive disorder. *J Child Psychol Psychiatry* 2011;**52**:1269–78. http://dx.doi.org/10.1111/j.1469-7610.2011.02419.x

220. de Haan E, Hoogduin KA, Buitelaar JK, Keijsers GP. Behavior therapy versus clomipramine for the treatment of obsessive–compulsive disorder in children and adolescents. *J Am Acad Child Adolesc Psychiatry* 1998;**37**:1022–9. http://dx.doi.org/10.1097/00004583-199810000-00011

221. DeVeaugh-Geiss J, Moroz G, Biederman J, Cantwell D, Fontaine R, Greist JH, *et al.* Clomipramine hydrochloride in childhood and adolescent obsessive–compulsive disorder: a multicenter trial. *J Am Acad Child Adolesc Psychiatry* 1992;**31**:45–9. http://dx.doi.org/10.1097/00004583-199201000-00008

222. Flament MF, Rapoport JL, Berg CJ, Sceery W, Kilts C, Mellström B, *et al.* Clomipramine treatment of childhood obsessive–compulsive disorder: a double-blind controlled study. *Arch Gen Psychiatry* 1985;**42**:977–83. http://dx.doi.org/10.1001/archpsyc.1985.01790330057007

223. Freeman JB, Garcia AM, Coyne L, Ale C, Przeworski A, Himle M, *et al.* Early childhood OCD: preliminary findings from a family-based cognitive–behavioural approach. *J Am Acad Child Adolesc Psychiatry* 2008;**47**:593–602. http://dx.doi.org/10.1097/CHI.0b013e31816765f9

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

224. Geller DA, Hoog SL, Heiligenstein JH, Ricardi RK, Tamura R, Kluszynski S, *et al.* Fluoxetine treatment for obsessive–compulsive disorder in children and adolescents: a placebo-controlled clinical trial. *J Am Acad Child Adolesc Psychiatry* 2001;**40**:773–9. http://dx.doi.org/10.1097/00004583-200107000-00011

225. GlaxoSmithKline. *A Randomized, Multicenter, 10-Week, Double-Blind, Placebo-Controlled, Flexible-Dose Study to Evaluate the Efficacy and Safety of Paroxetine in Children and Adolescents with Obsessive–Compulsive Disorder (OCD)*. 2001. Study number: 29060/704.

226. Liebowitz MR, Turner SM, Piacentini J, Beidel DC, Clarvit SR, Davies SO, *et al.* Fluoxetine in children and adolescents with OCD: a placebo-controlled trial. *J Am Acad Child Adolesc Psychiatry* 2002;**41**:1431–8. http://dx.doi.org/10.1097/00004583-200212000-00014

227. March JS, Johnston H, Jefferson JW, Kobak KA, Greist JH. Do subtle neurological impairments predict treatment resistance to clomipramine in children and adolescents with obsessive–compulsive disorder? *J Child Adolesc Psychopharmacol* 1990;**1**:133–40. http://dx.doi.org/10.1089/cap.1990.1.133

228. March JS, Biederman J, Wolkow R, Safferman A, Mardekian J, Cook EH, *et al.* Sertraline in children and adolescents with obsessive–compulsive disorder: a multicenter randomized controlled trial. *JAMA* 1998;**280**:1752–6. http://dx.doi.org/10.1001/jama.280.20.1752

229. Neziroglu F, Yaryura-Tobias JA, Walz J, McKay D. The effect of fluvoxamine and behavior therapy on children and adolescents with obsessive–compulsive disorder. *J Child Adolesc Psychopharmacol* 2000;**10**:295–306. http://dx.doi.org/10.1089/cap.2000.10.295

230. Piacentini J, Bergman RL, Chang S, Langley A, Peris T, Wood JJ, *et al.* Controlled comparison of family cognitive behavioral therapy and psychoeducation/relaxation training for child obsessive–compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 2011;**50**:1149–61. http://dx.doi.org/10.1016/j.jaac.2011.08.003

231. Riddle MA, Scahill L, King RA, Hardin MT, Anderson GM, Ort SI, *et al.* Double-blind, crossover trial of fluoxetine and placebo in children and adolescents with obsessive–compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 1992;**31**:1062–9. http://dx.doi.org/10.1097/00004583-199211000-00011

232. Riddle MA, Reeve EA, Yaryura-Tobias JA, Yang HM, Claghorn JL, Gaffney G, *et al.* Fluvoxamine for children and adolescents with obsessive–compulsive disorder: a randomized, controlled, multicenter trial. *J Am Acad Child Adolesc Psychiatry* 2001;**40**:222–9. http://dx.doi.org/10.1097/00004583-200102000-00017

233. Storch EA, Caporino NE, Morgan JR, Lewin AB, Rojas A, Brauer L, *et al.* Preliminary investigation of web-camera delivered cognitive–behavioural therapy for youth with obsessive–compulsive disorder. *Psychiatry Res* 2011;**189**:407–12. http://dx.doi.org/10.1016/j.psychres.2011.05.047

234. Storch EA, Bussing R, Small BJ, Geffken GR, McNamara JP, Rahman O, *et al.* Randomized, placebo-controlled trial of cognitive–behavioural therapy alone or combined with sertraline in the treatment of pediatric obsessive–compulsive disorder. *Behav Res Ther* 2013;**51**:823–9. http://dx.doi.org/10.1016/j.brat.2013.09.007

235. Williams TI, Salkovskis PM, Forrester L, Turner S, White H, Allsopp MA. A randomised controlled trial of cognitive behavioural treatment for obsessive compulsive disorder in children and adolescents. *Eur Child Adolesc Psychiatry* 2010;**19**:449–56. http://dx.doi.org/10.1007/s00787-009-0077-9

236. The Pediatric OCD Treatment Study. Cognitive–behaviour therapy, sertraline, and their combination for children and adolescents with obsessive–compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial. *JAMA* 2004;**292**:1969–76. http://dx.doi.org/10.1001/jama.292.16.1969

237. Knapp M, Henderson J, Patel A. Costs of Obsessive–Compulsive Disorder: A Review. In Maj M, Sartorius N, Okasha A, Zohar J, editors. *Obsessive–Compulsive Disorder*. New York, NY: Wiley; 2002. pp. 253–99. http://dx.doi.org/10.1002/0470861657.ch6

238. DuPont RL, Rice DP, Shiraki S, Rowland CR. Economic costs of obsessive–compulsive disorder. *Med Interface* 1995;**8**:102–9.

239. Greist JH, Bandelow B, Hollander E, Marazziti D, Montgomery SA, Nutt DJ, *et al.* WCA recommendations for the long-term treatment of obsessive–compulsive disorder in adults. *CNS Spectr* 2003;**8**(Suppl. 1):7–16.

240. Hankin CS, Koran L, Sheehan DV, Hollander E, Culpepper L, Black DW, *et al.* Patients with obsessive–compulsive disorder vs depression have comparable health care costs: a retrospective claims analysis of Florida Medicaid enrollees. *Ann Clin Psychiatry* 2011;**23**:285–96.

241. Koran LM, Leventhal J, Fireman B, Jacobsen A. Recognition and treatment of obsessive compulsive disorder in a pre-paid health plan: does adequate treatment reduce costs? *Eur Neuropsychopharmacol* 1997;**7**(Suppl. 2):243. http://dx.doi.org/10.1016/S0924-977X(97)88803-7

242. Tolin DF, Diefenbach GJ, Gilliam CM. Stepped care versus standard cognitive–behavioural therapy for obsessive–compulsive disorder: a preliminary study of efficacy and costs. *Depress Anxiety* 2011;**28**:314–23. http://dx.doi.org/10.1002/da.20804

243. McCrone P, Marks IM, Greist JH, Baer L, Kobak KA, Wenzel KW, *et al.* Cost-effectiveness of computer-aided behaviour therapy for obsessive–compulsive disorder. *Psychother Psychosom* 2007;**76**:249–50.

244. Gava I, Barbui C, Aguglia E, Carlino D, Churchill R, De Vanna M, *et al.* Psychological treatments versus treatment as usual for obsessive compulsive disorder (OCD). *Cochrane Database of Syst Rev* 2007;**2**:CD005333. http://dx.doi.org/10.1002/14651858.cd005333.pub2

245. Gellatly J, Bower P, McMillan D, Roberts C, Byford S, Bee P, *et al.* Obsessive Compulsive Treatment Efficacy Trial (OCTET) comparing the clinical and cost effectiveness of self-managed therapies: study protocol for a randomised controlled trial. *Trials* 2014;**15**:278. http://dx.doi.org/10.1186/1745-6215-15-278

246. Bamelis LL, Evers SM, Arntz A. Design of a multicentered randomized controlled trial on the clinical and cost effectiveness of schema therapy for personality disorders. *BMC Public Health* 2012;**12**:75. http://dx.doi.org/10.1186/1471-2458-12-75

247. Petrou S, Gray A. Economic evaluation using decision analytical modelling: design, conduct, analysis, and reporting. *BMJ* 2011;**342**:d1766. http://dx.doi.org/10.1136/bmj.d1766

248. Kaltenthaler E, Brazier J, De Nigris E, Tumur I, Ferriter M, Beverley C, *et al.* Computerised cognitive behaviour therapy for depression and anxiety update: a systematic review and economic evaluation. *Health Technol Assess* 2006;**10**(3). http://dx.doi.org/10.3310/hta10330

249. Pallanti S, Hollander E, Bienstock C, Koran L, Leckman J, Marazziti D, *et al.* (International Treatment Refractory OCD Consortium). Treatment non-response in OCD: methodological issues and operational definitions. *Int J Neuropsychopharmacol* 2002;**5**:181–91. http://dx.doi.org/10.1017/s1461145702002900

250. Farris SG, McLean CP, Van Meter PE, Simpson HB, Foa EB. Treatment response, symptom remission, and wellness in obsessive–compulsive disorder. *J Clin Psychiatry* 2013;**74**:685–90. http://dx.doi.org/10.4088/JCP.12m07789

251. Storch EA, Lewin AB, De Nadai AS, Murphy TK. Defining treatment response and remission in obsessive–compulsive disorder: a signal detection analysis of the Children's Yale–Brown Obsessive Compulsive Scale. *J Am Acad Child Adolesc Psychiatry* 2010;**49**:708–17. http://dx.doi.org/10.1016/j.jaac.2010.04.005

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

252. Guy W. *ECDEU Assessment Manual for Psychopharmacology*. Rockville, MD: National Institute for Mental Health; 1976.

253. Joint Formulary Committee. *British National Formulary* (online). London: BMJ Group and Pharmaceutical Press. URL: www.medicinescomplete.com (accessed 1 November 2014).

254. Curtis L. *Unit Costs of Health and Social Care*. Canterbury: Personal Social Services Research Unit; 2013.

255. Eaton WW, Roth KB, Bruce M, Cottler L, Wu L, Nestadt G, *et al.* The relationship of mental and behavioral disorders to all-cause mortality in a 27-year follow-up of 4 epidemiologic catchment area samples. *Am J Epidemiology* 2013;**178**:1366–77. http://dx.doi.org/10.1093/aje/kwt219

256. Office for National Statistics. *National Life Tables 2010–12. Secondary National Life Tables, 2010–12*. URL: www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-352834 (accessed 1 November 2014).

257. Scottish Intercollegiate Guidelines Network. *Guidelines: Search Filters for Observational Studies*. Edinburgh: Scottish Intercollegiate Network. URL: www.sign.ac.uk/methodology/filters.html (accessed 1 November 2014).

258. Mulhern B, Mukuria C, Barkham M, Knapp M, Byford S, Soeteman D, *et al.* Using generic preference-based measures in mental health: psychometric validity of the EQ–5D and SF–6D. *Br J Psychiatry* 2014;**205**:236–43. http://dx.doi.org/10.1192/bjp.bp.112.122283

259. Byford S, Barrett B, Despiegel N, Wade A. Impact of treatment success on health service use and cost in depression: longitudinal database analysis. *Pharmacoeconomics* 2011;**29**:157–70. http://dx.doi.org/10.2165/11537360-000000000-00000

260. National Institute for Health and Care Excellence. *Guide to the Methods of Technology Appraisal 2013*. London: National Institute for Health and Care Excellence; 2013.

261. Barton GR, Briggs AH, Fenwick EA. Optimal cost-effectiveness decisions: the role of the cost-effectiveness acceptability curve (CEAC), the cost-effectiveness acceptability frontier (CEAF), and the expected value of perfection information (EVPI). *Value Health* 2008;**11**:886–97. http://dx.doi.org/10.1111/j.1524-4733.2008.00358.x

262. van Balkom Anton JLM, van Oppen P, Vermeulen Alexander WA, van Dyck R, Nauta Mary CE, Vorst Harne CM. A meta-analysis on the treatment of obsessive compulsive disorder: a comparison of antidepressants, behavior, and cognitive therapy. *Clin Psychol Rev* 1994;**14**:359–81. http://dx.doi.org/10.1016/0272-7358(94)90033-7

263. Piccinelli M, Pini S, Bellantuono C, Wilkinson G. Efficacy of drug treatment in obsessive–compulsive disorder. A meta-analytic review. *Br J Psychiatry* 1995;**166**:424–43. http://dx.doi.org/10.1192/bjp.166.4.424

264. Geller DA, Biederman J, Stewart SE, Mullin B, Martin A, Spencer T, *et al.* Which SSRI? A meta-analysis of pharmacotherapy trials in pediatric obsessive–compulsive disorder. *Am J Psychiatry* 2003;**160**:1919–28. http://dx.doi.org/10.1176/appi.ajp.160.11.1919

265. Cuijpers P, Sijbrandij M, Koole SL, Andersson G, Beekman AT, Reynolds CF III. The efficacy of psychotherapy and pharmacotherapy in treating depressive and anxiety disorders: a meta-analysis of direct comparisons. *World Psychiatry* 2013;**12**:137–48. http://dx.doi.org/10.1002/wps.20038

266. Cuijpers P, Sijbrandij M, Koole SL, Andersson G, Beekman AT, Reynolds CF III. Adding psychotherapy to antidepressant medication in depression and anxiety disorders: a meta-analysis. *World Psychiatry* 2014;**13**:56–67. http://dx.doi.org/10.1002/wps.20089

267. Romanelli RJ, Wu FM, Gamba R, Mojtabai R, Segal JB. Behavioral therapy and serotonin reuptake inhibitor pharmacotherapy in the treatment of obsessive–compulsive disorder: a systematic review and meta-analysis of head-to-head randomized controlled trials. *Depress Anxiety* 2014;**31**:641–52. http://dx.doi.org/10.1002/da.22232

268. Rasmussen S, Hackett E, DuBoff E, Greist J, Halaris A, Koran LM, *et al.* A 2-year study of sertraline in the treatment of obsessive–compulsive disorder. *Int Clin Psychopharmacol* 1997;**12**:309–16. http://dx.doi.org/10.1097/00004850-199711000-00003

269. Skarphedinsson G, Hanssen-Bauer K, Kornor H, Heiervang ER, Landro NI, Axelsdottir B, *et al.* Standard individual cognitive behaviour therapy for paediatric obsessive–compulsive disorder: a systematic review of effect estimates across comparisons. *Nord J Psychiatry* 2014;**68**:1–12. http://dx.doi.org/10.3109/08039488.2014.941395

270. Lu G, Kounali D, Ades AE. Simultaneous multioutcome synthesis and mapping of treatment effects to a common scale. *Value Health* 2014;**17**:280–7. http://dx.doi.org/10.1016/j.jval.2013.12.006

271. Wood L, Egger M, Gluud LL, Schulz KF, Jüni P, Altman DG, *et al.* Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ* 2008;**336**:601–15. http://dx.doi.org/10.1136/bmj.39465.451748.AD

272. Huhn M, Tardy M, Spineli LM, Kissling W, Förstl H, Pitschel-Walz G, *et al.* Efficacy of pharmacotherapy and psychotherapy for adult psychiatric disorders: a systematic overview of meta-analyses. *JAMA Psychiatry* 2014;**71**:706–15. http://dx.doi.org/10.1001/jamapsychiatry.2014.112

273. Weinstein MC, O'Brien B, Hornberger J, Jackson J, Johannesson M, McCabe C, *et al.* Principles of good practice for decision analytic modeling in health-care evaluation: report of the ISPOR task force on good research practices: modeling studies. *Value Health* 2003;**6**:9–17. http://dx.doi.org/10.1046/j.1524-4733.2003.00234.x

274. Oppe M, Devlin NJ, van Hout B, Krabbe PF, de Charro F. A program of methodological research to arrive at the new international EQ-5D-5L valuation protocol. *Value Health* 2014;**17**:445–53. http://dx.doi.org/10.1016/j.jval.2014.04.002

275. Longworth L, Yang Y, Young T, Mulhern B, Hernandez Alava M, Mukuria C, *et al.* Use of generic and condition-specific measures of health-related quality of life in NICE decision-making: a systematic review, statistical modelling and survey. *Health Technol Assess* 2014;**18**(9). http://dx.doi.org/10.3310/hta18090

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 1 Search strategy

The CCDANCTR-Studies Register was initially searched (September–December 2012) using the following index terms:

Condition = obsess* or compulsi*

AND

Intervention = (Citalopram or (Clomipramin* or Clorimipramin* or Chlomipramin* or Chlorimipramin*) or Escitalopram or Fluoxetine or Fluvoxamine or Paroxetine or Sertraline or Venlafaxine or Duloxetine or Mirtazapine or SSRI* or Serotonin or cognitive* or behavi* or exposure or "response prevention")

The CCDANCTR-References Register was initially searched using a more sensitive set of free-text terms (to identify additional untagged/uncoded reports of trials):

((obsess* or compulsi* or OCD) AND (Citalopram or (Clomipramin* or Clorimipramin* or Chlomipramin* or Chlorimipramin*) or Escitalopram or Fluoxetine or Fluvoxamine or Paroxetine or Sertraline or Venlafaxine or Duloxetine or Mirtazapine or SSRI* or (Serotonin and (uptake or reuptake or re-uptake)) or SNRI* or CBT or cognitive* or behavioral or behavioural or exposure or ERP or "response prevention" or ((*therap* or train* or treatment*) and (behavi* or expos*))))

As the number of studies retrieved in this initial search was not very large (643 studies), in order to increase the sensitivity of the search we decided to repeat the search using the condition only, (obsess* or compulsi*), without any other terms.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 2 Table of excluded studies

TABLE 63 List of excluded studies

Number	Reference	Summary comment for exclusion
1	Aigner M, Demal U, Zitterl W, Bach M, Trappl E, Lenz G. Behavioural group therapy for obsessive–compulsive disorder. *Verhaltenstherapie* 2004;**14**:7–14	Controlled but not randomised
2	Akouchekian S, Jamshidian Z, Maracy MR, Almasi A, Davarpanah Jazi AH. Religious cognitive behavioural therapy in religious oriented obsessive compulsive disorder. The 19th European Congress of Psychiatry, Vienna, Austria, 12–15 March 2011	Duplicate: early congress abstract of the full paper
3	Akouchekian S, Jamshidian Z, Maracy MR, Almasi A, Davarpanah Jazi AH. Effectiveness of religious cognitive–behavioural therapy on religious oriented obsessive compulsive disorder and its co-morbidity. *J Isfahan Med School* 2011;**28**:1	Special subgroup of OCD patients with religious-oriented symptoms (in Arabic)
4	Askin R, Turan M, Cilli AS, Kaya N. Clomipramine versus sertraline in the treatment of obsessive compulsive disorder. *Bull Clin Psychopharmacol* 1999;**9**:133–8	Usable data only for dichotomous outcome. No variability measure for continuous outcome
5	van Balkom A, Haan ED, Oppen PV, Spinhoven P, Hoogduin L, Dyck RV. Cognitive–behavioural Therapy Versus the Combination with Fluvoxamine in the Treatment of OCD. 150th Annual Meeting of the American Psychiatric Association. San Diego, California, USA, 17–22 May 1997	Duplicate reporting: early congress abstract of the van Balkom *et al.* 1998 paper
6	Belloch A, Cabedo E, Carrió C, Fernández-Alvarez H, García F, Larsson C. Group versus individual cognitive treatment for obsessive–compulsive disorder: changes in non-OCD symptoms and cognitions at post-treatment and 1-year follow-up. *Psychiatry Res* 2011;**187**:174–9	Secondary analysis of Cabedo *et al.* 2010 paper, which has also been excluded
7	Black DW, Monahan P, Gable J, Blum N, Clancy G, Baker P. Hoarding and treatment response in 38 nondepressed subjects with obsessive–compulsive disorder. *J Clin Psychiatry* 1998;**59**:420–5	Duplicate data, paroxetine vs. placebo already included in Hollander *et al.* 2003.[180] CBT arm not randomised
8	Cabedo E, Belloch A, Carrio C, Larsson C, Fernández-Alvarez H, García F. Group versus individual cognitive treatment for obsessive–compulsive disorder: changes in severity at post-treatment and 1-year follow-up. *Behav Cogn Psychother* 2010;**38**:227–32	Control intervention not covered (comparison between different forms of the same therapy)
9	Denys D, van Megen HJ, van der Wee N, Westenberg HG. A double-blind switch study of paroxetine and venlafaxine in obsessive–compulsive disorder. *J Clin Psychiatry* 2004;**65**:37–43	Extension of the Denys *et al.* 2003[167] study in non-responders (treatment refractory population)
10	Dougherty DD, Jameson M, Deckersbach T, *et al.* Open-label study of high (30 mg) and moderate (20 mg) dose escitalopram for the treatment of obsessive–compulsive disorder. *Int Clin Psychopharmacol* 2009;**24**:306–11	Dose ranging study of the same drug: no comparator
11	Eli Lilly. *Fluoxetine Treatment for Obsessive Compulsive Disorder in Children and Adolescents*. Clinical Study Register. ID No. 3032. URL: www.lillytrials.com/results/prozac.pdf (accessed 5 February 2016)	Duplicate with Geller *et al.* 2001[224]

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 63 List of excluded studies (*continued*)

Number	Reference	Summary comment for exclusion
12	Fineberg NA, Hughes A, Gale TM, Roberts A. Group cognitive behaviour therapy in obsessive–compulsive disorder (OCD): a controlled study. *Int J Psychiatry Clin Pract* 2005;**9**:257–63	This paper used systematic and not random sampling
13	Franklin ME, Abramowitz JS, Bux DA Jr, Zoellner LA, Feeny NC. Cognitive–behavioural therapy with and without medication in the treatment of obsessive–compulsive disorder. *Prof Psychol Res Pract* 2002;**33**:162–8	Observational study stratified by medication: not an experimental study
14	Giasuddini NA, Nahar JS, Morshed NM, Balhara YP, Sobhan MA. Efficacy of combination of fluoxetine and cognitive behavioural therapy and fluoxetine alone for the treatment of obsessive compulsive disorder. *Pak J Pharm Sci* 2013;**26**:95–8	Uncertain if truly randomised (abstract does not mention randomised, baseline scores of the scale used almost marginally significantly different between the two groups with $p = 0.07$), unable to find if the symptom scale used (Dhaka University Obsessive–Compulsive Scale) has been validated or not – reference given unable to locate, this scale has not been used again in research
15	GlaxoSmithKline. *Paroxetine versus Placebo in the Treatment of Obsessive–Compulsive Disorder*. Clinical Study Register. 1993. URL: www.gsk-clinicalstudyregister.com/study/29060/116 (accessed 5 February 2016)	Early report of the Hollander *et al.* 2003[180] data set
16	GlaxoSmithKline. *A Double-Blind Study to Assess the Efficacy and Tolerance of a Flexible Dose of Paroxetine Compared with a Flexible Dose of Clomipramine and Placebo in the Treatment of Obsessive Compulsive Disorder.* Clinical Study Register. Study No. MY-1037/BRL-029060/1/CPMS-136. 1993. URL: www.gsk-clinicalstudyregister.com/files2/2287.pdf (accessed 5 February 2016)	Duplicate of Zohar and Judge 1996[213]
17	Goodman WK, Lydiard RB, Rubin A, Hackett E, Wolkow R, Londborg PD. Safety of sertraline in long-term OCD treatment: preliminary results of a multicenter study. 152nd Annual Meeting of the American Psychiatric Association, Washington, DC, 15–20 May 1999	Relapse prevention study
18	Goodman WK, Price LH, Delgado PL, Palumbo J, Krystal JH, Nagy LM, *et al.* Specificity of serotonin reuptake inhibitors in the treatment of obsessive–compulsive disorder: comparison of fluvoxamine and desipramine. *Arch Gen Psychiatry* 1990;**47**:577–85	See control intervention
19	Greist JH. Fluvoxamine in obsessive compulsive disorder: a multicenter parallel design double-blind placebo-controlled trial. *Clin Neuropharm* 1992;**15**(Suppl. 1):310B	Abstract report with no data given. This is one of the two pivotal studies of fluvoxamine from Solvay but only the second – Goodman *et al.* 1996[177] – has been published. Greist *et al.* 1995[126] in a meta-analysis has combined the two trials but no data can be used either
20	Greist JH, Jefferson JW, Kobak KA, Chouinard G, DuBoff E, Halaris A, *et al.* A 1 year double-blind placebo-controlled fixed dose study of sertraline in the treatment of obsessive–compulsive disorder. *Int Clin Psychopharmacol* 1995;**10**:57–65	Duplicate of the CCSG 1991[154]
21	Hewlett WA, Vinogradov S, Agras WS. Clomipramine, clonazepam, and clonidine treatment of obsessive–compulsive disorder. *J Clin Psychopharmacol* 1992;**12**:420–30	Comparator not covered (clonazepam, clonidine)

TABLE 63 List of excluded studies (*continued*)

Number	Reference	Summary comment for exclusion
22	Hoehn-Saric R, Ninan P, Black DW, Stahl S, Greist JH, Lydiard B, *et al.* Multicenter double-blind comparison of sertraline and desipramine for concurrent obsessive–compulsive and major depressive disorders. *Arch Gen Psychiatry* 2000;**57**:76–82	See diagnosis and control not covered
23	Hohagen F, Konig A, Rasche-Rauchle H, Hand I, Rey E, Aldenhoff J, *et al.* Behaviour therapy and fluvoxamine versus behaviour therapy and placebo: results of a multicenter study. Sixth World Congress of Biological Psychiatry, Nice, France, 22–27 June 1997	Duplicate: early congress abstract of the Hohagen *et al.* 1998[179] paper
24	Holland R, Vardy A, Bolt G. A comparison of fluvoxamine (FL) and clomipramine (CLO) in the treatment of obsessive compulsive disorder (OCD). *Clin Neuropharm* 1992;**15**(Suppl. 1):311B	Abstract congress about tolerability including previously published data from Solvay
25	Insel TR, Murphy DL, Cohen RM, Alterman I, Kilts C, Linnoila M. Obsessive–compulsive disorder. A double-blind trial of clomipramine and clorgyline. *Arch Gen Psychiatry* 1983;**40**:605–12	Control intervention not covered
26	Jakubovski E, Diniz JB, Valerio C, Fossaluza V, Belotto-Silva C, Gorenstein C, *et al.* Clinical predictors of long-term outcome in obsessive–compulsive disorder. *Depress Anxiety* 2013;**30**:763–72	Duplicate of Belotto-Silva *et al.* 2012:[160] secondary
27	Jenike MA, Baer L, Summergrad P, Weilburg JB, Holland A, Seymour R. Obsessive–compulsive disorder: a double-blind, placebo-controlled trial of clomipramine in 27 patients. *Am J Psychiatry* 1989;**146**:1328–30	Duplicate of CCSG 1991[154]
28	Jonsson H, Hougaard E, Bennedsen BE. Randomised comparative study of group versus individual cognitive behavioural therapy for obsessive compulsive disorder. *Acta Psychiatr Scand* 2011;**123**:387–97	Control intervention not covered (comparison between different forms of the same therapy)
29	Karabanow O. Double-blind controlled study in phobias and obsessions. *J Int Med Res* 1977;**5**(Suppl. 5):42–8	Not exclusively OCD (phobias): unstandardised diagnosis
30	Kearns C, Tone Y, Rush G, Lucey JV. Effectiveness of group-based cognitive–behavioural therapy in patients with obsessive–compulsive disorder. *Psychiatrist* 2010;**34**:6–9	Uncontrolled case series (not randomised)
31	Khan MN, Hotiana UA, Ahmad S. Escitalopram in the treatment of obsessive–compulsive disorder: a double blind placebo control trial. *J Ayub Med Coll Abbottabad* 2007;**19**:58–63	First phase of the study open label uncontrolled trial, second phase randomised responders only for relapse prevention
32	Koran LM, Cain JW, Dominguez RA, Rush AJ, Thiemann S. Are fluoxetine plasma levels related to outcome in obsessive–compulsive disorder? *Am J Psychiatry* 1996;**153**:1450–4	Duplicate of Tollefson *et al.*, 1994[127]
33	Kudo Y. A placebo controlled double blind study in obsessive compulsive disorder with fluvoxamine. *Eur Neuropsychopharmacol* 1995;**5**:371–2	Early congress report of the Nakajima *et al.* 1996[201] paper
34	Leonard HL, Swedo SE, Rapoport JL, Koby EV, Lenane MC, Cheslow DL, *et al.* Treatment of obsessive–compulsive disorder with clomipramine and desipramine in children and adolescents. A double-blind crossover comparison. *Arch Gen Psychiatry* 1989;**46**:1088–92	Comparator not covered

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 63 List of excluded studies (*continued*)

Number	Reference	Summary comment for exclusion
35	Ma JD, Wang CH, Li HF, Zhang XL, Zhang YL, Hou YH, *et al.* Cognitive-coping therapy for obsessive–compulsive disorder: a randomised controlled trial. *J Psychiatr Res* 2013;**47**:1785–90	Non-extractable data for non-resistant patients: this study included patients who were treatment resistant within the study but no separate data are given for those who were non-resistant
36	Mallya GK, White K, Waternaux C, Quay S. Short and long term treatment of obsessive compulsive disorder with fluvoxamine. *Ann Clin Psychiatry* 1992;**4**:77–80	Duplicate data also reported in Goodman *et al.* 1996[177]
37	Marks IM, Lelliott P, Basoglu M, Noshirvani H, Monteiro W, Cohen D, *et al.* Clomipramine, self-exposure and therapist-aided exposure for obsessive–compulsive rituals. *Br J Psychiatry* 1988;**152**:522–34	No extractable data for treatment comparisons
38	Marks IM, Stern RS, Mawson D, Cobb J, McDonald R. Clomipramine and exposure for obsessive–compulsive rituals. *Br J Psychiatry* 1980;**136**:1–25	No extractable data for treatment comparisons: OCD diagnosis not standardised
39	Mavissakalian MR, Jones B, Olson S, Perel JM. Clomipramine in obsessive–compulsive disorder: clinical response and plasma levels. *J Clin Psychopharmacol* 1990;**10**:261–8	Duplicate with CCSG 1991[154]
40	Montgomery SA. Clomipramine in obsessional neurosis: a placebo-controlled trial. *Pharmacol Med* 1980;**1**:189–92	Duplicate: crossover data at the point of cross-over, also reported later in Montgomery *et al.* 1990
41	Mundo E, Bianchi L, Bellodi L. Efficacy of fluvoxamine, paroxetine, and citalopram in the treatment of obsessive–compulsive disorder: a single-blind study. *J Clin Psychopharmacol* 1997;**17**:267–71	Dose-ranging study of the same drug: no comparator
42	Mundo E, Maina G, Uslenghi C. Multicentre, double-blind, comparison of fluvoxamine and clomipramine in the treatment of obsessive–compulsive disorder. *Int Clin Psychopharmacol* 2000;**15**:69–76	Early report of a subset of the data that also reported in Mundo *et al.* 2001[200] (14 out of the 40 centres)
43	Muroff J, Steketee G, Bratiotis C, Ross A. Group cognitive and behavioural therapy and bibliotherapy for hoarding: a pilot trial. *Depress Anxiety* 2012;**29**:597–604	Hoarding disorder not OCD
44	Nazari H, Momeni N, Jariani M, Tarrahi MJ. Comparison of eye movement desensitization and reprocessing with citalopram in treatment of obsessive compulsive disorder. *Int J Psychiatry Clin Pract* 2011;**15**:270–4	Main intervention not covered: eye movement desensitization and reprocessing
45	Olatunji BO, Rosenfield D, Tart CD, Cottraux J, Powers MB, Smits JA. Behavioural versus cognitive treatment of obsessive–compulsive disorder: an examination of outcome and mediators of change. *J Consult Clin Psychol* 2013;**81**:415–28	Reports same data with Cottraux *et al.* 2001,[166] but different method of analysis and treating missing data (multilevel instead of last observation carried forwards)
46	Omranifard V, Akuchakian S, Almasi A, Maraci MR. Effect of religious cognitive–behavour therapy on religious content obsessive compulsive disorder and marital satisfaction [conference abstract]. *Eur Psychiatry* 2011;**26**(Suppl. 1):1742	Duplicate with the Akouchakian 2011 paper, which has been excluded
47	Pigott TA, L'Heureux F, Rubenstein CS, Bernstein SE, Hill JL, Murphy DL. A double-blind, placebo controlled study of trazodone in patients with obsessive–compulsive disorder. *J Clin Psychopharmacol* 1992;**12**:156–62	Intervention not included (trazodone)

TABLE 63 List of excluded studies (*continued*)

Number	Reference	Summary comment for exclusion
48	Pigott TA, Pato MT, Bernstein SE, Grover GN, Hill JL, Tolliver TJ, *et al.* Controlled comparisons of clomipramine and fluoxetine in the treatment of obsessive–compulsive disorder. Behavioural and biological results. *Arch Gen Psychiatry* 1990;**47**:926–32	Data not extractable at the point of cross-over
49	Rapoport J, Elkins R, Mikkelsen E. Clinical controlled trial of chlorimipramine in adolescents with obsessive–compulsive disorder. *Psychopharmacol Bull* 1980;**16**:61–3	Duplicate data - this is an early report of the Flament *et al.* 1985[222] study (this is reported and cited in the later Flament study)
50	Richter P, Witheridge K, Daskalakis ZJ, Deluce J, Nebitt R, Rector N, *et al.* Investigation of predictors of drug response in obsessive compulsive disorder (OCD) [conference abstract]. *Eur Neuropsychopharmacol* 2010;**20**:529	Congress abstract only: crossover of escitalopram versus clomipramine but no usable data given
51	Rouillon F. A double-blind comparison of fluvoxamine and clomipramine in OCD. 11th European College of Neuropyschopharmacology Congress. Paris, France, 31 October–4 November 1998	Duplicate, early congress report of the Mundo *et al.* 2001[200] study
52	Shareh H, Gharaie B, Vahid MKA. [Comparison between metacognitive therapy, fluvoxamine and combined therapy in the improvement of thought control strategies and stop signal criteria in obsessive compulsive disorder.] *IJPCP* 2011;**17**:199–207	Duplicate publication of Shareh *et al.* 2010[206]
53	Shareh H, Gharraee B, Vahid MKA. [Comparison of metacognitive therapy, fluvoxamine and combined treatment in improving metacognitive beliefs and subjective distress of patients with obsessive–compulsive disorder.] *Adv Cog Sci* 2011;**12**:45–59	Secondary analysis of Sharreh *et al.* 2010[206]
54	Shavitt R, Valerio C, Diniz JB, Fossaluza V, Belotto-Silva C, Jakubovski J, *et al.* Clinical predictors of treatment outcome in obsessive–compulsive disorder: a 2-year follow-up [conference abstract]. *Eur Neuropsychopharmacol* 2011;**21**(Suppl. 3):530	Congress abstract: extension of the Belotto-Silva *et al.* 2012[160] dataset
55	Sibon I, Leyton M, Gravel P, Sookman D, Pinard G, Diksic M, *et al.* CBT vs sertraline in OCD: effects on brain regional serotonin synthesis index. ACNP, Waikoloa, HI, 11–15 December 2005	Congress abstract, data not given for analysis, unable to decide on inclusion criteria
56	Solyom L, Sookman D. A comparison of clomipramine hydrochloride (Anafranil) and behaviour therapy in the treatment of obsessive neurosis. *J Int Med Res* 1977;**5**(Suppl. 5):49–61	Not randomised
57	Stein DJ, Hollander E, Mullen LS, DeCaria CM, Liebowitz MR. Comparison of clomipramine, alprazolam and placebo in the treatment of obsessive compulsive disorder. *Hum Psychopharmacol* 1992;**7**:389–95	Continuous data not extractable for treatment comparisons
58	Stein DJ, Tonnior B, Andersen EW. Escitalopram in the treatment of OCD. Proceedings of the 159th Annual Meeting of the American Psychiatric Association, Toronto, ON, 20–25 May 2006	Early congress abstract of the full Stein *et al.* 2007[124] paper
59	Steketee G, Frost RO, Tolin DF, Rasmussen J, Brown TA. Waitlist-controlled trial of cognitive behaviour therapy for hoarding disorder. *Depress Anxiety* 2010;**27**:476–84	Hoarding disorder not OCD

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 63 List of excluded studies (*continued*)

Number	Reference	Summary comment for exclusion
60	Tamimi Raed R, Mavissakalian Matig R, Jones B, Olson S. Clomipramine versus fluvoxamine in obsessive–compulsive disorder. *Ann Clin Psychiatry* 1991;**3**:275–9	Unblinded (open-label) controlled trial
61	Turner SM, Jacob RG, Beidel DC, Himmelhoch J. Fluoxetine treatment of obsessive–compulsive disorder. *J Clin Psychopharmacol* 1985;**5**:207–12	Uncontrolled study, only one fluoxetine arm
62	Vallejo J, Olivares J, Marcos T, Bulbena A, Menchón JM. Clomipramine versus phenelzine in obsessive–compulsive disorder. A controlled clinical trial. *Br J Psychiatry* 1992;**161**:665–70	Comparator (phenelzine) not covered
63	van Balkom AJ, de Haan E, van Oppen P, Spinhoven P, Hoogduin KA, van Dyck R. Cognitive and behavioural therapies alone versus in combination with fluvoxamine in the treatment of obsessive compulsive disorder. *J Nerv Ment Dis* 1998;**186**:492–9	The usable comparison (CBT vs. BT for 16 weeks) has been fully reported in Van Oppen *et al.* 1995[209] study, therefore this reports is duplicate. Remaining arms cannot be used owing to the complexity of the design
64	Wheadon DE, Bushnell WD, Steiner MA. A fixed-dose comparison of 20, 40 or 60 mg paroxetine to placebo in the treatment of obsessive–compulsive disorder. The annual meeting of the American College of Neuropsychopharmacology, Honolulu, HI, 1993	Early report of the Hollander *et al.* 2003[180] data set
65	Wilhelm S, Steketee G, Fama JM, Buhlmann U, Teachman BA, Golan E. Modular cognitive therapy for obsessive–compulsive disorder: a wait-list controlled trial. *J Cogn Psychother* 2009;**23**:294–305	Not random assignment (but 'according to therapist availability')
66	Williams TI, Salkovskis P, White H, Turner S, Forrester E, Allsopp M. Trialled cognitive behaviour therapy for children with OCD: a randomised controlled trial. 32nd Congress of the British Association for Behavioural and Cognitive Psychotherapies (jointly with the European Association of Behavioural and Cognitive Therapies), Manchester, 7–11 September 2004	Duplicate: early congress abstract of the Williams *et al.* 2010[236] full paper
67	Wootton BM, Dear BF, Johnston L, Terides MD, Titov N. Remote treatment of obsessive–compulsive disorder: a randomised controlled trial. *J Obsess Compuls Relat Disord* 2013;**2**:375–84	Main aim of the paper to compare different form of same treatment
68	Yaryura-Tobias JA, Neziroglu FA. Venlafaxine in obsessive–compulsive disorder. *Arch Gen Psychiatry* 1996;**53**:653–4	This is a letter from a small pilot study that, according to the authors, is double blind but the results have not been published. The authors report very general trends and the study is negative. It is not possible to extract any information

CCSG, Clomipramine Collaborative Study Group.

Appendix 3 Publications in waiting status

TABLE 64 List of publications in waiting status

Study	Comment for waiting status
Bai X, Liu C, Li X. A comparative trial of paroxetine versus clomipramine in treatment of obsessive–compulsive neurosis. *Pract Clin Med* 2002;**13**:63–4	In Chinese
Huang SN, Ji QM, Xie SP. A clinical comparative study of venlafaxine and paroxetine in the treatment of obsessive–compulsive disorder. *Shandong Arch Psychiatry* 2003;**16**:129–30	In Chinese
Jianxun L, Hu X, Haiying D. Clinical controlled study of paroxetine and clomipramine in treatment of obsessive–compulsive disorder. *Chin J Psychiatry* 1998;**31**:215–17	In Chinese
Jing Ping, ZA. Controlled study of clomipramine and amitriptyline for treating obsessive–compulsive disorder. *Chin J Neurol Psychiatry* 1990;**23**:68–70	In Chinese
Lakatos A. Cognitive behaviour therapy of obsessive–compulsive neurosis. *Praxis der Klinischen Verhaltensmedizin und Rehabilitation* 1994;**7**:99–106	Unable to locate (article in German): small study ($n = 28$) comparing BT with CBT – e-mailed author
Lei BS. A cross-over treatment of obsessive–compulsive neurosis with imipramine and chlorimipramine. *Chin J Neurol Psychiatry* 1986;**19**:275–8	In Chinese
Li X, Li Z, Li Z, Huang K, Sun L. Comparative study of citalopram and clomipramine in treatment of obsessive–compulsive disorder. *J Clin Psychological Med* 2005;**15**:354–5	In Chinese
Liu X, Liu J, Long J. Paroxetine combined with cognitive behaviour therapy in treatment of obsessive–compulsive disorder. *Chin J Health Psychology* 2005;**13**:86–7	In Chinese
Liu Y, Yao C, Xu M. A comparative study of fluoxetine and sertraline in the treatment of obsessive–compulsive disorder. *Shandong Arch Psychiatry* 2004;**17**:204–6	In Chinese
Marconi P, Pancheri P, Catapano F, Maj M. Fluvoxamine vs clomipramine in obsessive–compulsive disorder. 10th World Congress of Psychiatry, 23–28 August 1996, Madrid, Spain	Congress report, no further details, no usable data, no further publication
Montgomery SA, Montgomery DB, Fineberg N. Early response with clomipramine in obsessive compulsive disorder a placebo controlled study. *Prog Neuro-Psychopharmacol Biol Psychiatry* 1990;**14**:719–27	Uncertain if duplicate data with the Montgomery SA. Clomipramine in obsessional neurosis: a placebo-controlled trial. *Pharmacological Med* 1980;**1**:189–92 study: e-mailed authors
Qing Y, Denghua T, Xiaoyang G. Comparative study of cognitive therapy on obsessional compulsive disorder. *Chin Mental Health J* 2004;**18**:421–2	In Chinese
Rajagopalan R, Niveditha, Vijayakumar. A comparative study of efficacy and tolerability of fluvoxamine and sertraline in treatment of obsessive–compulsive disorder. *Int J Pharm Pharm Sci* 2013;**5**(Suppl. 2):629–32	Another publication of the same study (the thesis of the first author) reports slightly different and inconsistent results, although it is the same study with the same patient population – e-mailed authors
Saboory S, Mehryar H, Ghareeb A. Comparing the effectiveness of cognitive–behavioural techniques, clomipramine and their combination in treatment of obsessive–compulsive disorder. *Andeesheh Va Raftar* 1998;**4**:25–34	In Arabic

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 64 List of publications in waiting status (*continued*)

Study	Comment for waiting status
Shaomei L, Fenglia H. Combination of clomipramine with exposure therapy in treatment of obsessive–compulsive disorder. *Chin Mental Health J* 2001;**15**:239–40	In Chinese
Song R, Zheng Z, Chen M. Contrast study of the effects of paroxetine and chlorimipramine on obsessive–compulsive disorder. *J Linyi Med Coll* 2005;**27**:327–8	In Chinese
Todorov C, Brassard M, Fontaine R, Vezina M, Elie R. Fluoxetine vs clomipramine in obsessive–compulsive disorder. 10th World Congress of Psychiatry, 23–28 August 1996, Madrid, Spain	Congress: abstract – no further data
Ushijima S, Kamijima K, Asai M, Murasaki M, Nakajima T, Kudo Y, *et al.* Clinical evaluation of sertraline hydrochloride, a selective serotonin reuptake inhibitor in the treatment of obsessive–compulsive disorder. *Jpn J Neuropsychopharmacol* 1997;**19**:603–23	In Japanese: unable to locate
Wang Y, Long J, Sun M. A comparative study of citalopram and clomipramine in the treatment of obsessive–compulsive disorder. *J Clin Psychosomatic Dis* 2005;**11**:17–18	In Chinese
Wu H, Luo Y, Chen C. Control study of fluvoxamine and chlorimipramine in treatment of obsession. *Nervous Dis Mental Health* 2005;**5**:101–2	In Chinese
Yargic LI, Enderer M, Imre H, Sen D, Yazici O. A randomised single blind comparison of clomipramine and fluvoxamine in OCD patients. *Noropsikiyatri Arsivi* 1995;**32**:70–5	In Turkish: unable to locate
Yu L, Jin W. Clinical comparing study of sertraline and clomipramine in treatment of obsessive–compulsive disorder. *Med J Chin People Health* 2006;**18**:169–71	In Chinese
Zhao JP. [A control study of clomipramine and amitriptyline for treating obsessive–compulsive disorder.] *Chin J Neurol Psychiatry* 1991;**24**:68–70	In Chinese
Zhu J, Zhang F, Zhou D. A comparative study of mirtazapine and chlorimipramine in treatment of obsessive–compulsive disorder. *Shandong Arch Psychiatry* 2005;**18**:84–5	In Chinese

Appendix 4 Main data extraction: adult subset

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 65 Main data extraction for adult subset

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
Albert *et al.*, 2002[155]	2	2001	VEN	8	YBOCS	26	26	25	4.81	1	25	18.36	7.11			
Albert *et al.*, 2002[155]	2	2001	CLO	9	YBOCS	47	47	25.7	5.07	7	40	17.3	6.15			
Ananth *et al.*, 1981[156]	2	1981	CLO	9	Severity Quest	10	10	122	NA	1	9	43	NA			
Ananth *et al.*, 1981[156]	2	1981	AMI	13	Severity Quest	10	10	113	NA	2	8	76	NA			
Anderson and Rees, 2007[157]	2	2007	CBT	11	YBOCS	21	17	24	6.2	4	17	16.7	6.8			
Anderson and Rees, 2007[157]	2	2007	Waitlist	2	YBOCS	17	14	24.1	5.1	3	14	23.5	6.4			
Andersson *et al.*, 2012[158]	2	2012	CBT	11	YBOCS	50	50	21.42	4.59	2	49	12.94	6.26			
Andersson *et al.*, 2012[158]	2	2012	PsychPLA	25	YBOCS	51	51	20.8	4.04	0	51	18.88	4.18			
Belloch *et al.*, 2008[159]	2	2008	BT	10	YBOCS	15	13	24.69	5.72	2	13	8.31	8.75			
Belloch *et al.*, 2008[159]	2	2008	CT	12	YBOCS	18	16	26.4	4.98	2	16	6.8	3.55			
Belotto-Silva *et al.*, 2012[160]	2	2012	FLX	3	YBOCS	88	88	25.82	5.1	33	88	20.29	8.05			
Belotto-Silva *et al.*, 2012[160]	2	2012	CBT	11	YBOCS	70	70	25.97	5.48	18	70	19.97	8.48			
Bergeron *et al.*, 2002[161]	2	2002	FLX	3	YBOCS	73	72	26.1	5.1	22	72	NA	NA	72	9.7	7.7
Bergeron *et al.*, 2002[161]	2	2002	SER	6	YBOCS	77	76	25.3	5	22	76	NA	NA	76	9.6	7.9
Bisserbe *et al.*, 1997[162]	2	1997	SER	6	YBOCS	86	86	27.86	NA	23	86	13.56	NA			

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
Bisserbe *et al.*, 1997[162]	2	1997	CLO	9	YBOCS	82	81	27.43	NA	35	81	15.72	NA			
CCSG1, 1991[154]	2	1991	CLO	9	YBOCS	118	118	26.3	5.5	17	102	16.23	0.73			
CCSG1, 1991[154]	2	1991	PLA	1	YBOCS	121	120	26	5.5	13	108	25.11	0.61			
CCSG1, 1991[154]	2	1991	CLO	9	YBOCS	142	134	26.2	4.9	14	120	14.7	0.68			
CCSG1, 1991[154]	2	1991	PLA	1	YBOCS	139	129	27.2	4.8	12	119	25.59	0.53			
Chouinard *et al.*, 1990[163]	2	1990	SER	6	YBOCS	43	43	23.4	4.9	6				43	3.79	5.22
Chouinard *et al.*, 1990[163]	2	1990	PLA	1	YBOCS	44	44	22.6	6.1	4				44	1.48	5.22
Cordioli *et al.*, 2003[164]	2	2003	CBT	11	YBOCS	23	23	26.7	4.9	1	23	15.1	7.8			
Cordioli *et al.*, 2003[164]	2	2003	Waitlist	2	YBOCS	24	24	24.7	5.2	1	24	23.2	5.5			
Cottraux *et al.*, 1993[165]	3	1993	FLV	4	NA	20	13	NA		7	13	NA				
Cottraux *et al.*, 1993[165]	3	1993	BT	10	NA	20	15	NA		5	15	NA				
Cottraux *et al.*, 1993[165]	3	1993	BT + FLV	15	NA	20	16	NA		4	16	NA				
Cottraux *et al.*, 2001[166]	2	2001	BT	10	YBOCS	33	32	28.5	4.9	3				30	12.1	7.8
Cottraux *et al.*, 2001[166]	2	2001	CT	12	YBOCS	32	30	28.6	5.1	2				30	12.5	8.2
Denys *et al.*, 2003[167]	2	2003	PAR	5	YBOCS	75	72	25.3	5.6	9	72	17.5	8	72	7.8	5.4
Denys *et al.*, 2003[167]	2	2003	VEN	8	YBOCS	75	73	26.9	5	4	73	19.7	8.6	73	7.2	7.5
Emmelkamp and Beens, 1991[168]	2	1991	CT	12	Maudsley OCI	15	10	17.2	6.2	5	10	12.3	7.3			

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 65 Main data extraction for adult subset (*continued*)

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
Emmelkamp and Beens, 1991[168]	2	1991	BT	10	Maudsley OCI	15	11	16.3	5.7	4	11	13.7	5.8			
Emmelkamp *et al.*, 1988[169]	2	1988	CT	12	Maudsley OCI	10	9	15.6	2.9	1	9	11.3	1.7			
Emmelkamp *et al.*, 1988[169]	2	1988	BT	10	Maudsley OCI	10	9	15.6	4	1	9	12.6	5.4			
Fals-Stewart *et al.*, 1993[170]	2	1993	BT	10	YBOCS	34	31	20.2	NA	3	31	12.1	NA			
Fals-Stewart *et al.*, 1993[170]	2	1993	PsychPLA	25	YBOCS	32	32	19.9	NA	0	32	18.1	NA			
Foa *et al.*, 2005[171]	4	2005	BT	10	YBOCS	37	29	24.6	4.8	16	29	11	7.9			
Foa *et al.*, 2005[171]	4	2005	CLO	9	YBOCS	47	36	26.3	4.4	20	36	18.2	7.8			
Foa *et al.*, 2005[171]	4	2005	BT + CLO	18	YBOCS	33	31	25.4	4.6	14	31	10.5	8.2			
Foa *et al.*, 2005[171]	4	2005	PLA	1	YBOCS	32	26	25	4	12	26	22.2	6.4			
Freeman *et al.*, 1994[172]	2	1994	FLV	4	YBOCS	34	34	26.2	NA	6					8.6	NA
Freeman *et al.*, 1994[172]	2	1994	CLO	9	YBOCS	32	30	25.5	NA	13					7.8	NA
Freeston *et al.*, 1997[173]	2	1997	CBT	11	YBOCS	15	15	25.1	5	3	15	12.2	9.6			
Freeston *et al.*, 1997[173]	2	1997	Waitlist	2	YBOCS	14	14	21.2	6	0	14	22	6			
GlaxoSmithKline, 2005[174]	3	1993	PLA	1	YBOCS	77	75	24.66	NA	20				75	4.61	0.87
GlaxoSmithKline, 2005[174]	3	1993	PAR	5	YBOCS	82	79	23.28	NA	28				79	5.61	0.84
GlaxoSmithKline, 2005[174]	3	1993	CLO	9	YBOCS	82	78	23.9	NA	28				78	7.73	0.84

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
GlaxoSmithKline, 2005[175]	2	1999	PAR	5	YBOCS	73	72	25.11	6.07	1	72	10.85	6.85	72	14.26	6.33
GlaxoSmithKline, 2005[175]	2	1999	CLO	9	YBOCS	73	69	24.07	5.74	4	69	10.88	6.86	69	13.19	6.48
Goodman *et al.*, 1989[176]	2	1989	PLA	1	YBOCS	23	21	25.6	6.6	6	21	28	7			
Goodman *et al.*, 1989[176]	2	1989	FLV	4	YBOCS	23	21	25	6	2	21	19.4	7			
Goodman *et al.*, 1996[177]	2	1996	PLA	1	YBOCS	80	78	24	NA	17				78	1.71	4.88
Goodman *et al.*, 1996[177]	2	1996	FLV	4	YBOCS	80	78	22.6	NA	23				78	3.95	6.28
Greist *et al.*, 1995[126]	2	1995	SER	6	YBOCS	241	240	23.8	5.3	65				240	5.57	6.19
Greist *et al.*, 1995[126]	2	1995	PLA	1	YBOCS	84	84	23.4	4.9	24				84	3.41	6.19
Greist *et al.*, 2002[178]	2	2002	BT	10	YBOCS	69	55	25.2	4.6	14	55	17.6	6.2			
Greist *et al.*, 2002[178]	2	2002	PsychPLA	25	YBOCS	75	66	25.8	5.1	9	66	24.1	6.7			
Hohagen *et al.*, 1998[179]	2	1998	BT + PLA	21	YBOCS	30	25	28.4	3.8	NA	25	15.9	7.9			
Hohagen *et al.*, 1998[179]	2	1998	BT + FLV	15	YBOCS	30	24	27.9	2.9	NA	24	12.4	6.8			
Hollander *et al.*, 2003[181]	2	2003	PLA	1	YBOCS	126	120	26.4	0.3	31	120	21	1	120	5.60	0.70
Hollander *et al.*, 2003[181]	2	2003	FLV	4	YBOCS	127	117	26.8	0.3	43	117	17.6	1.1	117	8.5	0.70
Hollander *et al.*, 2003[181]	4	2003	PLA	1	YBOCS	89	89	25.6	NA	15				89	3.33	NA

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 65 Main data extraction for adult subset (*continued*)

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
Hollander *et al.*, 2003[180]	4	2003	PAR-20	5	YBOCS	88	88	25.9	NA	14				88	4.14	NA
Hollander *et al.*, 2003[180]	4	2003	PAR-40	5	YBOCS	86	86	25.4	NA	20				86	6.35	NA
Hollander *et al.*, 2003[180]	4	2003	PAR-60	5	YBOCS	85	85	25.3	NA	19				85	7.34	NA
Jaurrieta *et al.*, 2008[182]	2	2008	CBT	11	YBOCS	19	19	25.2	7.7	NA	19	17.8	8.4			
Jaurrieta *et al.*, 2008[182]	2	2008	Waitlist	2	YBOCS	19	19	24.8	7.3	NA	19	24.6	8.9			
Jenike *et al.*, 1990[183]	2	1990	SER	6	YBOCS	10	10	22.8	6	0	10	20.6	9.2			
Jenike *et al.*, 1990[183]	2	1990	PLA	1	YBOCS	9	9	22.8	4.8	0	9	22.3	7.8			
Jenike *et al.*, 1990[184]	2	1990	PLA	1	YBOCS	20	20	22.7	6.1	0	20	21.8	7.6			
Jenike *et al.*, 1990[184]	2	1990	FLV	4	YBOCS	20	18	22.6	3.5	2	18	18.8	4			
Jenike *et al.*, 1997[185]	2	1997	PLA	1	YBOCS	21	19	18.9	6.2	3	18	18.7	6.1			
Jenike *et al.*, 1997[185]	2	1997	FLX	3	YBOCS	23	22	19	5.4	4	19	16.2	6.3			
Jones and Menzies, 1998[186]	2	1998	CT	12	Maudsley OCI	12	11	17.82	NA	1	11	14.27	NA			
Jones and Menzies, 1998[186]	2	1998	Waitlist	2	Maudsley OCI	11	10	17.6	NA	1	10	17.7	NA			
Kamijima *et al.*, 2004[187]	2	2004	PLA	1	YBOCS	96	94	23.4	4.72	NA	94	20.3	7.38			
Kamijima *et al.*, 2004[187]	2	2004	PAR	5	YBOCS	95	94	24.3	4.4	NA	94	15.8	8.09			
Khodarahimi, 2009[188]	2	2009	Waitlist	2	YBOCS	20	20	36.4	2.26	0	20	36.45	2.24			

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
Khodarahimi, 2009[188]	2	2009	BT	10	YBOCS	20	20	37.2	1.91	0	20	5.58	2.39			
Kobak *et al.*, 2005[189]	2	2005	PLA	1	YBOCS	30	30	23.47	5.54	9	30	19.87	7.46			
Kobak *et al.*, 2005[189]	2	2005	HYP	13	YBOCS	30	30	23.17	3.81	8	30	19.75	7.46			
Koran *et al.*, 1996[190]	2	1996	FLV	4	YBOCS	37	34	25.5	5.97	8	34	17.8	7.7			
Koran *et al.*, 1996[190]	2	1996	CLO	9	YBOCS	42	39	24.3	5.95	15	39	17	8.55			
Kronig *et al.*, 1999[191]	2	1999	SER	6	YBOCS	86	86	25.21	3.79	25				85	8.5	10.50
Kronig *et al.*, 1999[191]	2	1999	PLA	1	YBOCS	81	81	25.05	4.09	25				79	4.14	10.50
Lindsay *et al.*, 1997[192]	2	1997	BT	10	YBOCS	9	9	28.7	4.56	0	9	11	3.81			
Lindsay *et al.*, 1997[192]	2	1997	PsychPLA	25	YBOCS	9	9	24.44	6.98	0	9	25.89	5.8			
López-Ibor *et al.*, 1996[193]	2	1996	FLX	3	YBOCS	30	30	27.6	5.2	5	30			30	7.5	9.29
López-Ibor *et al.*, 1996[193]	2	1996	CLO	9	YBOCS	25	24	25.6	6.09	3	24			24	8.9	7.13
Mavissakalian *et al.*, 1985[194]	2	1985	CLO	9	OCNS	NA	7	74.5	4.74	NA	7	48	6.94			
Mavissakalian *et al.*, 1985[194]	2	1985	PLA	1	OCNS	NA	5	80	6.55	NA	5	69	8.51			
McLean *et al.*, 2001[195]	2	2001	CT	12	YBOCS	49	33	21.9	5.8	18	31	16.1	6.7			
McLean *et al.*, 2001[195]	2	2001	BT	10	YBOCS	44	40	21.8	4.6	12	32	13.2	7.2			

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 65 Main data extraction for adult subset (*continued*)

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
Milanfranchi *et al.*, 1997[196]	2	1997	CLO	9	YBOCS	13	13	27.5	6.8	1	12	16.5	11			
Milanfranchi *et al.*, 1997[196]	2	1997	FLV	4	YBOCS	13	13	29.7	5.5	0	13	18.4	9.2			
Montgomery *et al.*, 1993[197]	4	1993	PLA	1	YBOCS	57	56	23.25	6.86	15	56	20.04	NA	56	3.7	5.98
Montgomery *et al.*, 1993[197]	4	1993	FLX-20	3	YBOCS	53	52	23.79	4.91	14	53	18.66	NA	52	5.13	6.41
Montgomery *et al.*, 1993[197]	4	1993	FLX-40	3	YBOCS	52	52	25.52	5.59	13	52	19.06	NA	52	4.76	6.89
Montgomery *et al.*, 1993[197]	4	1993	FLX-60	3	YBOCS	55	54	22.98	7.18	14	54	17.71	NA	54	6.07	6.92
Montgomery *et al.*, 2001[198]	4	2001	CIT-20	7	YBOCS	102	102	25.1	3.9	16				102	8.4	7.3
Montgomery *et al.*, 2001[198]	4	2001	CIT-40	7	YBOCS	98	98	26	3.7	15				98	8.9	7.00
Montgomery *et al.*, 2001[198]	4	2001	CIT-60	7	YBOCS	100	100	25.9	4.5	15				100	10.4	6.90
Montgomery *et al.*, 2001[198]	4	2001	PLA	1	YBOCS	101	101	25.4	3.9	17				101	5.6	6.90
Mundo *et al.*, 1997[199]	3	1997	FLV	4	YBOCS	10	10	25.4	6.5	0	10	16.2	8.9			
Mundo *et al.*, 1997[199]	3	1997	PAR	5	YBOCS	9	9	30.5	3.9	0	9	21.6	7.6			
Mundo *et al.*, 1997[199]	3	1997	CIT	7	YBOCS	11	11	29.3	3.9	0	11	19.8	10.1			
Mundo *et al.*, 2001[200]	2	2001	CLO	9	YBOCS	112	112	25.4	6.1	26	112	13.4	NA			
Mundo *et al.*, 2001[200]	2	2001	FLV	4	YBOCS	115	115	26.5	5.6	19	115	14.3	NA			
Nakajima *et al.*, 1996[201]	2	1996	FLV	4	YBOCS	61	61	24.7	4.8	NA	61	NA	NA	61	7.1	7.03

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
Nakajima *et al.*, 1996[201]	2	1996	PLA	1	YBOCS	33	33	26.2	6.1	NA	33	NA	NA	33	1.9	7.20
Nakatani *et al.*, 2005[202]	3	2005	PsychPLA	25	YBOCS	9	8	30.5	3.7	1	8	28.4	5.5			
Nakatani *et al.*, 2005[202]	3	2005	FLV	4	YBOCS	11	10	28.4	3.8	1	10	20.2	9.4			
Nakatani *et al.*, 2005[202]	3	2005	BT	10	YBOCS	11	10	29.9	3.1	1	10	12.9	4.9			
O'Connor *et al.*, 1999[203]	4	1999	SRI	14	YBOCS	6	5	21	2.9	1	5	12	4.5			
O'Connor *et al.*, 1999[203]	4	1999	Waitlist	2	YBOCS	6	6	19.3	4.5	0	6	17.5	4			
O'Connor *et al.*, 1999[203]	4	1999	CBT	11	YBOCS	7	6	23.5	4	1	6	13.3	8.6			
O'Connor *et al.*, 1999[203]	4	1999	CBT + SRI	20	YBOCS	10	9	23.8	5.4	1	9	17.8	4.7			
O'Connor *et al.*, 2006[204]	2	2006	PLA	1	YBOCS	10	10	27.3	4.3	NA	10	25.4	3.5			
O'Connor *et al.*, 2006[204]	2	2006	FLV	4	YBOCS	11	11	28.3	3.9	NA	11	24	4.7			
Perse *et al.*, 1987[205]	2	1987	PLA	1	Maudsley OCI	10	8	NA	NA	2		NA	NA			
Perse *et al.*, 1987[205]	2	1987	FLV	4	Maudsley OCI	10	8	NA	NA	2		NA	NA			
Shareh *et al.*, 2010[206]	3	2010	FLV	4	YBOCS	7	6	25.83	5.77	1	6	16.66	3.2			
Shareh *et al.*, 2010[206]	3	2010	CBT	11	YBOCS	7	7	29	6.73	0	7	7	2.38			
Shareh *et al.*, 2010[206]	3	2010	FLV + CBT	16	YBOCS	7	6	26.16	7.98	1	6	8.5	2.42			

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

NIHR Journals Library www.journalslibrary.nihr.ac.uk

TABLE 65 Main data extraction for adult subset (*continued*)

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
Sousa *et al.*, 2006[207]	2	2006	SER	6	YBOCS	28	25	26.12	NA	3	25	18.76	NA			
Sousa *et al.*, 2006[207]	2	2006	CBT	11	YBOCS	28	25	25.08	NA	3	25	14.28	NA			
Stein *et al.*, 2007[124]	4	2007	PLA	1	YBOCS	115	113	27.7	4.2	18				113	8.46	0.76
Stein *et al.*, 2007[124]	4	2007	PAR	5	YBOCS	119	116	27.3	4	29				116	11.67	0.78
Stein *et al.*, 2007[124]	4	2007	ESCIT-10	19	YBOCS	116	112	26.6	3.7	24				112	11.43	0.78
Stein *et al.*, 2007[124]	4	2007	ESCIT-20	19	YBOCS	116	114	26.6	3.9	21				114	12.14	0.77
Thoren *et al.*, 1980[208]	2	1980	CLO	9	OCD symptom scale	NA	8	4.38	1.22	NA	8	2.94	1.15			
Thoren *et al.*, 1980[208]	2	1980	PLA	1	OCD symptom scale	NA	8	3.94	1.24	NA	8	3.69	1.46			
Tollefson *et al.*, 1994[127]	4	1994	PLA	1	YBOCS	89	89	24.3	5.7	13	76	23.6	7.5	89	0.8	5.66
Tollefson *et al.*, 1994[127]	4	1994	FLX-20	3	YBOCS	87	87	23.6	5.7	12	75	18.9	8.3			
Tollefson *et al.*, 1994[127]	4	1994	FLX-40	3	YBOCS	89	89	23.5	5.6	22	67	18.1	7.9			
Tollefson *et al.*, 1994[127]	4	1994	FLX-60	3	YBOCS	90	90	24.4	5.1	22	68	16.8	7.8			
Van Oppen *et al.*, 1995[209]	2	1995	CT	12	YBOCS	35	28	28.7	5.3	7	28	13.4	9.4			
Van Oppen *et al.*, 1995[209]	2	1995	BT	10	YBOCS	36	29	31.4	5	7	29	17.9	9			
Volavka *et al.*, 1985[210]	2	1985	CLO	9	SRONS	11	8	61.5	13.6	3	8	41.9	13.9			

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
Volavka *et al.*, 1985[210]	2	1985	IMI	13	SRONS	12	8	80.7	11.5	4	8	63.6	20.5			
Whittal *et al.*, 2005[211]	2	2005	CT	12	YBOCS	41	34	23.5	4.3	11	30	10.6	7.1			
Whittal *et al.*, 2005[211]	2	2005	BT	10	YBOCS	42	37	21.66	5.9	13	29	10.41	7.6			
Whittal *et al.*, 2010[212]	2	2010	CT	12	YBOCS	40	40	18.03	6.29	3	37	6.43	4.77			
Whittal *et al.*, 2010[212]	2	2010	PsychPLA	25	YBOCS	33	33	17.73	7.73	3	30	9.1	6.48			
Zohar and Judge, 1996[213]	3	1996	PLA	1	YBOCS	100	99	NA	NA	40				99	4.2	7.2
Zohar and Judge, 1996[213]	3	1996	PAR	5	YBOCS	205	201	NA	NA	53				201	6.4	7.1
Zohar and Judge, 1996[213]	3	1996	CLO	9	YBOCS	101	99	NA	NA	36				99	7	6.8

AMI, amitriptyline; BL_m, mean YBOCS (or other scale) at baseline; BLn, number at baseline; BL_sd, SD of YBOCS at baseline; CCSG, Clomipramine Collaborative Study Group; CGE_m, mean change in YBOCS from baseline; CGEn, number of patients with data for score changes; CGE_sd, SD of change; CIT, citalopram; CLO, clomipramine; Dr_*n*, total dropouts; ESCIT, escitalopram; FLV, fluvoxamine; FLX, fluoxetine; FU_mean, mean YBOCS at the end of study; FU_*n*, number at the end of study; FU_sd, SD of YBOCS (of other scale) at the end of study; HYP, hypericum; IMI, imipramine; NA, not available; OCI, Obssessive–Compulsive Inventory; OCNS, Obsessive–Compulsive Neurotic Scale; OCR, Obssessive–Compulsive Rating scale; PAR, paroxetine; PLA, placebo; PsychPLA, psychological placebo; SER, sertraline; SRI, serotonin reuptake inhibitor; SRONS, Self-Rating Obsessional Neurotic Scale; VEN, venlafaxine.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 5 Main data extraction: children and adolescents subset

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 66 Main data extraction for children and adolescents subset

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
Alaghband-Rad and Hakimshooshtary, 2009[215]	2	2009	FLX	3	CYBOCS	15	15	26.66	NA	NA	NA	15	NA			
Alaghband-Rad and Hakimshooshtary, 2009[215]	2	2009	CIT	7	CYBOCS	14	14	28	NA	NA	NA	16.9	NA			
Asbahr *et al.*, 2005[216]	2	2005	SER	6	CYBOCS	20	19	27	6.65	1	19	NA	NA			
Asbahr *et al.*, 2005[216]	2	2005	CBT	11	CYBOCS	20	20	26.3	4.9	0	20	NA	NA			
Barrett *et al.*, 2004[217]	2	2004	CBT	11	CYBOCS	24	22	23.64	4.3	NA	22	8.36	6.93			
Barrett *et al.*, 2004[217]	2	2004	Waitlist	2	CYBOCS	24	24	22.95	5.49	NA	24	24.04	4.14			
Bolton and Perrin, 2008[218]	2	2008	BT	10	CYBOCS	10	10	24	4.78	2	10	13.9	10.74			
Bolton and Perrin, 2008[218]	2	2008	Waitlist	2	CYBOCS	10	10	22	8.25	0	10	21.1	5.9			
Bolton *et al.*, 2011[219]	2	2011	Waitlist	2	CYBOCS	24	24	24,2	5	3	24	23.3	8.3			
Bolton *et al.*, 2011[219]	2	2011	CBT	11	CYBOCS	36	36	22.3	5	2	36	9.5	8			
de Haan *et al.*, 1998[220]	2	1998	CLO	9	CYBOCS	10	10	23.8	7.2	0	10	17.6	11.8			
de Haan *et al.*, 1998[220]	2	1998	BT	10	CYBOCS	13	12	21.5	5.9	1	12	9.1	9.1			
DeVeaugh-Geiss *et al.*, 1992[221]	2	1992	CLO	9	CYBOCS	31	31	27.1	NA	4	31	17.1	NA			
DeVeaugh-Geiss *et al.*, 1992[221]	2	1992	PLA	1	CYBOCS	29	29	28.4	NA	2	29	26	NA			
Flament *et al.*, 1985[222]	2	1985	CLO	9	OCR scale	NA	NA	NA	NA	NA	NA	9.1	3.6			
Flament *et al.*, 1985[222]	2	1985	PLA	1	OCR scale	NA	NA	NA	NA	NA	NA	12.1	4			
Freeman *et al.*, 2008[223]	2	2008	CBT	11	CYBOCS	22	22	22.95	3.84	6	22	14.45	8.16			
Freeman *et al.*, 2008[223]	2	2008	PsychPLA	25	CYBOCS	20	20	21.7	4.52	5	20	17.1	7.57			

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
Geller *et al.*, 2001[224]	2	2001	PLA	1	CYBOCS	32	32	26.3	4.6	12				32	5.2	7.4
Geller *et al.*, 2001[224]	2	2001	FLX	3	CYBOCS	71	71	24.5	5.1	22				71	9.5	9.2
GlaxoSmithKline, 2001[225]	2	2001	PAR	5	CYBOCS	100	98	24.4	4.95	35	98					
GlaxoSmithKline, 2001[225]	2	2001	PLA	1	CYBOCS	107	105	25.3	5.05	27	105					
Liebowitz *et al.*, 2002[226]	2	2002	PLA	1	CYBOCS	22	22	23.82	5.77	4	22	18.55	11.44			
Liebowitz *et al.*, 2002[226]	2	2002	FLX	3	CYBOCS	21	21	22.5	4.16	1	21	14.71	8.73			
March *et al.*, 1990[227]	2	1990	CLO	9	YBOCS	8	8	24.5	3.6	2	8	19.3	8.6			
March *et al.*, 1990[227]	2	1990	PLA	1	YBOCS	8	8	27.4	3.4	0	8	25.6	2.4			
March *et al.*, 1998[228]	2	1998	SER	6	CYBOCS	92	92	23.4	NA	18				92	6.8	0.87
March *et al.*, 1998[228]	2	1998	PLA	1	CYBOCS	95	95	22.2	NA	13				95	3.4	0.82
Neziroglu *et al.*, 2000[229]	2	2000	FLV	4	CYBOCS	5	5	22.8	4.21	0	5	19.2	3.56			
Neziroglu *et al.*, 2000[229]	2	2000	BT + FLV	15	CYBOCS	5	5	28	6.2	0	5	16.4	5.18			
Piacentini *et al.*, 2011[230]	2	2011	CBT	11	CYBOCS	49	49	24.7	0.71	8	49	13.3	1.33			
Piacentini *et al.*, 2011[230]	2	2011	PsychPLA	25	CYBOCS	22	22	25.3	0.97	5	22	17.2	2.14			
Riddle *et al.*, 1992[231]	2	1992	PLA	1	CYBOCS	6	6	20.2	7.7	1	6	14.8	7			
Riddle *et al.*, 1992[231]	2	1992	FLX	3	CYBOCS	7	7	24.3	4.2	1	7	13.6	5.7			
Riddle *et al.*, 2001[232]	2	2001	PLA	1	CYBOCS	63	63	24.2	4.8	27	63	20.9	8.5			
Riddle *et al.*, 2001[232]	2	2001	FLV	4	CYBOCS	57	57	24.2	4.4	19	57	18.2	8.6			
Storch *et al.*, 2011[233]	2	2011	CBT	11	CYBOCS	16	16	25.38	3.81	2	16	11.13	10.53			
Storch *et al.*, 2011[233]	2	2011	Waitlist	2	CYBOCS	15	15	21.27	2.74	0	15	18.53	8.11			
Storch *et al.*, 2013[234]	2	2013	SER + CBT	17	CYBOCS	14	14	23.64	4.48	6	14	15.43	9.72			
Storch *et al.*, 2013[234]	2	2013	CBT + PLA	22	CYBOCS	16	16	25.06	4.01	3	16	15.56	6.62			

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 66 Main data extraction for children and adolescents subset (*continued*)

Study	Number of arms	Year	Intervention	Coding of intervention	Scale used	Original *N* randomised	BLn	BL_m	BL_sd	Dr_*n*	FU_*n*	FU_mean	FU_sd	CGEn	CGE_m	CGE_sd
The Pediatric OCD Treatment Study, 2004[236]	4	2004	SER	6	CYBOCS	28	28	23.5	4.7	2	28	16.5	9.1			
The Pediatric OCD Treatment Study, 2004[236]	4	2004	CBT	11	CYBOCS	28	28	26	4.6	3	28	14	9.5			
The Pediatric OCD Treatment Study, 2004[236]	4	2004	SER + CBT	17	CYBOCS	28	28	23.8	3	3	28	11.2	8.6			
The Pediatric OCD Treatment Study, 2004[236]	4	2004	PLA	1	CYBOCS	28	28	25.2	3.3	7	28	21.5	5.4			
Williams *et al.*, 2010[235]	2	2010	CBT	11	CYBOCS	11	11	23.09	1.22	1	11	12.09	2.25			
Williams *et al.*, 2010[235]	2	2010	Waitlist	2	CYBOCS	10	10	21.05	1.84	1	10	19.6	2.03			

BL_m, mean CYBOCS (or other scale) at baseline; BLn, number at baseline; BL_sd, SD of CYBOCS at baseline; CGE_m, mean change in YBOCS from baseline; CGEn, number of patients with data for score changes; CGE_sd, SD of change; CIT, citalopram; CLO, clomipramine; Dr_*n*, total dropouts; FLV, fluvoxamine; FLX, fluoxetine; FU_mean, mean CYBOCS at the end of study; FU_*n*, number at the end of study; FU_sd, SD of CYBOCS (of other scale) at the end of study; NA, not available; PAR, paroxetine; PLA, placebo; PsychPLA, psychological placebo; SER, sertraline.

Appendix 6 Additional extraction: intervention details

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 67 Additional extraction: adult subset

Study	Setting[a]	Intervention	Average or mean dose at the end (mg)	SD of mean dose (mg)	Minimum dose during the study (mg)	Maximum dose during the study (mg)	Number of sessions	Duration of session (hours)
Albert *et al.*, 2002[155]	1	VEN	265	52.5	225	350		
Albert *et al.*, 2002[155]	1	CLO	168	28.9	150	225		
Ananth *et al.* 1981[156]	3	CLO	133.3	NA	75	300		
Ananth *et al.* 1981[156]	3	AMI	197.4	NA	75	300		
Anderson and Rees, 2007[157]	1	CBT					10	1
Anderson and Rees, 2007[157]	1	Waitlist					Waitlist	Waitlist
Anderson and Rees, 2007[157]	1	CBT					10	NA
Anderson and Rees, 2007[157]	1	PsychPLA					PsychPLA	PsychPLA
Belloch *et al.*, 2008[159]	1	BT					20	1
Belloch *et al.*, 2008[159]	1	CT					18	1
Belotto-Silva *et al.*, 2012[160]	1	FLX	80	Fixed				
Belotto-Silva *et al.*, 2012[160]	1	CBT					12	2
Bergeron *et al.*, 2002[161]	1	FLX	56.7	23	20	80		
Bergeron *et al.*, 2002[161]	1	SER	139.5	58.5	50	200		
Bisserbe *et al.*, 1997[162]	1	SER	136	NA	50	200		
Bisserbe *et al.*, 1997[162]	1	CLO	110	NA	50	200		
CCSG1, 1991[154]	1	CLO	234.5	NA	100	300		
CCSG1, 1991[154]	1	PLA	PLA					
CCSG2, 1991[154]	1	CLO	218.8	NA	100	300		
CCSG2, 1991[154]	1	PLA	PLA					
Chouinard *et al.*, 1990[163]	1	SER	185	NA	50	200		
Chouinard *et al.*, 1990[163]	1	PLA	PLA	PLA	PLA	PLA		
Cordiolo *et al.*, 2003[164]	1	CBT					12	2

Study	Setting[a]	Intervention	Average or mean dose at the end (mg)	SD of mean dose (mg)	Minimum dose during the study (mg)	Maximum dose during the study (mg)	Number of sessions	Duration of session (hours)
Cordiolo *et al.*, 2003[164]	1	Waitlist					Waitlist	Waitlist
Cottraux *et al.*, 1993[165]	1	FLV	282	NA	NA	300		
Cottraux *et al.*, 1993[165]	1	BT					25	NA
Cottraux *et al.*, 1993[165]	1	BT + FLV	282	NA	NA	300	25	NA
Cottraux *et al.*, 2001[166]	1	BT					20	1
Cottraux *et al.*, 2001[166]	1	CT					20	1
Denys *et al.*, 2003[167]	1	PAR	60	Fixed		60		
Denys *et al.*, 2003[167]	1	VEN	300	Fixed		300		
Emmelkamp and Beens, 1991[168]	1	CT					31	NA
Emmelkamp and Beens, 1991[168]	1	BT					31	1.5
Emmelkamp *et al.*, 1988[169]	1	CT					10	1
Emmelkamp *et al.*, 1988[169]	1	BT					10	1
Fals-Stewart *et al.*, 1993[170]	1	BT					24	1
Fals-Stewart *et al.*, 1993[170]	1	PsychPLA						
Foa *et al.*, 2005[171]	1	BT					15	2
Foa *et al.*, 2005[171]	1	CLO	235	34		250		
Foa *et al.*, 2005[171]	1	BT + CLO	194	48		250	15	2
Foa *et al.*, 2005[171]	1	PLA	PLA					
Freeman *et al.*, 1994[172]	1	FLV	200	NA	150	250		
Freeman *et al.*, 1994[172]	1	CLO	200	NA	150	250		

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 67 Additional extraction: adult subset (*continued*)

Study	Setting[a]	Intervention	Average or mean dose at the end (mg)	SD of mean dose (mg)	Minimum dose during the study (mg)	Maximum dose during the study (mg)	Number of sessions	Duration of session (hours)
Freeston *et al.*, 1997[173]	1	CBT					40	1.5
Freeston *et al.*, 1997[173]	1	Waitlist					Waitlist	Waitlist
GlaxoSmithKline, 2005[174]	1	PLA	PLA	PLA	PLA	PLA		
GlaxoSmithKline, 2005[174]	1	PAR	NA	NA		60		
GlaxoSmithKline, 2005[174]	1	CLO	NA	NA		250		
GlaxoSmithKline, 2005[175]	9	PAR	NA	NA		50		
GlaxoSmithKline, 2005[175]	9	CLO	NA	NA		275		
Goodman *et al.*, 1989[176]	1	PLA	PLA					
Goodman *et al.*, 1989[176]	1	FLV	255	60		300		
Goodman *et al.*, 1996[177]	1	PLA	PLA					
Goodman *et al.*, 1996[177]	1	FLV	245	NA	100	300		
Greist *et al.*, 1995[126]	1	SER	50/100/200	Fixed				
Greist *et al.*, 1995[126]	1	PLA	PLA					
Greist *et al.*, 2002[178]	1	BT					11	1
Greist *et al.*, 2002[178]	1	PsychPLA					PsychPLA	PsychPLA
Hohagen *et al.*, 1998[179]	2	BT + PLA	PLA	PLA	PLA	PLA		
Hohagen *et al.*, 1998[179]	2	BT + FLV	288.1	NA		300		
Hollander *et al.*, 2003[181]	1	PLA	PLA					
Hollander *et al.*, 2003[181]	1	FLV	271	NA	100	300		
Hollander *et al.*, 2003[180]	1	PLA	PLA	PLA	PLA	PLA		
Hollander *et al.*, 2003[180]	1	PAR-20	20	Fixed	Fixed	Fixed		
Hollander *et al.*, 2003[180]	1	PAR-40	40	Fixed	Fixed	Fixed		

Study	Setting[a]	Intervention	Average or mean dose at the end (mg)	SD of mean dose (mg)	Minimum dose during the study (mg)	Maximum dose during the study (mg)	Number of sessions	Duration of session (hours)
Hollander *et al.*, 2003[180]	1	PAR-60	60	Fixed	Fixed	Fixed		
Jaurrieta *et al.*, 2008[182]	1	CBT					20	0.75 hours (45 minutes)
Jaurrieta *et al.*, 2008[182]	1	Waitlist					Waitlist	Waitlist
Jenike *et al.*, 1990[183]	9	SER	200	Fixed		200		
Jenike *et al.*, 1990[183]	9	PLA	PLA	PLA				
Jenike *et al.*, 1990[184]	1	PLA	PLA					
Jenike *et al.*, 1990[184]	1	FLV	294	23.6	100	300		
Jenike *et al.*, 1997[185]	1	PLA	PLA	PLA	PLA	PLA		
Jenike *et al.*, 1997[185]	1	FLX	77.9	6.3		80		
Jones and Menzies, 1998[186]	1	CT					8	1
Jones and Menzies, 1998[186]	1	Waitlist						
Kamijima *et al.*, 2004[187]	9	PLA	PLA	PLA	PLA	PLA		
Kamijima *et al.*, 2004[187]	9	PAR	45	5	40	50		
Khodarahimi, 2009[188]	1	Waitlist					Waitlist	Waitlist
Khodarahimi, 2009[188]	1	BT					12	1.5
Kobak *et al.*, 2005[189]	1	PLA	PLA					
Kobak *et al.*, 2005[189]	1	HYP	1663.64	303.22	600	1800		
Koran *et al.*, 1996[190]	1	FLV	255	NA	100	300		
Koran *et al.*, 1996[190]	1	CLO	201	NA	100	250		
Kronig *et al.*, 1999[191]	1	SER	165	55	50	200		
Kronig *et al.*, 1999[191]	1	PLA	PLA	PLA	PLA	PLA		
Lindsay *et al.*, 1997[192]	1	BT					15	1

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 67 Additional extraction: adult subset (*continued*)

Study	Setting[a]	Intervention	Average or mean dose at the end (mg)	SD of mean dose (mg)	Minimum dose during the study (mg)	Maximum dose during the study (mg)	Number of sessions	Duration of session (hours)
Lindsay *et al.*, 1997[192]	1	PsychPLA					PsychPLA	PsychPLA
López-Ibor *et al.*, 1996[193]	9	FLX	40	Fixed		40		
López-Ibor *et al.*, 1996[193]	9	CLO	150	Fixed		150		
Mavissakalian *et al.*, 1985[194]	1	CLO	228.5	NA	100	300		
Mavissakalian *et al.*, 1985[194]	1	PLA	PLA					
McLean *et al.*, 2001[195]	1	CT					12	2.5
McLean *et al.*, 2001[195]	1	BT					12	2.5
Milanfranchi *et al.*, 1997[196]	1	CLO	300	0		300		
Milanfranchi *et al.*, 1997[196]	1	FLV	300	0		300		
Montgomery *et al.*, 1993[197]	9	PLA	PLA					
Montgomery *et al.*, 1993[197]	9	FLX-20	20	Fixed				
Montgomery *et al.*, 1993[197]	9	FLX-40	40	Fixed				
Montgomery *et al.*, 1993[197]	9	FLX-60	60	Fixed				
Montgomery *et al.*, 2001[198]	9	CIT-20	20	Fixed				
Montgomery *et al.*, 2001[198]	9	CIT-40	40	Fixed				
Montgomery *et al.*, 2001[198]	9	CIT-60	60	Fixed				
Montgomery *et al.*, 2001[198]	9	PLA	PLA					
Mundo *et al.*, 1997[199]	2	FLV	290	31	150	300		
Mundo *et al.*, 1997[199]	2	PAR	53.3	10	20	60		
Mundo *et al.*, 1997[199]	2	CIT	50.9	10.4	20	60		
Mundo *et al.*, 2001[200]	9	CLO	NA	NA	150	300		
Mundo *et al.*, 2001[200]	9	FLV	NA	NA	150	300		

Study	Setting[a]	Intervention	Average or mean dose at the end (mg)	SD of mean dose (mg)	Minimum dose during the study (mg)	Maximum dose during the study (mg)	Number of sessions	Duration of session (hours)
Nakajima *et al.*, 1996[201]	9	FLV	193.5	64	NA	150–300		
Nakajima *et al.*, 1996[201]	9	PLA	PLA	PLA	PLA	PLA		
Nakatani *et al.*, 2005[202]	1	PsychPLA						
Nakatani *et al.*, 2005[202]	1	FLV	190	21	150	200		
Nakatani *et al.*, 2005[202]	1	BT					12	0.75 hours (45 minutes)
O'Connor *et al.*, 1999[203]	1	SRI	NA	NA	NA	NA		
O'Connor *et al.*, 1999[203]	1	Waitlist						
O'Connor *et al.*, 1999[203]	1	CBT					20	1
O'Connor *et al.*, 1999[203]	1	CBT + SRI	NA	NA	NA	NA	20	1
O'Connor *et al.*, 2006[204]	1	PLA	PLA					
O'Connor *et al.*, 2006[204]	1	FLV	NA	NA	100	300		
Perse *et al.*, 1987[205]	1	PLA	PLA					
Perse *et al.*, 1987[205]	1	FLV	Not reported	NA		300		
Shareh *et al.*, 2010[206]	1	FLV	NA	NA	50	300		
Shareh *et al.*, 2010[206]	1	CBT					10	1
Shareh *et al.*, 2010[206]	1	FLV + CBT	NA	NA	50	300	10	1
Sousa *et al.*, 2006[207]	1	SER	100	Fixed				
Sousa *et al.*, 2006[207]	1	CBT					12	2
Stein *et al.*, 2007[124]	1	PLA	PLA	PLA	PLA	PLA		
Stein *et al.*, 2007[124]	1	PAR	40	Fixed	Fixed	Fixed		
Stein *et al.*, 2007[124]	1	ESCIT-10	10	Fixed	Fixed	Fixed		
Stein *et al.*, 2007[124]	1	ESCIT-20	20	Fixed	Fixed	Fixed		

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 67 Additional extraction: adult subset (*continued*)

Study	Setting[a]	Intervention	Average or mean dose at the end (mg)	SD of mean dose (mg)	Minimum dose during the study (mg)	Maximum dose during the study (mg)	Number of sessions	Duration of session (hours)
Thoren *et al.*, 1980[208]	2	CLO	150	Fixed		150		
Thoren *et al.*, 1980[208]	2	PLA	PLA					
Tollefson *et al.*, 1994[127]	1	PLA	PLA					
Tollefson *et al.*, 1994[127]	1	FLX-20	20	Fixed				
Tollefson *et al.*, 1994[127]	1	FLX-40	40	Fixed				
Tollefson *et al.*, 1994[127]	1	FLX-60	60	Fixed				
Van Oppen *et al.*, 1995[209]	1	CT					16	0.75 hours (45 minutes)
Van Oppen *et al.*, 1995[209]	1	BT					16	0.75 hours (45 minutes)
Volavka *et al.*, 1985[210]	1	CLO	275	53.5		300		
Volavka *et al.*, 1985[210]	1	IMI	262.5	74.4		300		
Whittal *et al.*, 2005[211]	1	CT					12	1
Whittal *et al.*, 2005[211]	1	BT					12	1
Whittal *et al.*, 2010[212]	1	CT					12	1
Whittal *et al.*, 2010[212]	1	PsychPLA					PsychPLA	PsychPLA
Zohar and Judge, 1996[213]	9	PLA	PLA					
Zohar and Judge, 1996[213]	9	PAR	49.3	13.7	20	60		
Zohar and Judge, 1996[213]	9	CLO	204.5	65.1	50	250		

AMI, amitriptyline; CCSG, Clomipramine Collaborative Study Group; CIT, citalopram; CLO, clomipramine; ESCIT, escitalopram; FLV, fluvoxamine; FLX, fluoxetine; HYP, hypericum; IMI, imipramine; NA, not available; PAR, paroxetine; PLA, placebo; PsychPLA, psychological placebo; SER, sertraline; SRI, serotonin reuptake inhibitor; VEN, venlafaxine.
a 1 = outpatients, 2 = inpatients, 3 = mixed, 9 = unclear.

TABLE 68 Additional extraction: children and adolescents subset

Study	Setting[a]	Intervention	Average or mean dose at the end (mg)	SD of mean dose (mg)	Minimum dose during the study (mg)	Maximum dose during the study (mg)	Number of sessions	Duration of session (hours)
Alaghband-Rad and Hakimshooshtary, 2009[215]	1	FLX	20	Fixed				
Alaghband-Rad and Hakimshooshtary, 2009[215]	1	CIT	20	Fixed				
Asbahr *et al.*, 2005[216]	1	SER	137.5	57.1	25	200		
Asbahr *et al.*, 2005[216]	1	CBT					12	1.5
Barrett *et al.*, 2004[217]	1	CBT					14	1.5
Barrett *et al.*, 2004[217]	1	PsychPLA					Waitlist	Waitlist
Bolton and Perrin, 2008[218]	1	BT					10	1 to 1.5
Bolton and Perrin, 2008[218]	1	PsychPLA					Waitlist	Waitlist
Bolton *et al.*, 2011[219]	1	PsychPLA					Waitlist	Waitlist
Bolton *et al.*, 2011[219]	1	CBT					12	1
de Haan *et al.*, 1998[220]	1	CLO	2.5 mg/kg	0.63	NA	3 mg/kg		
de Haan *et al.*, 1998[220]	1	BT						
DeVeaugh-Geiss *et al.*, 1992[221]	1	CLO	NA	NA	75	200		
DeVeaugh-Geiss *et al.*, 1992[221]	1	PLA	PLA					
Flament *et al.*, 1985[222]	1	CLO	141	30	100	200		
Flament *et al.*, 1985[222]	1	PLA	PLA					
Freeman *et al.*, 2008[223]	1	CBT					12	1
Freeman *et al.*, 2008[223]	1	PsychPLA					12	1
Geller *et al.*, 2001[224]	1	PLA	PLA					
Geller *et al.*, 2001[224]	1	FLX	24.6	NA	20	60		

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 68 Additional extraction: children and adolescents subset (*continued*)

Study	Setting[a]	Intervention	Average or mean dose at the end (mg)	SD of mean dose (mg)	Minimum dose during the study (mg)	Maximum dose during the study (mg)	Number of sessions	Duration of session (hours)
GlaxoSmithKline, 2001[225]	1	PAR	NA	NA	20	50		
GlaxoSmithKline, 2001[225]	1	PLA	PLA	PLA	PLA	PLA		
Liebowitz *et al.*, 2002[226]	9	PLA	PLA					
Liebowitz *et al.*, 2002[226]	9	FLX	64.8	18.9	20	80		
March *et al.*, 1990[227]	1	CLO	190	NA		200		
March *et al.*, 1990[227]	1	PLA	PLA					
March *et al.*, 1998[228]	1	SER	167	NA		200		
March *et al.*, 1998[228]	1	PLA	180					
Neziroglu *et al.*, 2000[229]	9	FLV	200	Fixed		200		
Neziroglu *et al.*, 2000[229]	9	BT + FLV	200	Fixed		200	20	1.5
Piacentini *et al.*, 2011[230]	1	CBT					12	1.5
Piacentini *et al.*, 2011[230]	1	PsychPLA					12	1.5
Riddle *et al.*, 1992[231]	1	PLA	PLA					
Riddle *et al.*, 1992[231]	1	FLX	20	Fixed				
Riddle *et al.*, 2001[232]	9	PLA	PLA					
Riddle *et al.*, 2001[232]	9	FLV	165	50	50	200		
Storch *et al.*, 2011[233]	1	CBT					12	1–1.5 hours
Storch *et al.*, 2011[233]	1	PsychPLA					Waitlist	Waitlist
Storch *et al.*, 2013[234]	1	SER + CBT	164.3	NA		200	14	1
Storch *et al.*, 2013[234]	1	CBT + PLA					14	1

Study	Setting[a]	Intervention	Average or mean dose at the end (mg)	SD of mean dose (mg)	Minimum dose during the study (mg)	Maximum dose during the study (mg)	Number of sessions	Duration of session (hours)
The Pediatric OCD Treatment Study, 2004[236]	1	SER	170	33		200		
The Pediatric OCD Treatment Study, 2004[236]	1	CBT					12	1
The Pediatric OCD Treatment Study, 2004[236]	1	SER + CBT	133	64		200	14	1
The Pediatric OCD Treatment Study, 2004[236]	1	PLA	PLA	PLA	PLA	PLA		
Williams *et al.*, 2010[235]	1	CBT					10	1
Williams *et al.*, 2010[235]	1	PsychPLA					PsychPLA	PsychPLA

CIT, citalopram; CLO, clomipramine; FLV, fluvoxamine; FLX, fluoxetine; NA, not available; PAR, paroxetine; PLA, placebo; PsychPLA, psychological placebo; SER, sertraline.
a 1 = outpatients, 2 = inpatients, 3 = mixed, 9 = unclear.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 7 Quality assessment of trials

TABLE 69 Quality assessment: randomisation – allocation section

Study	Sequence generation	Sequence generation comment	Allocation concealment	Allocation concealment comment
Alaghband-Rad and Hakimshooshtary, 2009[215]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc. ('consenting subjects were randomly assigned to start with either')	Unclear	No description
Albert *et al.*, 2002[155]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Ananth *et al.* 1981[156]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Anderson and Rees 2007[157]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Andersson *et al.*, 2012[158]	Low risk	Computer-based randomisation	Unclear	No description
Asbahr *et al.*, 2005[216]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Barrett *et al.*, 2004[217]	Low risk	Block randomisation	Unclear	No description
Belloch *et al.*, 2008[159]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Belotto-Silva *et al.*, 2012[160]	Low risk	Minimisation using computer program	Low risk	Allocation for each group was determined without the knowledge of the professionals responsible for screening and recruitment of patients
Bergeron *et al.*, 2002[161]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc. ('patients were randomised to 24 weeks of double-blind treatment with flexible doses of . . .')	Unclear	No description
Bisserbe *et al.*, 1997[162]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 69 Quality assessment: randomisation – allocation section (*continued*)

Study	Sequence generation	Sequence generation comment	Allocation concealment	Allocation concealment comment
Bolton and Perrin, 2008[218]	Low risk	Participants were randomly assigned to ERP or a waitlist control condition by use of random number tables. A colleague independent of the trial selected a random sequence of 20 numbers including 10 even and 10 odd numbers, and then made each kind represent 1 of the 2 conditions on a database containing 20 separate pages, the assignment sequence being unknown to the trial team. Assignment of the nth case was made after informed consent to participate in the trial by accessing the relevant separate page of the assignment database	Low risk	Participants were randomly assigned to ERP or a waitlist control condition by use of random number tables. A colleague independent of the trial selected a random sequence of 20 numbers including 10 even and 10 odd, and then made each kind represent one of the two conditions on a database containing 20 separate pages, the assignment sequence being unknown to the trial team. Assignment of the nth case was made after informed consent to participate in the trial by accessing the relevant separate page of the assignment database
Bolton *et al.*, 2011[219]	Low risk	Randomisation was carried out independently of the study team using sampling without replacement in blocks of six. The randomisation was stratified depending on whether or not the participant was receiving current stable medication for OCD	Low risk	Assignment of the next recruited participant was placed in a sealed envelope and held by an independent administrator, and this information was provided to the research assessor in written form or by telephone following consent to enter the trial
CCSG1, 1991[154]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
CCSG2, 1991[154]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Chouinard *et al.*, 1990[163]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Cordioli *et al.*, 2003[164]	Low risk	Computer-based randomisation	Low risk	The random allocation was done by a researcher not involved in the clinical trial
Cottraux *et al.*, 1993[165]	Unclear	Description only includes 'random', 'randomly generated', 'randomised'	Unclear	No description
Cottraux *et al.*, 2001[166]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
de Haan *et al.*, 1998[220]	Unclear	Description only includes 'random', 'randomly generated', 'randomised'	Unclear	No description
Denys *et al.*, 2003[167]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
DeVeaugh-Geiss *et al.*, 1992[221]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description

TABLE 69 Quality assessment: randomisation – allocation section (*continued*)

Study	Sequence generation	Sequence generation comment	Allocation concealment	Allocation concealment comment
Emmelkamp and Beens 1991[168]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Emmelkamp *et al.*, 1988[169]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Fals-Stewart *et al.*, 1993[170]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Flament *et al.*, 1985[222]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Foa *et al.*, 2005[171]	Low risk	Block randomisation	Unclear	No description
Freeman *et al.*, 1994[172]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Freeman *et al.*, 2008[223]	Unclear	Description only includes 'random', 'randomly generated', 'randomised'	Unclear	No description
Freeston *et al.*, 1997[173]	Unclear	The authors describe the process but they do not present how they got the random numbers. Therefore unclear	Unclear	No description
Geller *et al.*, 2001[224]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc.	Unclear	No description
GlaxoSmithKline, 2005[174]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
GlaxoSmithKline, 2005[175]	Unclear	Description only includes 'random', 'randomly generated', 'randomised'	Unclear	No description
GlaxoSmithKline, 2001[225]	Low risk	Stratified by age randomisation	Unclear	No description
Goodman *et al.*, 1989[176]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Goodman *et al.*, 1996[177]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Greist *et al.*, 1995[126]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Greist *et al.*, 2002[178]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Hohagen *et al.*, 1998[179]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc.	Unclear	No description
Hollander *et al.*, 2003[181]	Unclear	Description only includes 'random', 'randomly generated', 'randomised'	Unclear	No description

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 69 Quality assessment: randomisation – allocation section (*continued*)

Study	Sequence generation	Sequence generation comment	Allocation concealment	Allocation concealment comment
Hollander *et al.*, 2003[180]	Low risk	A computer-based randomisation	Low risk	Central randomisation by SmithKline Beecham plc
Jaurrieta *et al.*, 2008[182]	Low risk	Tables of random numbers	Low risk	The random allocation was performed by a researcher not involved in the clinical trial
Jenike *et al.*, 1990[183]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Jenike *et al.*, 1990[184]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Jenike *et al.*, 1997[185]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc.	Unclear	No description
Jones and Menzies, 1998[186]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Kamijima *et al.*, 2004[187]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Khodarahimi, 2009[188]	Low risk	Description includes block randomisation in groups of three	Unclear	No description
Kobak *et al.*, 2005[189]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Koran *et al.*, 1996[190]	Low risk	Patients were randomly assigned to double-blind treatment with fluvoxamine or clomipramine in approximately equal numbers in accordance with a randomisation schedule	Unclear	No description
Kronig *et al.*, 1999[191]	Low risk	Randomly assigned via computer-generated codes	Unclear	No description
Liebowitz 2002[226]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc.	Unclear	No description
Lindsay *et al.*, 1997[192]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
López-Ibor *et al.*, 1996[193]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
March 1990[227]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
March 1998[228]	Low risk	Computer-generated randomisation algorithm	Unclear	No description
Mavissakalian *et al.*, 1985[194]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
McLean *et al.*, 2001[195]	Low risk	Block randomisation	Unclear	No description

TABLE 69 Quality assessment: randomisation – allocation section (*continued*)

Study	Sequence generation	Sequence generation comment	Allocation concealment	Allocation concealment comment
Milanfranchi *et al.*, 1997[196]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc.	Unclear	No description
Montgomery *et al.*, 1993[197]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc.	Unclear	No description
Montgomery *et al.*, 2001[198]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Mundo *et al.*, 1997[199]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Mundo *et al.*, 2001[200]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc.	Unclear	No description
Nakajima *et al.*, 1996[201]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc.	Unclear	No description
Nakatani *et al.*, 2005[202]	Unclear	Description only includes 'random', 'randomly generated', 'randomised'	Low risk	Central randomisation: *A study coordinator who did not know any further information of the subjects randomly assigned them to one of three treatment conditions*
Neziroglu *et al.*, 2000[229]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
O'Connor *et al.*, 1999[203]	High risk	Three clients had definite preferences (at least initially) regarding whether they preferred medication or non-medication. This choice was respected, so allocation to groups was not entirely random	Unclear	No description
O'Connor *et al.*, 2006[204]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Low risk	Pharmacy-controlled randomisation: *The code was controlled through random allocation by the hospital pharmacy who revealed the code only at the end of follow-up*
Perse *et al.*, 1987[205]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Piacentini *et al.*, 2011[230]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 69 Quality assessment: randomisation – allocation section (*continued*)

Study	Sequence generation	Sequence generation comment	Allocation concealment	Allocation concealment comment
Riddle *et al.*, 1992[231]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc.	Low risk	Pharmacy-controlled randomisation
Riddle *et al.*, 2001[232]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Shareh *et al.*, 2010[206]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc. ('21 patients who met all the conditions to participate in the study were randomly assigned to one of the three')	Unclear	No description
Sousa *et al.*, 2006[207]	Low risk	Computer-generated random numbers	Unclear	No description
Stein *et al.*, 2007[124]	Low risk	A computer-generated randomisation list	Low risk	Sealed opaque envelopes
Storch *et al.*, 2011[233]	Low risk	Computer-based randomisation	Unclear	No description
Storch *et al.*, 2013[234]	Low risk	A computer-based randomisation	Unclear	No description
The Pediatric OCD Treatment Study, 2004[236]	Low risk	Patients were randomly assigned (within site) to treatment using a computer-generated randomised permuted blocking procedure using a block size of four	Low risk	Concealment methods followed standard recommendations
Thoren *et al.*, 1980[208]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Tollefson *et al.*, 1994[127]	Unclear	Description includes only 'random', 'randomly generated', 'randomised', etc.	Unclear	No description
Van Oppen *et al.*, 1995[209]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Volavka *et al.*, 1985[210]	Low risk	Computer-generated random numbers were used in blocks	Low risk	Central randomisation by the manufacturer of the drug
Whittal *et al.*, 2005[211]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Whittal *et al.*, 2010[212]	Unclear	Description includes only 'random', 'randomly generated', 'randomised'	Unclear	No description
Williams *et al.*, 2010[235]	Low risk	Tables of random numbers	Low risk	Only the trial administrator was aware which participants were in which group
Zohar and Judge 1996[213]	Unclear	Description only includes 'random', 'randomly generated', 'randomised'	Unclear	No description

CCSG, Clomipramine Collaborative Study Group.

TABLE 70 Quality assessment: blinding section

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Alaghband-Rad and Hakimshooshtary, 2009[215]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	*The CYBOCS was administrated by an experienced clinician (MS)*
Albert *et al.*, 2002[155]	High risk	Open-label treatment, as in the outcome assessment the authors report that the patients were instructed not to reveal their current treatment to evaluators	High risk	Open label treatment for clinicians; the term single blind was used to refer to independent evaluators	Low risk	Independent evaluators and patients were also instructed not to reveal their current treatment
Ananth *et al.* 1981[156]	Low risk	Identical pills and description includes 'double blind'	Low risk	Identical pills and description includes 'double blind'	Unclear	No description
Anderson and Rees 2007[157]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Unclear	No description
Andersson *et al.*, 2012[158]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	The assessors were blinded to treatment allocation at the post-treatment interview and were instructed to guess to which treatment condition the participant had been randomised in order to control for blinding integrity
Asbahr *et al.*, 2005[216]	High risk	No description of blindness regarding the drug and not possible to blind the psychological intervention	High risk	No description of blindness regarding the drug and not possible to blind the psychological intervention	Low risk	Two independent evaluators who were blinded to treatment assignment, performed all clinician-rated instruments. Subjects were not assessed by their own therapist and were asked not to reveal any information about their treatment to the independent evaluators

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 70 Quality assessment: blinding section (*continued*)

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Barrett *et al.*, 2004[217]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Unclear	No description
Belloch *et al.*, 2008[159]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	The evaluator was blind to the treatment received by patients
Belotto-Silva *et al.*, 2012[160]	High risk	Psychological intervention in group format compared with drug	High risk	The principal CBT therapist was the main author of the manuscript	Low risk	Follow-up assessments administered by a rater who was blind to the patient treatment condition
Bergeron *et al.*, 2002[161]	Unclear	Description includes only 'double blind'	Unclear	Description only includes 'double blind'	Unclear	*Efficacy assessments were conducted exclusively by psychiatrists with expertise in treatment research. Rater training on the primary outcome measures was conducted at an investigator meeting. As often as possible the same rater completed all of the ratings of a given patient*
Bisserbe *et al.*, 1997[162]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
Bolton and Perrin, 2008[218]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	High risk	The rater undertaking the CYBOCS assessment was not involved in the treatment of the case, but no attempt was made to achieve blindness of rater to condition because of the great difficulty associated with preserving it in this intensive treatment condition, especially in children

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Bolton *et al.*, 2011[219]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	CYBOCS and ADIS–C/P assessments were made by trained independent evaluators in the research team, masters' or doctoral-level psychologists, kept blinded to the randomisation status
CCSG1, 1991[154]	Low risk	Identical capsules	Low risk	Identical capsules and states double blind	Unclear	No description
CCSG2, 1991[154]	Low risk	Identical capsules	Low risk	Identical capsules and states double blind	Unclear	No description
Chouinard *et al.*, 1990[163]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
Cordioli *et al.*, 2003[164]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	Patients of both groups were rated by three independent raters, blinded for patient group allocation
Cottraux *et al.*, 1993[165]	Unclear	Stated as double blind (expect FLV + BT group which is single blind)	Unclear	Stated as double blind (expect FLV + BT group which is single blind)	Unclear	No description
Cottraux *et al.*, 2001[166]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	The evaluator was independent and did not take part in the treatment. He or she had no information about the treatment under way
de Haan *et al.*, 1998[220]	High risk	Abstract says that open clomipramine was used and BT not possible to blind	High risk	Abstract says that open clomipramine was used and BT not possible to blind	Unclear	No description

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

DOI: 10.3310/hta20430

TABLE 70 Quality assessment: blinding section (*continued*)

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Denys *et al.*, 2003[167]	Low risk	The study drugs were packaged so that the units were identical, and each subject received the appropriate dosage	Low risk	The study drugs were packaged so that the units were identical, and each subject received the appropriate dosage	Low risk	Two trained investigators, blind to the patient's assigned condition, completed the scales at baseline and on each visit
DeVeaugh-Geiss *et al.*, 1992[221]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
Emmelkamp and Beens 1991[168]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	In addition, an independent assessor, a clinical psychologist who was blind with respect to the treatment condition rated the patients at assessment II (pretest) and after the first (assessment III) and second (assessment V) treatment block
Emmelkamp *et al.*, 1988[169]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	In addition, an independent assessor, a clinical psychologist who was blind with respect to the treatment condition, rated the patients at pre- and post-test
Fals-Stewart *et al.*, 1993[170]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Unclear	No description
Flament *et al.*, 1985[222]	Low risk	Identical pills and description includes 'double blind'	Low risk	Identical pills and description includes 'double blind'	Low risk	Two independent psychiatrists blinded to the patients' treatment

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Foa *et al.*, 2005[171]	Unclear	Description includes only double blind for medication and placebo. Blinding not possible for psychological intervention	Low risk	Independent evaluators, who remained blind to treatment assignment, conducted the assessments. Psychiatrists were blind to patients' medication assignment and therapy status. The therapists who provided exposure and ritual prevention were blind to patients' medication status. Patients were reminded not to discuss their treatment in order to maintain the blinding	Low risk	Independent evaluators, who remained blind to treatment assignment, conducted the assessments. Psychiatrists were blind to patients' medication assignment and therapy status. The therapists who provided exposure and ritual prevention were blind to patients' medication status. Patients were reminded not to discuss their treatment in order to maintain the blinding
Freeman *et al.*, 1994[172]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
Freeman *et al.*, 2008[223]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	Trained independent evaluators (i.e. child clinical psychologists and child psychiatrists) who were blind
Freeston *et al.*, 1997[173]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	High risk	*The rater was aware of treatment status*
Geller *et al.*, 2001[224]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
GlaxoSmithKline, 2005[174]	Unclear	Description only includes 'double blind'	Unclear	Description only includes 'double blind'	Unclear	Description includes only 'double blind'
GlaxoSmithKline, 2005[175]	Unclear	Description only includes 'double blind'	Unclear	Description only includes 'double blind'	Unclear	Description includes only 'double blind'

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 70 Quality assessment: blinding section (*continued*)

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
GlaxoSmithKline, 2001[225]	Low risk	Both double-blind medications (i.e. paroxetine and placebo) were in the form of white, oval, film-coated tablets for oral administration once daily. They were identical in size, shape and colour	Low risk	Both double-blind medications (i.e. paroxetine and placebo) were in the form of white, oval, film-coated tablets for oral administration once daily. They were identical in size, shape and colour	Unclear	No description
Goodman *et al.*, 1989[176]	Low risk	'Identical appearing tablets' and double blind	Low risk	'Identical appearing tablets' and double blind	Low risk	Experienced raters blind to drug assignment assessed symptoms of OCD
Goodman *et al.*, 1996[177]	Unclear	Description only includes 'double blind'	Unclear	Description only includes 'double blind'	Unclear	No description
Greist *et al.*, 1995[126]	Unclear	Description only includes 'double blind'	Unclear	Description only includes 'double blind'	Unclear	No description
Greist *et al.*, 2002[178]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	High risk	Self-rated YBOCS by patients
Hohagen *et al.*, 1998[179]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Low risk	The YBOCS was used weekly by an independent rater to rate patients' symptoms
Hollander *et al.*, 2003[181]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
Hollander *et al.*, 2003[180]	Low risk	Description includes 'double blind' and 'identical tablets and identical coded bottles'	Low risk	Description includes 'double blind' and 'identical tablets and identical coded bottles'	Unclear	No description
Jaurrieta *et al.*, 2008[182]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Unclear	Vague description unable to decide if high risk or not; therefore, unclear

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Jenike *et al.*, 1990[183]	Low risk	Identically appearing placebo capsules	Low risk	Identically appearing placebo capsules	Unclear	No description
Jenike *et al.*, 1990[184]	Low risk	Identical appearing placebo capsules	Low risk	Identical appearing placebo capsules	Low risk	The authors give details on the rigorous procedure they followed about measuring YBOCS (giving intraclass correlation coefficients) and they state that: *the raters were provided with standardized instructions and the same rater assessed each individual patient throughout the course of the study*
Jenike *et al.*, 1997[185]	Unclear	No description	Unclear	No description	Unclear	No description
Jones and Menzies, 1998[186]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	High risk	Self-rated instruments
Kamijima *et al.*, 2004[187]	Unclear	Description includes only 'double blind'	Unclear	Description only includes 'double blind'	Unclear	No description
Khodarahimi, 2009[188]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Unclear	No description
Kobak *et al.*, 2005[189]	Low risk	The authors describe 'matched' placebo	Low risk	The authors describe 'matched' placebo	Unclear	No description

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 70 Quality assessment: blinding section (*continued*)

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Kobak *et al.*, 2005[189]	Low risk	Blinding was accomplished by having all study patients take the same number of capsules daily and medications supplied in identical capsules for oral administration	Low risk	Blinding was accomplished by having all study patients take the same number of capsules daily and medications supplied in identical capsules for oral administration	Unclear	No description
Kronig *et al.*, 1999[191]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
Liebowitz *et al.*, 2002[226]	Unclear	Study is only described as 'placebo-controlled'	Unclear	Study is only described as 'placebo-controlled'	Low risk	Independent evaluators assessing symptoms were blind to treatment assignment
Lindsay *et al.*, 1997[192]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Unclear	No description
López-Ibor *et al.*, 1996[193]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
March *et al.*, 1990[227]	Low risk	Identical pills and description includes 'double blind'	Low risk	Identical pills and description includes 'double blind'	Unclear	No description
March *et al.*, 1998[228]	Low risk	Identical blisters	Low risk	Identical blisters	Unclear	No description
Mavissakalian *et al.*, 1985[194]	Unclear	Description only includes 'double blind'	Unclear	Description only includes 'double blind'	Unclear	No description
McLean *et al.*, 2001[195]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Unclear	No description

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Milanfranchi *et al.*, 1997[196]	Low risk	Description includes 'double blind' and also the authors note how the two drugs were similar ('the drugs were administered in capsules containing either 50 mg of FLV or 50 mg of CLO; the clomipramine dose was distributed in two comfits of 25 mg in the same capsule')	Low risk	Description includes 'double blind' and also the authors note how the two drugs were similar ('the drugs were administered in capsules containing either 50 mg of FLV or 50 mg of CLO; the clomipramine dose was distributed in two comfits of 25 mg in the same capsule')	Unclear	No description
Montgomery *et al.*, 1993[197]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
Montgomery *et al.*, 2001[198]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
Mundo *et al.*, 1997[199]	High risk	Mentioned that patients were not blinded for medication	High risk	The authors report that this is a single blind study, with the blinding referring to independent raters, therefore we can assume that the health-care providers were not blinded	Low risk	The ratings were all made under blind conditions
Mundo *et al.*, 2001[200]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
Nakajima *et al.*, 1996[201]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	No description
Nakatani *et al.*, 2005[202]	High risk	No description but due to the nature of intervention this is high risk	Unclear	No description	Low risk	*Clinical ratings were undertaken blindly at baseline, week 4, 8 and 12 by 4 clinically experienced psychiatrists*

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 70 Quality assessment: blinding section (*continued*)

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Neziroglu *et al.*, 2000[229]	High risk	Psychological intervention was added to one of the groups and, therefore, blinding was not possible	High risk	Psychological intervention was added to one of the groups and, therefore, blinding was not possible	Unclear	No description
O'Connor *et al.*, 1999[203]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	The same clinician carried out all ratings post treatment and was blind to treatment-group membership
O'Connor *et al.*, 2006[204]	Low risk	Paper discusses how placebos were similar ('The active and inactive medication was given in identical tablet form of 50 mg units and were identical in appearance')	Low risk	Paper discusses how placebos were similar ('The active and inactive medication was given in identical tablet form of 50 mg units and were identical in appearance')	Low risk	An independent assessor administered the YBOCS at pre-, mid- and post-treatment and follow-ups
Perse *et al.*, 1987[205]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Low risk	Each of the three physician investigators made independent blind clinical ratings
Piacentini *et al.*, 2011[230]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	Trained evaluators blinded to treatment condition conducted assessments with families
Riddle *et al.*, 1992[231]	Low risk	Paper discusses how placebos were similar ('placebo capsules were prepared by filling identical opaque jackets with lactose powder')	Low risk	Paper discusses how placebos were similar ('placebo capsules were prepared by filling identical opaque jackets with lactose powder')	Unclear	No description

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Riddle *et al.*, 2001[232]	Low risk	Description includes 'double blind' and 'identical placebo capsule'	Low risk	Description includes 'double blind' and 'identical placebo capsule'	Low risk	The authors give details on the rigorous procedure they followed about measuring CYBOCS
Shareh *et al.*, 2010[206]	High risk	No description but owing to the nature of intervention this is high risk	High risk	No description of blindness in the paper, therefore high risk	Unclear	No description
Sousa *et al.*, 2006[207]	High risk	Psychological intervention was added to one of the groups and, therefore, blinding was not possible	High risk	Psychological intervention was added to one of the groups and, therefore, blinding was not possible	Low risk	Two psychiatrists blind to the type of treatment were used as independent evaluators
Stein *et al.*, 2007[124]	Low risk	Double blind and identical appearance of study medications	Low risk	Double blind and identical appearance of study medications	Low risk	The authors give details on the rigorous procedure they followed about measuring YBOCS ('Only those investigators who had actively participated in rater training sessions prior to inclusion of patients into the study were allowed to rate patients. Rater training was undertaken to increase inter-rater reliability, and was chaired by an experienced psychiatrist'). Patient ratings were assessed by the same investigator at each visit, whenever possible

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 70 Quality assessment: blinding section (*continued*)

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Storch *et al.*, 2011[233]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	Independent evaluators blinded to treatment
Storch *et al.*, 2013[234]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Low risk	Independent evaluators trained by the authors in the administration of scales
Thoren *et al.*, 1980[208]	Low risk	Identical pills and description includes 'double blind'	Low risk	Identical pills and description includes 'double blind'	Unclear	No description
Tollefson *et al.*, 1994[127]	Unclear	No description	Unclear	'Patients were examined by the treating clinicians who were blinded to the study medication' but no further information	Unclear	No description
Van Oppen *et al.*, 1995[209]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Unclear	No description
Volavka *et al.*, 1985[210]	Low risk	Identical capsules	Low risk	Identical capsules and double blind	Unclear	No description
The Pediatric OCD Treatment Study, 2004[236]	Unclear	Except in emergencies, participants and clinicians remained masked in the pills-only conditions. However, it is not possible to blind the psychological intervention	Unclear	Except in emergencies, participants and clinicians remained masked in the pills-only conditions. However, it is not possible to blind the psychological intervention	Low risk	Independent evaluators
Whittal *et al.*, 2005[211]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	The assessors were blind to treatment type. With few exceptions, the same assessor was used at pre- and post-treatment, and follow-up

Study	Blinding of participants	Blinding of participants comment	Blinding of those delivering the intervention	Blinding of those delivering comment	Blinding of the outcome assessor	Blinding of outcome assessors comment
Whittal *et al.*, 2010[212]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Unclear	No description
Williams *et al.*, 2010[235]	High risk	Psychological interventions not possible to blind	High risk	Psychological interventions not possible to blind	Low risk	Assessors were blind to the allocation of the participants, and the participants were instructed not to reveal whether or not they had received treatment
Zohar and Judge 1996[213]	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'	Unclear	Description includes only 'double blind'

ADIS–C/P, Anxiety Disorders Interview Schedule for DSM-IV, child and parent versions; CCSG, Clomipramine Collaborative Study Group; CLO, clomipramine; FLU, fluvoxamine.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 71 Quality assessment: outcome reporting/other biases

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Alaghband-Rad and Hakimshooshtary, 2009[215]	High risk	No description of how the handled missing data, no ITT analysis. Overall attrition 17%; no further details	High risk	SDs not given for CYBOCS	High risk	No data for number of children screened initially, excluded because not eligible. Standard of reporting not high despite this being a relatively recent trial
Albert *et al.*, 2002[155]	High risk	Missing data not imputed, completers analysis. Differential attrition almost reached 15%	High risk	Data for completers only, even though they reported that they have also carried out LOCF as well, they only present the results for the visitwise analysis	High risk	Differential attrition ≈15%
Ananth *et al.* 1981[156]	High risk	Completers analysis	Low risk		Low risk	Not any other
Anderson and Rees, 2007[157]	Low risk	Completers analysis reported in detail although the authors have also used ITT but only giving *F*-statistics and *p*-values	High risk	The results of the ITT analysis are not given in full; therefore, only the completers analysis can be included	Low risk	Not any other
Andersson *et al.*, 2012[158]	Low risk	One dropout only and therefore they performed completers analysis. Unlikely that this may have influenced their results, and also they examined blinding integrity. Therefore, could be low risk	Low risk		Low risk	Not any other
Asbahr *et al.*, 2005[216]	Low risk	The authors reported that they did not use ITT because only one patient dropped out. Could be low risk for this reason	High risk	No detailed measures for CYBOCS for follow-up measurements, only *F*-tests and figures	Low risk	Not any other

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Barrett *et al.*, 2004[217]	Unclear	It is not clear from the description whether this is a completers or ITT analysis	High risk	Dropouts not per arm	Low risk	Not any other
Belloch *et al.*, 2008[159]	High risk	Completers analysis	Low risk		Low risk	Not any other
Belotto-Silva *et al.*, 2012[160]	Low risk	Missing data have been imputed using appropriate methods ('Intention-to-treat and last-observation-carried-forward analyses were conducted in order to make conservative estimates of symptom severity for individuals whose outcome measures were missing'). Dropout rates were 25.7% in the CBT ($n = 18$) and 37.5% in the SSRI group ($n = 33$). Overall attrition > 20% and some evidence of differential attrition but reasons for dropouts given and judgement is that there is no serious risk for differential bias. Overall, low risk	Low risk		Low risk	Not any other serious risk (see comment for differential attrition in column 3 – *Incomplete outcome comment* – of this table)
Bergeron *et al.*, 2002[161]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). However, overall attrition rate high (> 30%) without differential attrition	Low risk		High risk	Overall attrition high (> 30%)

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 71 Quality assessment: outcome reporting/other biases (*continued*)

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Bisserbe *et al.*, 1997[162]	Low risk	The authors report that they used ITT and 'last efficacy assessment' for those who dropped out	High risk	SDs not given	High risk	High attrition 35% and evidence of differential attrition > 15% (27% vs. 43%)
Bolton and Perrin, 2008[218]	Low risk	ITT analysis and LOCF as stated in the methods section	Low risk		Low risk	Not any other
Bolton *et al.*, 2011[219]	Low risk	ITT analysis and LOCF as stated in the methods section	Low risk		Low risk	Not any other
CCSG1, 1991[154]	Unclear	In the methods section they do not mention how they handled missing data. In the results, although they mention that in the efficacy analysis that all patients and not just the completers have been used, it is not clear from figures and tables that this is the case	High risk	In the results, although they mention that in the efficacy analysis all patients and not just the completers have been used, it is not clear from figures and tables that this is the case. Therefore, evidence for selective reporting	High risk	They report deviations from the protocol: *Because the physicians' and patients' global ratings did not satisfy the statistical assumptions for logistic regression, i.e., the analysis that had been intended, these scores were analysed by the Wilcoxon rank-sum test*
CCSG2, 1991[154]	Unclear	In the methods section they do not mention how they handled missing data. In the results, although they mention that in the efficacy analysis all patients and not just the completers have been used it is not clear from figures and tables that this is the case	High risk	In the results, although they mention that in the efficacy analysis all patients and not just the completers have been used it is not clear from figures and tables that this is the case. Therefore, evidence for selective reporting	High risk	They report deviations from the protocol: *Because the physicians' and patients' global ratings did not satisfy the statistical assumptions for logistic regression, i.e., the analysis that had been intended, these scores were analysed by the Wilcoxon rank-sum test*

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Chouinard *et al.*, 1990[163]	Low risk	The authors report that 'no patients were excluded from analysis' and LOCF was used to handle missing data – low attrition	High risk	SDs not given	Low risk	Not any other
Cordioli *et al.*, 2003[164]	Low risk	ITT analysis and LOCF as stated in the methods section. Overall attrition low	Low risk		Low risk	Not any other
Cottraux *et al.*, 1993[165]	High risk	No description of how the handled missing data, completers and no ITT analysis. High attrition rate: 45%	Low risk		High risk	Very high attrition (45%). Not standardised scale of overall OCD symptoms
Cottraux *et al.*, 2001[166]	High risk	Completers analysis reported although the authors point out that they have also used ITT with LOCF	High risk	Completers analysis only reported. Regarding the results of the ITT, there were no differences	Low risk	Not any other
de Haan *et al.*, 1998[220]	Low risk	Although this is completers analysis, just one dropout so possibly no effect	Low risk		Low risk	Not any other
Denys *et al.*, 2003[167]	Low risk	ITT analysis and LOCF as stated in the methods section	Low risk		Low risk	Not any other
DeVeaugh-Geiss *et al.*, 1992[221]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Low attrition and no evidence of differential attrition	High risk	SDs not given	Low risk	Not any other

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 71 Quality assessment: outcome reporting/other biases (*continued*)

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Emmelkamp and Beens 1991[168]	High risk	There were dropouts but the authors focused only on the completers analysis	Low risk		High risk	Dropout rate 8/31 = 26%
Emmelkamp *et al.*, 1988[169]	High risk	Two dropped out but the authors conducted completers analysis	Low risk		Low risk	Not any other
Fals-Stewart *et al.*, 1993[170]	High risk	Completers analysis	High risk	SDs not reported	Low risk	Not any other
Flament *et al.*, 1985[222]	Unclear	Crossover trial	High risk	Not sufficient data for baseline and first crossover	Low risk	Not any other
Foa *et al.*, 2005[171]	Low risk	Linear mixed-effects model to account for missing data	Low risk		High risk	Overall attrition high (29%) and evidence of > 15% differential attrition between placebo and BT + CLO groups
Freeman *et al.*, 1994[172]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Overall attrition high (26%) and some evidence for differential attrition (17% vs. 34%)	High risk	SDs not given	High risk	Overall attrition high (26%) and evidence for differential attrition > 15% (17% FLV vs. 34% CLO)
Freeman *et al.*, 2008[223]	Low risk	ITT analysis and LOCF as stated in the methods section. Overall attrition moderate 26% but no evidence of differential attrition	Low risk		High risk	Overall attrition > 25% (= 26%); no differential attrition however

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Freeston *et al.*, 1997[173]	Low risk	ITT analysis although not exactly sure which method they have used for missing data, possibly LOCF though	Low risk		Low risk	Not any other
Geller *et al.*, 2001[224]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Overall attrition high (33%); no evidence of differential attrition	Low risk		High risk	Overall attrition high (> 33%)
GlaxoSmithKline, 2005[174]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Overall high attrition (32%), but no evidence of differential attrition > 15%	Low risk		High risk	No publication: high attrition of 32%
GlaxoSmithKline, 2005[175]	Unclear	Report describes ITT as the method of the analysis but from the table it is not clear	Low risk		High risk	No publication: company report
GlaxoSmithKline, 2001[225]	High risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Overall high attrition (31%) but no evidence of differential attrition > 15%	Low risk		High risk	No publication: high attrition of 31%
Goodman *et al.*, 1989[176]	Low risk	'Dropouts were subjected to endpoint analysis'	Low risk		High risk	Differential attrition (8% vs. 26%) but in favour of active treatment rather than placebo

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skaphinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

NIHR Journals Library www.journalslibrary.nihr.ac.uk

TABLE 71 Quality assessment: outcome reporting/other biases (*continued*)

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Goodman *et al.*, 1996[177]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Overall attrition moderate (23%), but no evidence for differential attrition	High risk	Absolute values for YBOCS at follow-up not given for the ITT population, only figures and change values	Low risk	Not any other
Greist *et al.*, 1995[126]	Unclear	Tables for end-point analysis report *N* for all patients randomised, but there is no discussion of how the missing data were handled or if they used ITT, although it seems that this is ITT analysis	Low risk		High risk	High attrition of 27% overall with no evidence of differential attrition
Greist *et al.*, 2002[178]	Low risk	LOCF and ITT	Low risk		Low risk	Not any other
Hohagen *et al.*, 1998[179]	Unclear	No discussion of dropouts	Low risk		High risk	The authors state that owing to significant imbalance in the two groups at baseline, they dropped the outliers in both therefore reducing the sample for analysis to 25 and 24, respectively
Hollander *et al.*, 2003[181]	Low risk	Missing data have been imputed using appropriate methods (LOCF, ITT). Overall attrition 31%, but no evidence of differential attrition (> 15% between treatments)	High risk	SEs given instead of SDs, high attrition	Low risk	Not any other
Hollander *et al.*, 2003[180]	Low risk	ITT analysis and LOCF as stated in the methods section	High risk	SDs not given	Low risk	Not any other

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Jaurrieta *et al.*, 2008[182]	Low risk	ITT analysis and LOCF as stated in the methods section. Overall attrition < 25% (= 21%)	High risk	Dropouts not per arm	Low risk	Not any other
Jenike *et al.*, 1990[183]	Low risk	No dropouts	Low risk		Low risk	Not any other
Jenike *et al.*, 1990[184]	High risk	No description of how the handled missing data, completers and no ITT analysis. Low attrition rate (45%)	High risk	Baseline data only for completers	Low risk	Not any other
Jenike *et al.*, 1997[185]	Low risk	No methods for imputing but the authors note that 'All analyses were conducted for both patients who completed the study and all patients in intent-to-treat analyses. In all cases, the pattern of results was identical across both analyses'. Therefore, one can assume low risk	Low risk		Unclear	ITT analysis not reported but they mention that results were similar with completers
Jones and Menzies, 1998[186]	Unclear	No discussion of dropouts, possibly no dropouts	Low risk		Low risk	Not any other
Kamijima *et al.*, 2004[187]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF)	High risk	No description of dropouts per arm reported	Low risk	Not any other
Khodarahimi, 2009[188]	High risk	No discussion of dropouts	Low risk		Low risk	Not any other
Kobak *et al.*, 2005[189]	Low risk	ITT and LOCF	Low risk		Low risk	Not any other

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

NIHR Journals Library www.journalslibrary.nihr.ac.uk

TABLE 71 Quality assessment: outcome reporting/other biases (*continued*)

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Kobak *et al.*, 2005[189]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Overall attrition however high (29%) and some evidence for differential attrition	Low risk		High risk	Differential attrition despite missing data handling (21% FLV vs. 36% CLO)
Kronig *et al.*, 1999[191]	Low risk	The authors report LOCF	High risk	No detailed follow-up data, figures only and *F*-tests and *p*-values	High risk	High attrition (30%) but no evidence of differential attrition
Liebowitz *et al.*, 2002[226]	Low risk	Missing data have been imputed using appropriate methods. Low overall attrition (12%) and low differential attrition	Low risk		Low risk	Not any other serious risk
Lindsay *et al.*, 1997[192]	Unclear	The authors do not discuss any dropouts but it is unclear if this was a completers analysis or there were no dropouts	Unclear	No discussion of dropouts, therefore unable to decide if completers or not	Low risk	Not any other
López-Ibor *et al.*, 1996[193]	Low risk	ITT and LOCF	Low risk		Low risk	Not any other
March *et al.*, 1990[227]	Low risk	There were two dropouts and the authors say that they did an ITT analysis by using the mean treatment score of the treatment group	Low risk		Low risk	Not any other
March *et al.*, 1998[228]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Low attrition of 16% and no evidence of differential attrition	High risk	SDs not given	Low risk	Not any other

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Mavissakalian *et al.*, 1985[194]	High risk	Completers analysis	High risk	Original number randomised not reported	Low risk	Not any other
McLean *et al.*, 2001[195]	High risk	Completers analysis	Low risk		Low risk	Not any other
Milanfranchi *et al.*, 1997[196]	High risk	One dropout only but no LOCF	Low risk		Low risk	Not any other
Montgomery *et al.*, 1993[197]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Overall attrition high (25%), no evidence of differential attrition	Low risk		Low risk	Not any other
Montgomery *et al.*, 2001[198]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Low attrition and no evidence of differential attrition	Low risk		Low risk	Not any other
Mundo *et al.*, 1997[199]	Low risk	No dropouts, therefore no need to handle missing data	Low risk		Low risk	Not any other
Mundo *et al.*, 2001[200]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Attrition 20%	High risk	SDs not given for follow-up	Low risk	Not any other
Nakajima *et al.*, 1996[201]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF)	Low risk		Low risk	Not any other
Nakatani *et al.*, 2005[202]	High risk	No description of how missing data were handled, completers and no ITT analysis	Low risk		Low risk	Not any other

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 71 Quality assessment: outcome reporting/other biases (*continued*)

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Neziroglu *et al.*, 2000[229]	Low risk	No dropouts according to the authors	Low risk		Low risk	Not any other
O'Connor *et al.*, 1999[203]	High risk	Completers analysis	High risk	No baseline data for dropouts, only for completers	Low risk	Not any other
O'Connor *et al.*, 2006[204]	High risk	No description of how the handled missing data, completers and no ITT analysis	Low risk		Low risk	Not any other
Perse *et al.*, 1987[205]	High risk	Missing data not imputed, completers analysis	High risk	Not full reporting of means and SDs	Low risk	Not any other
Piacentini *et al.*, 2011[230]	Low risk	ITT analysis and LOCF as stated in the methods section. Moderate attrition and no evidence of differential attrition	Low risk		Low risk	Not any other
Riddle *et al.*, 1992[231]	Low risk	Missing data have been imputed using appropriate methods ('Intention-to-treat' and 'the 4-week data for those two subjects were carried over to week 8')	Low risk		Low risk	Very small sample size, initial protocol for crossover not feasible in the end, but no evidence for risk for the first 8 weeks of analysis included in this meta-analysis
Riddle *et al.*, 2001[232]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Overall attrition high (38%) but no evidence for differential attrition	Low risk		High risk	Very high attrition (38%)
Shareh *et al.*, 2010[206]	High risk	No description of how the handled missing data, completers and no ITT analysis	Low risk		High risk	No standard reporting despite this being a recent trial, no flow chart, potentially high risk

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Sousa *et al.*, 2006[207]	Low risk	No dropouts with at least one baseline evaluation, therefore it can be considered that there are no missing data	High risk	SDs not given	Low risk	Not any other
Stein *et al.*, 2007[124]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF)	Low risk		Low risk	Not any other
Storch *et al.*, 2011[233]	Low risk	ITT analysis and LOCF as stated in the methods section	Low risk		Low risk	Not any other
Storch *et al.*, 2013[234]	Low risk	Missing data have been imputed using appropriate methods [random-effects models in SAS (SAS Institute Inc., Cary, NC, USA) with MLE instead of LOCF, which is more conservative]. Overall high attrition (30%) and evidence of differential attrition (> 15%)	Low risk		High risk	High attrition (30%) and evidence of differential attrition (> 15%) between some of the arms
The Pediatric OCD Treatment Study, 2004[236]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF)	Low risk		Low risk	Not any other
Thoren *et al.*, 1980[208]	High risk	Completers analysis	High risk	No details for dropouts	Low risk	Not any other
Tollefson *et al.*, 1994[127]	Low risk	They have used appropriate methods (LOCF and ITT) but see reporting issues	High risk	SDs not given for ITT analysis, therefore only completers analysis can be used	High risk	Reporting should be better, reliance on secondary outcomes
Van Oppen *et al.*, 1995[209]	High risk	Completers analysis	High risk	Baseline data only for completers	Low risk	Not any other

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 71 Quality assessment: outcome reporting/other biases (*continued*)

Study ID (author and year)	Incomplete outcome data	Incomplete outcome comment	Selective outcome reporting	Selective outcome comment	Any other potential threats to validity	Any other comment
Volavka *et al.*, 1985[210]	High risk	Completers analysis	Low risk		Low risk	Not any other
Whittal *et al.*, 2005[211]	High risk	Completers analysis	Low risk		Low risk	Not any other
Whittal *et al.*, 2010[212]	High risk	Completers analysis	Low risk		Low risk	Not any other
Williams *et al.*, 2010[235]	Low risk	ITT analysis and LOCF as stated in the methods section. Moderate attrition and no evidence of differential attrition	High risk	SEs given instead of SDs	Low risk	Not any other
Zohar and Judge, 1996[213]	Low risk	Missing data have been imputed using appropriate methods (ITT and LOCF). Overall high attrition (30%), but no evidence of differential attrition > 15%	Low risk		High risk	High attrition (30%)

CCSG, Clomipramine Collaborative Study Group; CLO, clomipramine; FLU, fluvoxamine; ITT, intention to treat; LOCF, last observation carried forward; MLE, maximum likelihood estimation; SE, standard error.

TABLE 72 Quality assessment: analysis section

Study	Imputation for missing data	Imputation method	ITT analysis
Alaghband-Rad and Hakimshooshtary, 2009[215]	No		No
Albert *et al.*, 2002[155]	No		No
Ananth *et al.* 1981[156]	No		No
Anderson and Rees, 2007[157]	Unclear	No description given	Unclear
Andersson *et al.*, 2012[158]	No		No
Asbahr *et al.*, 2005[216]	No		No
Barrett *et al.*, 2004[217]	Unclear	Unclear	Unclear
Belloch *et al.*, 2008[159]	No		No
Belotto-Silva *et al.*, 2012[160]	Yes	LOCF	Yes
Bergeron *et al.*, 2002[161]	Yes	LOCF	Yes
Bisserbe *et al.*, 1997[162]	Yes	LOCF	Yes
Bolton and Perrin, 2008[218]	Yes	LOCF	Yes
Bolton *et al.*, 2011[219]	Yes	LOCF	Yes
CCSG1, 1991[154]	Unclear	Unclear	Unclear
CCSG2, 1991[154]	Unclear	Unclear	Unclear
Chouinard *et al.*, 1990[163]	Yes	LOCF	Yes
Cordioli *et al.*, 2003[164]	Yes	LOCF	Yes
Cottraux *et al.*, 1993[165]	No		No
Cottraux *et al.*, 2001[166]	No		No
de Haan *et al.*, 1998[220]	No		No
Denys *et al.*, 2003[167]	Yes	LOCF	Yes
DeVeaugh-Geiss *et al.*, 1992[221]	Yes	LOCF	Yes
Emmelkamp and Beens 1991[168]	No		No
Emmelkamp *et al.*, 1988[169]	No		No
Fals-Stewart *et al.*, 1993[170]	No		No
Flament *et al.*, 1985[222]	Unclear	Unclear	Unclear
Foa *et al.*, 2005[171]	Yes	Linear mixed-effects models	Yes
Freeman *et al.*, 1994[172]	Yes	LOCF	Yes
Freeman *et al.*, 2008[223]	Yes	LOCF	Yes
Freeston *et al.*, 1997[173]	Yes	Unclear	Yes
Geller *et al.*, 2001[224]	Yes	LOCF	Yes
GlaxoSmithKline, 2005[174]	Yes	LOCF	Yes
GlaxoSmithKline, 2005[175]	Unclear	Unclear	Unclear
GlaxoSmithKline, 2001[225]	Yes	LOCF	Yes
Goodman *et al.*, 1989[176]	Yes	LOCF	Yes
Goodman *et al.*, 1996[177]	Yes	LOCF	Yes

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 72 Quality assessment: analysis section (*continued*)

Study	Imputation for missing data	Imputation method	ITT analysis
Greist *et al.*, 1995[126]	Unclear	Unclear	Unclear
Greist *et al.*, 2002[178]	Yes	LOCF	Yes
Hohagen *et al.*, 1998[179]	Unclear	Unclear	No
Hollander *et al.*, 2003[180]	Yes	LOCF	Yes
Hollander *et al.*, 2003[181]	Yes	LOCF	Yes
Jaurrieta *et al.*, 2008[182]	Yes	LOCF	Yes
Jenike *et al.*, 1990[183]	NA	NA	NA
Jenike *et al.*, 1990[184]	No		No
Jenike *et al.*, 1997[185]	No		No
Jones and Menzies, 1998[186]	Unclear	Unclear	Unclear
Kamijima *et al.*, 2004[187]	Yes	LOCF	Yes
Khodarahimi, 2009[188]	No	Unclear	Unclear
Kobak *et al.*, 2005[189]	Yes	LOCF	Yes
Koran *et al.*, 1996[190]	Yes	LOCF	Yes
Kronig *et al.*, 1999[191]	Yes	LOCF	Yes
Liebowitz *et al.*, 2002[226]	Yes	LOCF	Yes
Lindsay *et al.*, 1997[192]	Unclear	Unclear	Unclear
López-Ibor *et al.*, 1996[193]	Yes	LOCF	Yes
March *et al.*, 1990[227]	Yes	Other	Yes
March *et al.*, 1998[228]	Yes	LOCF	Yes
Mavissakalian *et al.*, 1985[194]	No		No
McLean *et al.*, 2001[195]	No		No
Milanfranchi *et al.*, 1997[196]	No		No
Montgomery *et al.*, 1993[197]	Yes	LOCF	Yes
Montgomery *et al.*, 2001[198]	Yes	LOCF	Yes
Mundo *et al.*, 1997[199]	No		Yes
Mundo *et al.*, 2001[200]	Yes	LOCF	Yes
Nakajima *et al.*, 1996[201]	Yes	LOCF	Yes
Nakatani *et al.*, 2005[202]	No		No
Neziroglu *et al.*, 2000[229]	NA	NA	Yes
O'Connor *et al.*, 1999[203]	No		No
O'Connor *et al.*, 2006[204]	No		No
Perse *et al.*, 1987[205]	No		No
Piacentini *et al.*, 2011[230]	Yes	LOCF	Yes
Riddle *et al.*, 1992[231]	Yes	LOCF	Yes
Riddle *et al.*, 2001[232]	Yes	LOCF	Yes
Shareh *et al.*, 2010[206]	No		No
Sousa *et al.*, 2006[207]	NA	NA	NA

TABLE 72 Quality assessment: analysis section (*continued*)

Study	Imputation for missing data	Imputation method	ITT analysis
Stein *et al.*, 2007[124]	Yes	LOCF	Yes
Storch *et al.*, 2011[233]	Yes	LOCF	Yes
Storch *et al.*, 2013[234]	Yes	MLE	Yes
The Pediatric OCD Treatment Study, 2004[236]	Yes	LOCF	Yes
Thoren *et al.*, 1980[208]	No		No
Tollefson *et al.*, 1994[127]	No		No
Van Oppen *et al.*, 1995[209]	No		No
Volavka *et al.*, 1985[210]	No		No
Whittal *et al.*, 2005[211]	No		No
Whittal *et al.*, 2010[212]	No		No
Williams *et al.*, 2010[235]	Yes	LOCF	Yes
Zohar and Judge, 1996[213]	Yes	LOCF	Yes

CCSG, Clomipramine Collaborative Study Group; ITT, intention to treat; LOCF, last observation carried forward; MLE, maximum likelihood estimation; NA, not applicable.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 8 Detailed results of network meta-analysis

Adult subset: clinical effectiveness (Yale–Brown Obsessive–Compulsive Scale)

Network geometry

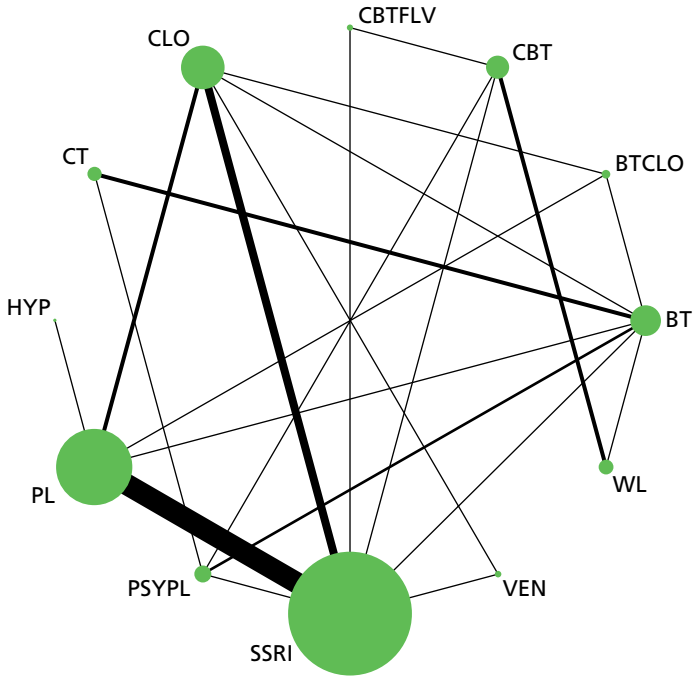


FIGURE 26 Network plot for class effects (the plot for individual effects is included in the main report). BTCLO, BT + clomipramine; CBTFLV, CBT + fluvoxamine; CLO, clomipramine; HYP, hypericum; PL, placebo; PSYPL, psychological placebo; VEN, venlafaxine; WL, waitlist.

TABLE 73 Model fit: consistency model

Model fit								
	Dbar	***Dhat***	***DIC***	***pD***				
mu.sd	2.773	2.773	2.773	4.24×10^{-12}				
sd1	386.1	382.1	390.2	4.046				
y	370.1	259.4	480.8	110.7				
total	759	644.2	873.7	114.7				
	Mean	***SD***	***MC_error***	***val2.5pc***	***Median***	***val97.5pc***	***Start***	***Sample***
sdev	3.128	0.3794	0.002615	2.462	3.102	3.95	50,001	100,000
totresdev	104.6	14.35	0.06465	78.34	103.9	134.6	50,001	100,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 74 Model fit: inconsistency model

Model fit								
	Dbar	***Dhat***	***DIC***	***pD***				
mu.sd	2.773	2.773	2.773	5.16×10^{-12}				
sd1	386.1	382.1	390.2	4.054				
y	370.8	262.6	479.1	108.3				
total	759.8	647.4	872.1	112.3				
	Mean	***SD***	***MC_error***	***val2.5pc***	***Median***	***val97.5pc***	***Start***	***Sample***
sdev	1.78	0.3462	0.003119	1.18	1.755	2.534	60,001	120,000
totresdev	105.8	14.46	0.06664	79.48	105.2	135.8	60,001	120,000

Data synthesis: consistency model (network meta-analysis)

Key: intervention (class)

1. Placebo (1).
2. Waitlist (2).
3. Fluoxetine (3).
4. Fluvoxamine (3).
5. Paroxetine (3).
6. Sertraline (3).
7. Citalopram (3).
8. Venlafaxine (4).
9. Clomipramine (5).
10. BT (6).
11. CBT (7).
12. CT (8).
13. Hypericum (9).
14. Fluvoxamine + CBT (10).
15. BT+ clomipramine (11).
16. Escitalopram (3).
17. Psychological placebo (12).

TABLE 75 Data synthesis: adults – class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[1,2]	5.62	2.378	0.02451	0.9106	5.635	10.26	50,001	100,000
class.mean.diff[1,3]	–3.493	0.8465	0.0126	–5.116	–3.503	–1.814	50,001	100,000
class.mean.diff[1,4]	–3.217	2.577	0.01525	–8.262	–3.225	1.885	50,001	100,000
class.mean.diff[1,5]	–4.724	1.078	0.009793	–6.851	–4.728	–2.601	50,001	100,000
class.mean.diff[1,6]	–14.48	2.131	0.02531	–18.61	–14.51	–10.23	50,001	100,000
class.mean.diff[1,7]	–5.374	1.898	0.02087	–9.098	–5.377	–1.632	50,001	100,000
class.mean.diff[1,8]	–13.36	2.59	0.02797	–18.4	–13.39	–8.21	50,001	100,000
class.mean.diff[1,9]	–0.1555	3.716	0.01768	–7.456	–0.1629	7.124	50,001	100,000
class.mean.diff[1,10]	–7.521	3.222	0.02186	–13.89	–7.517	–1.173	50,001	100,000
class.mean.diff[1,11]	–12.97	3.165	0.01717	–19.18	–12.97	–6.738	50,001	100,000
class.mean.diff[1,12]	–4.147	2.324	0.02623	–8.649	–4.171	0.4895	50,001	100,000
class.mean.diff[2,3]	–9.114	2.349	0.02079	–13.67	–9.133	–4.459	50,001	100,000
class.mean.diff[2,4]	–8.838	3.395	0.02372	–15.47	–8.856	–2.141	50,001	100,000
class.mean.diff[2,5]	–10.34	2.462	0.02028	–15.14	–10.36	–5.475	50,001	100,000
class.mean.diff[2,6]	–20.1	2.272	0.01427	–24.52	–20.13	–15.55	50,001	100,000
class.mean.diff[2,7]	–10.99	1.715	0.008719	–14.31	–11.01	–7.601	50,001	100,000
class.mean.diff[2,8]	–18.98	2.694	0.01744	–24.21	–19	–13.62	50,001	100,000
class.mean.diff[2,9]	–5.776	4.413	0.0298	–14.44	–5.784	2.911	50,001	100,000
class.mean.diff[2,10]	–13.14	3.501	0.01671	–19.98	–13.15	–6.262	50,001	100,000
class.mean.diff[2,11]	–18.59	3.719	0.02054	–25.88	–18.6	–11.23	50,001	100,000
class.mean.diff[2,12]	–9.768	2.455	0.01473	–14.51	–9.796	–4.857	50,001	100,000
class.mean.diff[3,4]	0.2759	2.553	0.01126	–4.731	0.2721	5.325	50,001	100,000
class.mean.diff[3,5]	–1.231	1.109	0.00638	–3.408	–1.231	0.9418	50,001	100,000
class.mean.diff[3,6]	–10.99	2.129	0.02277	–15.14	–11.01	–6.752	50,001	100,000
class.mean.diff[3,7]	–1.88	1.85	0.01643	–5.517	–1.878	1.763	50,001	100,000
class.mean.diff[3,8]	–9.866	2.587	0.02559	–14.91	–9.878	–4.739	50,001	100,000
class.mean.diff[3,9]	3.338	3.815	0.02117	–4.134	3.339	10.82	50,001	100,000
class.mean.diff[3,10]	–4.028	3.19	0.01734	–10.36	–4.016	2.212	50,001	100,000
class.mean.diff[3,11]	–9.476	3.211	0.01784	–15.78	–9.473	–3.137	50,001	100,000
class.mean.diff[3,12]	–0.6541	2.312	0.02379	–5.139	–0.6794	3.949	50,001	100,000
class.mean.diff[4,5]	–1.507	2.519	0.01091	–6.501	–1.502	3.436	50,001	100,000
class.mean.diff[4,6]	–11.26	3.229	0.02526	–17.57	–11.29	–4.862	50,001	100,000
class.mean.diff[4,7]	–2.156	3.074	0.0198	–8.191	–2.164	3.879	50,001	100,000
class.mean.diff[4,8]	–10.14	3.547	0.02778	–17.08	–10.16	–3.114	50,001	100,000
class.mean.diff[4,9]	3.062	4.517	0.02292	–5.836	3.084	11.9	50,001	100,000
class.mean.diff[4,10]	–4.304	4.033	0.02118	–12.26	–4.292	3.584	50,001	100,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 75 Data synthesis: adults – class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[4,11]	–9.752	3.988	0.01997	–17.62	–9.746	–1.905	50,001	100,000
class.mean.diff[4,12]	–0.93	3.354	0.02612	–7.449	–0.9471	5.711	50,001	100,000
class.mean.diff[5,6]	–9.756	2.191	0.02149	–14.02	–9.771	–5.404	50,001	100,000
class.mean.diff[5,7]	–0.6494	2.008	0.016	–4.604	–0.642	3.293	50,001	100,000
class.mean.diff[5,8]	–8.635	2.638	0.02443	–13.79	–8.651	–3.385	50,001	100,000
class.mean.diff[5,9]	4.569	3.876	0.02024	–3.072	4.582	12.15	50,001	100,000
class.mean.diff[5,10]	–2.797	3.291	0.01753	–9.323	–2.794	3.677	50,001	100,000
class.mean.diff[5,11]	–8.245	3.177	0.01566	–14.48	–8.238	–1.984	50,001	100,000
class.mean.diff[5,12]	0.577	2.384	0.02248	–4.048	0.559	5.333	50,001	100,000
class.mean.diff[6,7]	9.106	2.089	0.01435	4.97	9.109	13.18	50,001	100,000
class.mean.diff[6,8]	1.12	1.561	0.008178	–1.955	1.122	4.192	50,001	100,000
class.mean.diff[6,9]	14.32	4.282	0.03056	5.879	14.34	22.7	50,001	100,000
class.mean.diff[6,10]	6.959	3.54	0.0212	–0.04063	6.976	13.87	50,001	100,000
class.mean.diff[6,11]	1.511	3.379	0.01985	–5.158	1.517	8.135	50,001	100,000
class.mean.diff[6,12]	10.33	1.547	0.006452	7.289	10.33	13.38	50,001	100,000
class.mean.diff[7,8]	–7.986	2.532	0.01758	–12.97	–7.981	–3.008	50,001	100,000
class.mean.diff[7,9]	5.218	4.167	0.02699	–2.976	5.23	13.37	50,001	100,000
class.mean.diff[7,10]	–2.147	3.121	0.01332	–8.307	–2.136	3.987	50,001	100,000
class.mean.diff[7,11]	–7.596	3.495	0.01823	–14.46	–7.606	–0.7485	50,001	100,000
class.mean.diff[7,12]	1.226	2.173	0.01469	–3.029	1.22	5.541	50,001	100,000
class.mean.diff[8,9]	13.2	4.535	0.03276	4.261	13.19	22.11	50,001	100,000
class.mean.diff[8,10]	5.838	3.814	0.02375	–1.666	5.839	13.33	50,001	100,000
class.mean.diff[8,11]	0.3902	3.698	0.02294	–6.854	0.3933	7.678	50,001	100,000
class.mean.diff[8,12]	9.212	1.973	0.009613	5.341	9.213	13.1	50,001	100,000
class.mean.diff[9,10]	–7.366	4.933	0.02833	–17.08	–7.357	2.351	50,001	100,000
class.mean.diff[9,11]	–12.81	4.871	0.02431	–22.35	–12.81	–3.281	50,001	100,000
class.mean.diff[9,12]	–3.992	4.379	0.03134	–12.55	–3.996	4.653	50,001	100,000
class.mean.diff[10,11]	–5.448	4.415	0.02175	–14.08	–5.445	3.286	50,001	100,000
class.mean.diff[10,12]	3.374	3.619	0.02194	–3.661	3.354	10.53	50,001	100,000
class.mean.diff[11,12]	8.822	3.563	0.02118	1.849	8.797	15.84	50,001	100,000

TABLE 76 Data synthesis: adults – individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[1,2]	5.62	2.378	0.02451	0.9106	5.635	10.26	50,001	100,000
treat.mean.diff[1,3]	–3.463	0.9264	0.01216	–5.268	–3.478	–1.584	50,001	100,000
treat.mean.diff[1,4]	–3.604	0.8429	0.01194	–5.292	–3.594	–1.947	50,001	100,000
treat.mean.diff[1,5]	–3.416	0.878	0.01195	–5.105	–3.431	–1.611	50,001	100,000
treat.mean.diff[1,6]	–3.498	0.9257	0.0124	–5.304	–3.506	–1.628	50,001	100,000
treat.mean.diff[1,7]	–3.488	1.065	0.01272	–5.622	–3.498	–1.309	50,001	100,000
treat.mean.diff[1,8]	–3.217	2.577	0.01525	–8.262	–3.225	1.885	50,001	100,000
treat.mean.diff[1,9]	–4.724	1.078	0.009793	–6.851	–4.728	–2.601	50,001	100,000
treat.mean.diff[1,10]	–14.48	2.131	0.02531	–18.61	–14.51	–10.23	50,001	100,000
treat.mean.diff[1,11]	–5.374	1.898	0.02087	–9.098	–5.377	–1.632	50,001	100,000
treat.mean.diff[1,12]	–13.36	2.59	0.02797	–18.4	–13.39	–8.21	50,001	100,000
treat.mean.diff[1,13]	–0.1555	3.716	0.01768	–7.456	–0.1629	7.124	50,001	100,000
treat.mean.diff[1,14]	–7.521	3.222	0.02186	–13.89	–7.517	–1.173	50,001	100,000
treat.mean.diff[1,15]	–12.97	3.165	0.01717	–19.18	–12.97	–6.738	50,001	100,000
treat.mean.diff[1,16]	–3.483	1.088	0.01272	–5.611	–3.498	–1.234	50,001	100,000
treat.mean.diff[1,17]	–4.147	2.324	0.02623	–8.649	–4.171	0.4895	50,001	100,000
treat.mean.diff[2,3]	–9.083	2.36	0.02061	–13.68	–9.102	–4.405	50,001	100,000
treat.mean.diff[2,4]	–9.225	2.329	0.02016	–13.77	–9.237	–4.628	50,001	100,000
treat.mean.diff[2,5]	–9.036	2.384	0.02101	–13.68	–9.06	–4.306	50,001	100,000
treat.mean.diff[2,6]	–9.118	2.358	0.02042	–13.73	–9.134	–4.45	50,001	100,000
treat.mean.diff[2,7]	–9.108	2.451	0.0212	–13.89	–9.127	–4.253	50,001	100,000
treat.mean.diff[2,8]	–8.838	3.395	0.02372	–15.47	–8.856	–2.141	50,001	100,000
treat.mean.diff[2,9]	–10.34	2.462	0.02028	–15.14	–10.36	–5.475	50,001	100,000
treat.mean.diff[2,10]	–20.1	2.272	0.01427	–24.52	–20.13	–15.55	50,001	100,000
treat.mean.diff[2,11]	–10.99	1.715	0.008719	–14.31	–11.01	–7.601	50,001	100,000
treat.mean.diff[2,12]	–18.98	2.694	0.01744	–24.21	–19	–13.62	50,001	100,000
treat.mean.diff[2,13]	–5.776	4.413	0.0298	–14.44	–5.784	2.911	50,001	100,000
treat.mean.diff[2,14]	–13.14	3.501	0.01671	–19.98	–13.15	–6.262	50,001	100,000
treat.mean.diff[2,15]	–18.59	3.719	0.02054	–25.88	–18.6	–11.23	50,001	100,000
treat.mean.diff[2,16]	–9.103	2.457	0.02115	–13.9	–9.118	–4.223	50,001	100,000
treat.mean.diff[2,17]	–9.768	2.455	0.01473	–14.51	–9.796	–4.857	50,001	100,000
treat.mean.diff[3,4]	–0.1412	0.8752	0.004168	–2.196	–0.04312	1.62	50,001	100,000
treat.mean.diff[3,5]	0.04729	0.8874	0.003442	–1.843	0.009691	2.033	50,001	100,000
treat.mean.diff[3,6]	–0.03457	0.8854	0.00315	–2.019	–0.00726	1.857	50,001	100,000
treat.mean.diff[3,7]	–0.02461	1.042	0.004036	–2.315	–0.00442	2.256	50,001	100,000
treat.mean.diff[3,8]	0.2457	2.602	0.01119	–4.871	0.2425	5.377	50,001	100,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 76 Data synthesis: adults – individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[3,9]	–1.261	1.182	0.006338	–3.63	–1.254	1.055	50,001	100,000
treat.mean.diff[3,10]	–11.02	2.155	0.0226	–15.23	–11.04	–6.742	50,001	100,000
treat.mean.diff[3,11]	–1.911	1.853	0.01622	–5.549	–1.902	1.728	50,001	100,000
treat.mean.diff[3,12]	–9.896	2.606	0.02546	–14.98	–9.912	–4.757	50,001	100,000
treat.mean.diff[3,13]	3.308	3.832	0.02092	–4.217	3.312	10.81	50,001	100,000
treat.mean.diff[3,14]	–4.058	3.21	0.01732	–10.43	–4.039	2.225	50,001	100,000
treat.mean.diff[3,15]	–9.506	3.231	0.01754	–15.86	–9.5	–3.137	50,001	100,000
treat.mean.diff[3,16]	–0.01967	1.048	0.003805	–2.314	–0.0041	2.276	50,001	100,000
treat.mean.diff[3,17]	–0.6843	2.33	0.02355	–5.218	–0.7018	3.94	50,001	100,000
treat.mean.diff[4,5]	0.1885	0.8269	0.004488	–1.409	0.06661	2.146	50,001	100,000
treat.mean.diff[4,6]	0.1066	0.8689	0.003919	–1.676	0.02994	2.116	50,001	100,000
treat.mean.diff[4,7]	0.1166	0.9929	0.004682	–1.94	0.03256	2.417	50,001	100,000
treat.mean.diff[4,8]	0.3869	2.571	0.0118	–4.653	0.377	5.462	50,001	100,000
treat.mean.diff[4,9]	–1.12	1.083	0.005907	–3.24	–1.131	1.036	50,001	100,000
treat.mean.diff[4,10]	–10.88	2.099	0.02222	–14.96	–10.91	–6.69	50,001	100,000
treat.mean.diff[4,11]	–1.769	1.831	0.01591	–5.365	–1.776	1.866	50,001	100,000
treat.mean.diff[4,12]	–9.755	2.557	0.0251	–14.73	–9.778	–4.697	50,001	100,000
treat.mean.diff[4,13]	3.449	3.816	0.02111	–4.032	3.454	10.95	50,001	100,000
treat.mean.diff[4,14]	–3.917	3.147	0.01687	–10.14	–3.912	2.281	50,001	100,000
treat.mean.diff[4,15]	–9.365	3.198	0.01756	–15.62	–9.371	–3.02	50,001	100,000
treat.mean.diff[4,16]	0.1215	1.012	0.004475	–1.937	0.02962	2.493	50,001	100,000
treat.mean.diff[4,17]	–0.5431	2.283	0.02332	–4.964	–0.566	4.005	50,001	100,000
treat.mean.diff[5,6]	–0.08186	0.8859	0.003587	–2.096	–0.0227	1.769	50,001	100,000
treat.mean.diff[5,7]	–0.0719	0.9897	0.004086	–2.309	–0.01626	2.029	50,001	100,000
treat.mean.diff[5,8]	0.1984	2.501	0.01046	–4.704	0.1935	5.125	50,001	100,000
treat.mean.diff[5,9]	–1.309	1.101	0.005826	–3.508	–1.304	0.848	50,001	100,000
treat.mean.diff[5,10]	–11.06	2.156	0.023	–15.27	–11.08	–6.784	50,001	100,000
treat.mean.diff[5,11]	–1.958	1.898	0.0166	–5.704	–1.955	1.762	50,001	100,000
treat.mean.diff[5,12]	–9.944	2.61	0.02578	–15.06	–9.961	–4.784	50,001	100,000
treat.mean.diff[5,13]	3.26	3.821	0.02081	–4.243	3.263	10.76	50,001	100,000
treat.mean.diff[5,14]	–4.105	3.218	0.0176	–10.49	–4.092	2.212	50,001	100,000
treat.mean.diff[5,15]	–9.554	3.214	0.01765	–15.88	–9.547	–3.232	50,001	100,000
treat.mean.diff[5,16]	–0.06696	0.9761	0.003684	–2.261	–0.01811	2.024	50,001	100,000
treat.mean.diff[5,17]	–0.7316	2.342	0.02399	–5.301	–0.7494	3.927	50,001	100,000
treat.mean.diff[6,7]	0.009959	1.039	0.003995	–2.271	0.001729	2.285	50,001	100,000
treat.mean.diff[6,8]	0.2803	2.596	0.01146	–4.789	0.2729	5.417	50,001	100,000
treat.mean.diff[6,9]	–1.227	1.173	0.006392	–3.552	–1.224	1.095	50,001	100,000
treat.mean.diff[6,10]	–10.98	2.153	0.02246	–15.16	–11.01	–6.708	50,001	100,000

TABLE 76 Data synthesis: adults – individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[6,11]	–1.876	1.859	0.01605	–5.532	–1.881	1.798	50,001	100,000
treat.mean.diff[6,12]	–9.862	2.604	0.0253	–14.93	–9.871	–4.706	50,001	100,000
treat.mean.diff[6,13]	3.342	3.835	0.02118	–4.181	3.344	10.86	50,001	100,000
treat.mean.diff[6,14]	–4.023	3.209	0.01722	–10.39	–4.009	2.274	50,001	100,000
treat.mean.diff[6,15]	–9.472	3.23	0.01747	–15.82	–9.468	–3.113	50,001	100,000
treat.mean.diff[6,16]	0.0149	1.044	0.003616	–2.26	0.001961	2.338	50,001	100,000
treat.mean.diff[6,17]	–0.6497	2.333	0.02343	–5.19	–0.6678	3.987	50,001	100,000
treat.mean.diff[7,8]	0.2703	2.644	0.01148	–4.932	0.262	5.48	50,001	100,000
treat.mean.diff[7,9]	–1.237	1.304	0.007012	–3.847	–1.229	1.338	50,001	100,000
treat.mean.diff[7,10]	–10.99	2.24	0.0231	–15.36	–11.01	–6.56	50,001	100,000
treat.mean.diff[7,11]	–1.886	1.982	0.01693	–5.806	–1.884	2.029	50,001	100,000
treat.mean.diff[7,12]	–9.872	2.677	0.02598	–15.12	–9.893	–4.573	50,001	100,000
treat.mean.diff[7,13]	3.332	3.87	0.02124	–4.254	3.332	10.93	50,001	100,000
treat.mean.diff[7,14]	–4.033	3.265	0.01785	–10.52	–4.013	2.361	50,001	100,000
treat.mean.diff[7,15]	–9.482	3.281	0.01792	–15.91	–9.484	–3.001	50,001	100,000
treat.mean.diff[7,16]	0.004941	1.13	0.003898	–2.469	-3.77×10^{-4}	2.509	50,001	100,000
treat.mean.diff[7,17]	–0.6597	2.418	0.02409	–5.361	–0.6761	4.163	50,001	100,000
treat.mean.diff[8,9]	–1.507	2.519	0.01091	–6.501	–1.502	3.436	50,001	100,000
treat.mean.diff[8,10]	–11.26	3.229	0.02526	–17.57	–11.29	–4.862	50,001	100,000
treat.mean.diff[8,11]	–2.156	3.074	0.0198	–8.191	–2.164	3.879	50,001	100,000
treat.mean.diff[8,12]	–10.14	3.547	0.02778	–17.08	–10.16	–3.114	50,001	100,000
treat.mean.diff[8,13]	3.062	4.517	0.02292	–5.836	3.084	11.9	50,001	100,000
treat.mean.diff[8,14]	–4.304	4.033	0.02118	–12.26	–4.292	3.584	50,001	100,000
treat.mean.diff[8,15]	–9.752	3.988	0.01997	–17.62	–9.746	–1.905	50,001	100,000
treat.mean.diff[8,16]	–0.2654	2.646	0.0116	–5.501	–0.2571	4.944	50,001	100,000
treat.mean.diff[8,17]	–0.93	3.354	0.02612	–7.449	–0.9471	5.711	50,001	100,000
treat.mean.diff[9,10]	–9.756	2.191	0.02149	–14.02	–9.771	–5.404	50,001	100,000
treat.mean.diff[9,11]	–0.6494	2.008	0.016	–4.604	–0.642	3.293	50,001	100,000
treat.mean.diff[9,12]	–8.635	2.638	0.02443	–13.79	–8.651	–3.385	50,001	100,000
treat.mean.diff[9,13]	4.569	3.876	0.02024	–3.072	4.582	12.15	50,001	100,000
treat.mean.diff[9,14]	–2.797	3.291	0.01753	–9.323	–2.794	3.677	50,001	100,000
treat.mean.diff[9,15]	–8.245	3.177	0.01566	–14.48	–8.238	–1.984	50,001	100,000
treat.mean.diff[9,16]	1.242	1.316	0.006932	–1.352	1.236	3.89	50,001	100,000
treat.mean.diff[9,17]	0.577	2.384	0.02248	–4.048	0.559	5.333	50,001	100,000
treat.mean.diff[10,11]	9.106	2.089	0.01435	4.97	9.109	13.18	50,001	100,000
treat.mean.diff[10,12]	1.12	1.561	0.008178	–1.955	1.122	4.192	50,001	100,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 76 Data synthesis: adults – individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[10,13]	14.32	4.282	0.03056	5.879	14.34	22.7	50,001	100,000
treat.mean.diff[10,14]	6.959	3.54	0.0212	–0.04063	6.976	13.87	50,001	100,000
treat.mean.diff[10,15]	1.511	3.379	0.01985	–5.158	1.517	8.135	50,001	100,000
treat.mean.diff[10,16]	11	2.241	0.02308	6.548	11.01	15.4	50,001	100,000
treat.mean.diff[10,17]	10.33	1.547	0.006452	7.289	10.33	13.38	50,001	100,000
treat.mean.diff[11,12]	–7.986	2.532	0.01758	–12.97	–7.981	–3.008	50,001	100,000
treat.mean.diff[11,13]	5.218	4.167	0.02699	–2.976	5.23	13.37	50,001	100,000
treat.mean.diff[11,14]	–2.147	3.121	0.01332	–8.307	–2.136	3.987	50,001	100,000
treat.mean.diff[11,15]	–7.596	3.495	0.01823	–14.46	–7.606	–0.7485	50,001	100,000
treat.mean.diff[11,16]	1.891	1.985	0.0168	–2.03	1.891	5.813	50,001	100,000
treat.mean.diff[11,17]	1.226	2.173	0.01469	–3.029	1.22	5.541	50,001	100,000
treat.mean.diff[12,13]	13.2	4.535	0.03276	4.261	13.19	22.11	50,001	100,000
treat.mean.diff[12,14]	5.838	3.814	0.02375	–1.666	5.839	13.33	50,001	100,000
treat.mean.diff[12,15]	0.3902	3.698	0.02294	–6.854	0.3933	7.678	50,001	100,000
treat.mean.diff[12,16]	9.877	2.678	0.02587	4.591	9.889	15.14	50,001	100,000
treat.mean.diff[12,17]	9.212	1.973	0.009613	5.341	9.213	13.1	50,001	100,000
treat.mean.diff[13,14]	–7.366	4.933	0.02833	–17.08	–7.357	2.351	50,001	100,000
treat.mean.diff[13,15]	–12.81	4.871	0.02431	–22.35	–12.81	–3.281	50,001	100,000
treat.mean.diff[13,16]	–3.327	3.874	0.02134	–10.94	–3.331	4.227	50,001	100,000
treat.mean.diff[13,17]	–3.992	4.379	0.03134	–12.55	–3.996	4.653	50,001	100,000
treat.mean.diff[14,15]	–5.448	4.415	0.02175	–14.08	–5.445	3.286	50,001	100,000
treat.mean.diff[14,16]	4.038	3.274	0.01775	–2.386	4.023	10.51	50,001	100,000
treat.mean.diff[14,17]	3.374	3.619	0.02194	–3.661	3.354	10.53	50,001	100,000
treat.mean.diff[15,16]	9.487	3.285	0.01803	3.003	9.481	15.93	50,001	100,000
treat.mean.diff[15,17]	8.822	3.563	0.02118	1.849	8.797	15.84	50,001	100,000
treat.mean.diff[16,17]	–0.6646	2.418	0.0241	–5.384	–0.6767	4.141	50,001	100,000

TABLE 77 Data synthesis: adults – inconsistency model (pairwise comparison)

d	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
d[1,3]	–2.656	1.064	0.006615	–4.722	–2.666	–0.5367	60,001	120,000
d[1,4]	–3.577	0.9644	0.005258	–5.513	–3.566	–1.704	60,001	120,000
d[1,5]	–2.839	0.8353	0.004452	–4.48	–2.844	–1.174	60,001	120,000
d[1,6]	–2.85	1.188	0.006132	–5.182	–2.854	–0.503	60,001	120,000
d[1,7]	–3.653	1.32	0.008286	–6.255	–3.651	–1.056	60,001	120,000
d[1,9]	–6.278	0.9656	0.004634	–8.154	–6.291	–4.34	60,001	120,000
d[1,10]	–11.76	2.598	0.0167	–16.87	–11.77	–6.617	60,001	120,000
d[1,13]	–0.0795	2.658	0.01658	–5.297	–0.08029	5.112	60,001	120,000
d[1,15]	–12.25	2.599	0.01664	–17.29	–12.26	–7.094	60,001	120,000
d[1,16]	–3.281	1.563	0.008429	–6.38	–3.275	–0.1997	60,001	120,000
d[2,10]	–30.86	1.945	0.00709	–34.72	–30.86	–27	60,001	120,000
d[2,11]	–7.392	1.452	0.0107	–10.25	–7.395	–4.542	60,001	120,000
d[3,6]	0.1054	2.22	0.009702	–4.27	0.106	4.466	60,001	120,000
d[3,9]	–1.422	2.862	0.0203	–7.063	–1.414	4.208	60,001	120,000
d[3,11]	–0.3179	2.244	0.01055	–4.766	–0.3078	4.083	60,001	120,000
d[4,5]	5.399	4.21	0.0448	–2.866	5.41	13.59	60,001	120,000
d[4,7]	3.603	4.507	0.05032	–5.237	3.594	12.44	60,001	120,000
d[4,9]	–0.1027	1.331	0.007964	–2.735	–0.1039	2.515	60,001	120,000
d[4,10]	–7.277	3.785	0.05031	–14.74	–7.247	0.05766	60,001	120,000
d[4,11]	–9.656	2.408	0.01619	–14.4	–9.656	–4.914	60,001	120,000
d[4,14]	–8.149	2.426	0.0168	–12.92	–8.147	–3.367	60,001	120,000
d[4,17]	8.227	3.961	0.05129	0.4291	8.253	15.93	60,001	120,000
d[5,7]	Not estimable							
d[5,8]	0.6068	2.106	0.008706	–3.561	0.6089	4.744	60,001	120,000
d[5,9]	1.06	2.109	0.009106	–3.096	1.06	5.213	60,001	120,000
d[5,16]	Not estimable							
d[6,9]	2.581	2.123	0.009151	–1.611	2.584	6.762	60,001	120,000
d[6,11]	–3.44	2.711	0.01678	–8.768	–3.438	1.924	60,001	120,000
d[8,9]	–1.071	2.502	0.0164	–5.988	–1.08	3.865	60,001	120,000
d[9,10]	Not estimable							
d[9,15]	Not estimable							
d[10,12]	–0.3039	1.246	0.008738	–2.747	–0.3015	2.147	60,001	120,000
d[10,15]	Not estimable							
d[10,17]	8.424	1.437	0.008111	5.641	8.405	11.31	60,001	120,000
d[11,14]	Not estimable							
d[11,17]	5.937	2.105	0.01018	1.741	5.942	10.06	60,001	120,000
d[12,17]	2.673	2.301	0.01049	–1.86	2.686	7.185	60,001	120,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 78 Data synthesis: adults – median ranks (class effects)

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	10.37	0.6439	0.003308	9	10	11	50,001	100,000
rk.class[2]	11.89	0.3477	0.001867	11	12	12	50,001	100,000
rk.class[3]	7.882	1.128	0.007899	5	8	10	50,001	100,000
rk.class[4]	7.852	2	0.009506	4	8	11	50,001	100,000
rk.class[5]	6.353	1.27	0.007864	4	6	9	50,001	100,000
rk.class[6]	1.585	0.6645	0.002948	1	1	3	50,001	100,000
rk.class[7]	5.892	1.42	0.008825	4	6	9	50,001	100,000
rk.class[8]	2.294	0.8118	0.004527	1	2	4	50,001	100,000
rk.class[9]	9.666	2.042	0.01036	4	10	12	50,001	100,000
rk.class[10]	4.733	1.776	0.007904	2	4	9	50,001	100,000
rk.class[11]	2.369	1.104	0.00559	1	3	4	50,001	100,000
rk.class[12]	7.116	1.826	0.01607	4	7	10	50,001	100,000

TABLE 79 Data synthesis: adults – median ranks (individual effects)

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	15.36	0.6554	0.00344	14	15	16	50,001	100,000
rk[2]	16.89	0.3588	0.00192	16	17	17	50,001	100,000
rk[3]	10.46	2.306	0.01013	6	11	14	50,001	100,000
rk[4]	10.03	2.199	0.01102	6	10	14	50,001	100,000
rk[5]	10.61	2.204	0.01088	6	11	14	50,001	100,000
rk[6]	10.35	2.314	0.009603	6	10	14	50,001	100,000
rk[7]	10.35	2.498	0.01192	5	10	14	50,001	100,000
rk[8]	10.56	4.078	0.01757	4	12	16	50,001	100,000
rk[9]	7.078	2.24	0.01174	4	7	13	50,001	100,000
rk[10]	1.585	0.6645	0.002947	1	1	3	50,001	100,000
rk[11]	6.683	2.744	0.01967	4	6	14	50,001	100,000
rk[12]	2.295	0.8165	0.004561	1	2	4	50,001	100,000
rk[13]	13.71	3.736	0.01859	4	15	17	50,001	100,000
rk[14]	5.252	2.984	0.01282	2	4	14	50,001	100,000
rk[15]	2.38	1.168	0.005787	1	3	4	50,001	100,000
rk[16]	10.35	2.504	0.01141	5	10	14	50,001	100,000
rk[17]	9.053	3.823	0.03553	4	8	15	50,001	100,000

Children and adolescent/clinical effectiveness (CYBOCS)

Network geometry

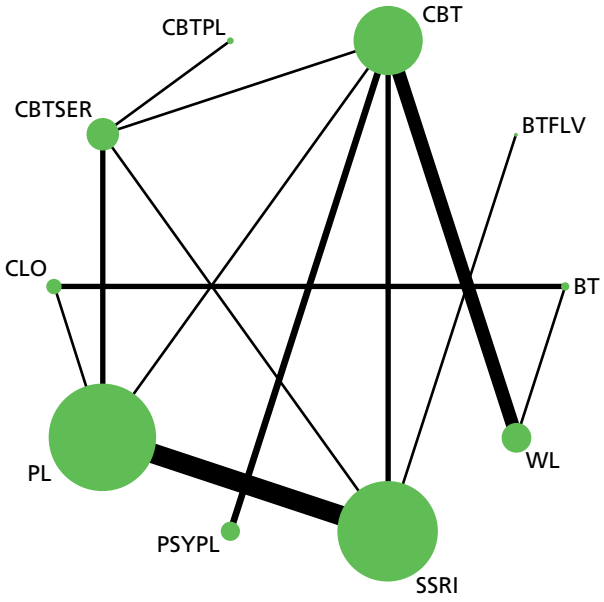


FIGURE 27 Network plot for class effects (the plot for individual effects is included in the main report). BTFLV, BT + fluvoxamine; CBTPL, CBT + placebo; CBTSER, CBT + sertraline; CLO, clomipramine; PL, placebo; PSYPL, psychological placebo; WL, waitlist.

TABLE 80 Model fit: children and adolescents – consistency model

Model fit								
	Dbar	***Dhat***	***DIC***	***pD***				
mu.sd	2.773	2.773	2.773	4.24×10^{-12}				
sd1	139.7	135.2	144.2	4.505				
y	156.2	110.9	201.6	45.36				
total	298.7	248.8	348.5	49.87				
	Mean	***SD***	***MC_error***	***val2.5pc***	***Median***	***val97.5pc***	***Start***	***Sample***
sdev	2.083	1.352	0.0313	0.1306	1.888	5.233	50,001	100,000
totresdev	35.04	7.992	0.07331	20.81	34.58	52.19	50,001	100,000

TABLE 81 Model fit: children and adolescents – inconsistency model

Model fit								
	Dbar	***Dhat***	***DIC***	***pD***				
mu.sd	2.773	2.773	2.773	6.30×10^{-12}				
sd1	139.7	135.2	144.2	4.504				
y	558.8	108.9	1009	449.9				
total	701.2	246.8	1156	454.4				
	Mean	***SD***	***MC_error***	***val2.5pc***	***Median***	***val97.5pc***	***Start***	***Sample***
sdev	2.062	1.506	0.02984	0.07666	1.809	5.782	70,000	140,001
totresdev	34.27	7.881	0.0579	20.53	33.71	51.36	70,000	140,001

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Data synthesis: consistency model (network meta-analysis)

Key

Treatment	Treatment ID	Class ID
Placebo	1	1
Waitlist	2	2
Psychological placebo	3	3
Fluoxetine	4	4
Fluvoxamine	5	4
Sertraline	6	4
Clomipramine	7	5
BT	8	6
CBT	9	7
BT + fluvoxamine	10	8
CBT + sertraline	11	9
CBT + placebo	12	10

TABLE 82 Data synthesis: children and adolescents – class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[1,2]	3.10E + 00	3.212	0.05846	–3.792	3.275	9.03	50,001	100,000
class.mean.diff[1,3]	–5.374	3.736	0.05499	–12.9	–5.318	2.011	50,001	100,000
class.mean.diff[1,4]	–3.577	2.379	0.01829	–8.57	–3.586	1.515	50,001	100,000
class.mean.diff[1,5]	–5.645	3.004	0.03301	–11.36	–5.736	0.6411	50,001	100,000
class.mean.diff[1,6]	–8.467	4.206	0.06413	–16.98	–8.355	–0.3873	50,001	100,000
class.mean.diff[1,7]	–8.664	2.798	0.04855	–14.38	–8.643	–3.139	50,001	100,000
class.mean.diff[1,8]	–6.123	4.247	0.04411	–14.49	–6.139	2.453	50,001	100,000
class.mean.diff[1,9]	–10.3	2.899	0.03269	–16.16	–10.27	–4.582	50,001	100,000
class.mean.diff[1,10]	–10.22	4.864	0.0634	–19.84	–10.19	–0.6097	50,001	100,000
class.mean.diff[2,3]	–8.474	3.04	0.03171	–14.15	–8.61	–2.028	50,001	100,000
class.mean.diff[2,4]	–6.678	3.848	0.05634	–13.96	–6.843	1.556	50,001	100,000
class.mean.diff[2,5]	–8.745	4.027	0.06251	–16.1	–9.018	–0.08619	50,001	100,000
class.mean.diff[2,6]	–11.57	3.843	0.04655	–19.04	–11.63	–3.788	50,001	100,000
class.mean.diff[2,7]	–11.77	1.782	0.02223	–14.91	–11.91	–7.83	50,001	100,000
class.mean.diff[2,8]	–9.223	5.273	0.07134	–19.09	–9.409	1.857	50,001	100,000
class.mean.diff[2,9]	–13.41	3.719	0.05122	–20.39	–13.52	–5.562	50,001	100,000
class.mean.diff[2,10]	–13.32	5.388	0.07379	–23.62	–13.42	–2.244	50,001	100,000
class.mean.diff[3,4]	1.796	4.285	0.05382	–6.692	1.727	10.48	50,001	100,000
class.mean.diff[3,5]	–0.2708	4.495	0.05865	–8.874	–0.3962	9.083	50,001	100,000
class.mean.diff[3,6]	–3.093	4.648	0.05348	–12.43	–3.028	6.046	50,001	100,000

TABLE 82 Data synthesis: children and adolescents – class effects (*continued*)

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[3,7]	–3.291	2.472	0.02408	–8.218	–3.284	1.637	50,001	100,000
class.mean.diff[3,8]	–0.7488	5.572	0.06654	–11.55	–0.7911	10.54	50,001	100,000
class.mean.diff[3,9]	–4.931	4.171	0.05001	–13.15	–4.954	3.422	50,001	100,000
class.mean.diff[3,10]	–4.842	5.686	0.07099	–16.03	–4.884	6.517	50,001	100,000
class.mean.diff[4,5]	–2.067	3.803	0.03652	–9.524	–2.189	5.901	50,001	100,000
class.mean.diff[4,6]	–4.889	4.752	0.06341	–14.6	–4.8	4.28	50,001	100,000
class.mean.diff[4,7]	–5.087	3.497	0.04683	–12.33	–5.027	1.864	50,001	100,000
class.mean.diff[4,8]	–2.545	4.413	0.04026	–11.24	–2.6	6.461	50,001	100,000
class.mean.diff[4,9]	–6.727	3.563	0.03146	–14.02	–6.7	0.4664	50,001	100,000
class.mean.diff[4,10]	–6.638	5.296	0.06311	–17.16	–6.637	3.873	50,001	100,000
class.mean.diff[5,6]	–2.822	4.143	0.0641	–11.37	–2.708	4.944	50,001	100,000
class.mean.diff[5,7]	–3.02	3.772	0.05265	–10.9	–2.876	4.19	50,001	100,000
class.mean.diff[5,8]	–0.478	5.187	0.05526	–11.06	–0.4075	9.66	50,001	100,000
class.mean.diff[5,9]	–4.66	4.054	0.04384	–13.04	–4.557	3.127	50,001	100,000
class.mean.diff[5,10]	–4.571	5.637	0.07232	–15.96	–4.49	6.375	50,001	100,000
class.mean.diff[6,7]	–0.1977	3.979	0.04858	–7.957	–0.2628	7.793	50,001	100,000
class.mean.diff[6,8]	2.344	5.954	0.07583	–9.139	2.32	14.35	50,001	100,000
class.mean.diff[6,9]	–1.838	4.766	0.06176	–11.08	–1.904	7.805	50,001	100,000
class.mean.diff[6,10]	–1.749	6.167	0.08015	–13.74	–1.834	10.65	50,001	100,000
class.mean.diff[7,8]	2.542	5.002	0.06231	–7.198	2.474	12.75	50,001	100,000
class.mean.diff[7,9]	–1.64	3.354	0.04181	–8.257	–1.633	5.06	50,001	100,000
class.mean.diff[7,10]	–1.551	5.131	0.06601	–11.68	–1.547	8.672	50,001	100,000
class.mean.diff[8,9]	–4.182	5.044	0.05016	–14.35	–4.165	5.715	50,001	100,000
class.mean.diff[8,10]	–4.093	6.354	0.06923	–16.77	–4.056	8.517	50,001	100,000
class.mean.diff[9,10]	0.08868	3.909	0.04742	–7.601	0.1137	7.812	50,001	100,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 83 Data synthesis: children and adolescents – individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[1,2]	3.101	3.212	0.05846	–3.792	3.275	9.03	50,001	100,000
treat.mean.diff[1,3]	–5.374	3.736	0.05499	–12.9	–5.318	2.011	50,001	100,000
treat.mean.diff[1,4]	–3.58	1.693	0.01926	–7.014	–3.588	–0.08378	50,001	100,000
treat.mean.diff[1,5]	–3.273	2.073	0.02171	–7.39	–3.334	1.127	50,001	100,000
treat.mean.diff[1,6]	–3.903	1.69	0.01729	–7.466	–3.845	–0.5958	50,001	100,000
treat.mean.diff[1,7]	–5.645	3.004	0.03301	–11.36	–5.736	0.6411	50,001	100,000
treat.mean.diff[1,8]	–8.467	4.206	0.06413	–16.98	–8.355	–0.3873	50,001	100,000
treat.mean.diff[1,9]	–8.664	2.798	0.04855	–14.38	–8.643	–3.139	50,001	100,000
treat.mean.diff[1,10]	–6.123	4.247	0.04411	–14.49	–6.139	2.453	50,001	100,000
treat.mean.diff[1,11]	–10.3	2.899	0.03269	–16.16	–10.27	–4.582	50,001	100,000
treat.mean.diff[1,12]	–10.22	4.864	0.0634	–19.84	–10.19	–0.6097	50,001	100,000
treat.mean.diff[2,3]	–8.474	3.04	0.03171	–14.15	–8.61	–2.028	50,001	100,000
treat.mean.diff[2,4]	–6.68	3.558	0.06036	–13.32	–6.846	0.9085	50,001	100,000
treat.mean.diff[2,5]	–6.373	3.71	0.05793	–13.18	–6.567	1.58	50,001	100,000
treat.mean.diff[2,6]	–7.004	3.324	0.05219	–13.24	–7.145	0.04082	50,001	100,000
treat.mean.diff[2,7]	–8.745	4.027	0.06251	–16.1	–9.018	–0.08619	50,001	100,000
treat.mean.diff[2,8]	–11.57	3.843	0.04655	–19.04	–11.63	–3.788	50,001	100,000
treat.mean.diff[2,9]	–11.77	1.782	0.02223	–14.91	–11.91	–7.83	50,001	100,000
treat.mean.diff[2,10]	–9.223	5.273	0.07134	–19.09	–9.409	1.857	50,001	100,000
treat.mean.diff[2,11]	–13.41	3.719	0.05122	–20.39	–13.52	–5.562	50,001	100,000
treat.mean.diff[2,12]	–13.32	5.388	0.07379	–23.62	–13.42	–2.244	50,001	100,000
treat.mean.diff[3,4]	1.794	4.023	0.05669	–5.995	1.719	10.03	50,001	100,000
treat.mean.diff[3,5]	2.101	4.162	0.05531	–6.055	2.018	10.64	50,001	100,000
treat.mean.diff[3,6]	1.47	3.83	0.05047	–6.121	1.457	9.187	50,001	100,000
treat.mean.diff[3,7]	–0.2708	4.495	0.05865	–8.874	–0.3962	9.083	50,001	100,000
treat.mean.diff[3,8]	–3.093	4.648	0.05348	–12.43	–3.028	6.046	50,001	100,000
treat.mean.diff[3,9]	–3.291	2.472	0.02408	–8.218	–3.284	1.637	50,001	100,000
treat.mean.diff[3,10]	–0.7488	5.572	0.06654	–11.55	–0.7911	10.54	50,001	100,000
treat.mean.diff[3,11]	–4.931	4.171	0.05001	–13.15	–4.954	3.422	50,001	100,000
treat.mean.diff[3,12]	–4.842	5.686	0.07099	–16.03	–4.884	6.517	50,001	100,000
treat.mean.diff[4,5]	0.307	2.246	0.01943	–4.344	0.1259	5.191	50,001	100,000
treat.mean.diff[4,6]	–0.3238	1.993	0.01728	–4.802	–0.129	3.582	50,001	100,000
treat.mean.diff[4,7]	–2.065	3.406	0.03578	–8.647	–2.177	5.01	50,001	100,000
treat.mean.diff[4,8]	–4.887	4.487	0.06599	–14.04	–4.789	3.696	50,001	100,000
treat.mean.diff[4,9]	–5.085	3.17	0.05022	–11.62	–5.016	1.052	50,001	100,000
treat.mean.diff[4,10]	–2.543	4.315	0.04213	–11.05	–2.564	6.081	50,001	100,000
treat.mean.diff[4,11]	–6.725	3.245	0.03557	–13.33	–6.666	–0.326	50,001	100,000

TABLE 83 Data synthesis: children and adolescents – individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[4,12]	–6.636	5.077	0.06581	–16.73	–6.632	3.319	50,001	100,000
treat.mean.diff[5,6]	–0.6308	2.251	0.01714	–5.809	–0.3063	3.693	50,001	100,000
treat.mean.diff[5,7]	–2.372	3.627	0.03927	–9.412	–2.481	5.184	50,001	100,000
treat.mean.diff[5,8]	–5.194	4.632	0.06495	–14.65	–5.112	3.752	50,001	100,000
treat.mean.diff[5,9]	–5.392	3.358	0.04913	–12.33	–5.295	1.14	50,001	100,000
treat.mean.diff[5,10]	–2.85	3.731	0.03711	–10.18	–2.877	4.587	50,001	100,000
treat.mean.diff[5,11]	–7.032	3.437	0.03377	–14.08	–6.998	–0.2872	50,001	100,000
treat.mean.diff[5,12]	–6.943	5.199	0.06297	–17.36	–6.922	3.356	50,001	100,000
treat.mean.diff[6,7]	–1.741	3.389	0.03599	–8.13	–1.877	5.471	50,001	100,000
treat.mean.diff[6,8]	–4.563	4.383	0.06104	–13.39	–4.497	3.961	50,001	100,000
treat.mean.diff[6,9]	–4.761	2.92	0.043	–10.69	–4.737	1.034	50,001	100,000
treat.mean.diff[6,10]	–2.22E+00	4.337	0.04293	–10.64	–2.267	6.639	50,001	100,000
treat.mean.diff[6,11]	–6.401	2.992	0.02854	–12.35	–6.394	–0.4037	50,001	100,000
treat.mean.diff[6,12]	–6.312	4.927	0.06145	–16.05	–6.315	3.455	50,001	100,000
treat.mean.diff[7,8]	–2.822	4.143	0.0641	–11.37	–2.708	4.944	50,001	100,000
treat.mean.diff[7,9]	–3.02	3.772	0.05265	–10.9	–2.876	4.19	50,001	100,000
treat.mean.diff[7,10]	–0.478	5.187	0.05526	–11.06	–0.4075	9.66	50,001	100,000
treat.mean.diff[7,11]	–4.66	4.054	0.04384	–13.04	–4.557	3.127	50,001	100,000
treat.mean.diff[7,12]	–4.571	5.637	0.07232	–15.96	–4.49	6.375	50,001	100,000
treat.mean.diff[8,9]	–0.1977	3.979	0.04858	–7.957	–0.2628	7.793	50,001	100,000
treat.mean.diff[8,10]	2.344	5.954	0.07583	–9.139	2.32	14.35	50,001	100,000
treat.mean.diff[8,11]	–1.838	4.766	0.06176	–11.08	–1.904	7.805	50,001	100,000
treat.mean.diff[8,12]	–1.749	6.167	0.08015	–13.74	–1.834	10.65	50,001	100,000
treat.mean.diff[9,10]	2.542	5.002	0.06231	–7.198	2.474	12.75	50,001	100,000
treat.mean.diff[9,11]	–1.64	3.354	0.04181	–8.257	–1.633	5.06	50,001	100,000
treat.mean.diff[9,12]	–1.551	5.131	0.06601	–11.68	–1.547	8.672	50,001	100,000
treat.mean.diff[10,11]	–4.182	5.044	0.05016	–14.35	–4.165	5.715	50,001	100,000
treat.mean.diff[10,12]	–4.093	6.354	0.06923	–16.77	–4.056	8.517	50,001	100,000
treat.mean.diff[11,12]	0.08868	3.909	0.04742	–7.601	0.1137	7.812	50,001	100,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 84 Data synthesis: children and adolescents – inconsistency model (pairwise comparison)

d	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
d[1,4]	–3.525	2.099	0.0166	–7.589	–3.553	0.8077	70,000	140,001
d[1,5]	–2.687	2.984	0.01831	–8.731	–2.705	3.354	70,000	140,001
d[1,6]	–3.989	2.122	0.01392	–8.452	–3.963	0.2112	70,000	140,001
d[1,7]	–7.623	3.303	0.02624	–14.21	–7.667	–0.9719	70,000	140,001
d[1,9]	–7.299	3.282	0.02647	–13.95	–7.278	–0.8807	70,000	140,001
d[1,11]	–10.12	3.166	0.02212	–16.58	–10.09	–3.844	70,000	140,001
d[2,8]	–7.051	4.672	0.05982	–16.17	–7.073	2.047	70,000	140,001
d[2,9]	–12.34	1.828	0.01991	–15.6	–12.47	–8.35	70,000	140,001
d[3,9]	–3.206	2.514	0.02367	–8.194	–3.214	1.915	70,000	140,001
d[5,10]	–2.811	3.829	0.04023	–10.26	–2.79	4.759	70,000	140,001
d[6,9]	Not estimable							
d[6,11]	Not estimable							
d[7,8]	–8.57	5.227	0.07107	–18.81	–8.609	1.701	70,000	140,001
d[9,11]	Not estimable							
d[11,12]	0.1554	3.988	0.04839	–7.703	0.1543	7.952	70,000	140,001

TABLE 85 Data synthesis: children and adolescents – median ranks (class effects)

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	8.879	0.7007	0.007675	7	9	10	50,001	100,000
rk.class[2]	9.707	0.7274	0.009997	7	10	10	50,001	100,000
rk.class[3]	5.887	1.851	0.02335	2	6	9	50,001	100,000
rk.class[4]	6.933	1.447	0.0142	3	7	9	50,001	100,000
rk.class[5]	5.574	1.831	0.02318	2	6	9	50,001	100,000
rk.class[6]	3.808	2.143	0.03	1	4	8	50,001	100,000
rk.class[7]	3.44	1.435	0.01966	1	3	6	50,001	100,000
rk.class[8]	5.212	2.385	0.02745	1	5	10	50,001	100,000
rk.class[9]	2.555	1.41	0.01666	1	2	6	50,001	100,000
rk.class[10]	3.005	2.204	0.0301	1	2	8	50,001	100,000

TABLE 86 Data synthesis: children and adolescents – median ranks (individual effects)

Mean	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	10.84	0.7791	0.008764	9	11	12	50,001	100,000
rk[2]	11.64	0.9671	0.01322	8	12	12	50,001	100,000
rk[3]	6.508	2.503	0.03344	2	6	11	50,001	100,000
rk[4]	7.963	1.701	0.02002	4	8	11	50,001	100,000
rk[5]	8.28	1.734	0.01771	4	9	11	50,001	100,000
rk[6]	7.667	1.621	0.01517	4	8	10	50,001	100,000
rk[7]	6.065	2.39	0.02953	2	6	11	50,001	100,000
rk[8]	4.057	2.571	0.03552	1	4	10	50,001	100,000
rk[9]	3.519	1.598	0.02183	1	3	7	50,001	100,000
rk[10]	5.701	2.976	0.03297	1	6	12	50,001	100,000
rk[11]	2.587	1.512	0.01737	1	2	6	50,001	100,000
rk[12]	3.171	2.57	0.03467	1	2	10	50,001	100,000

Adults/acceptability (total dropouts)

Network geometry

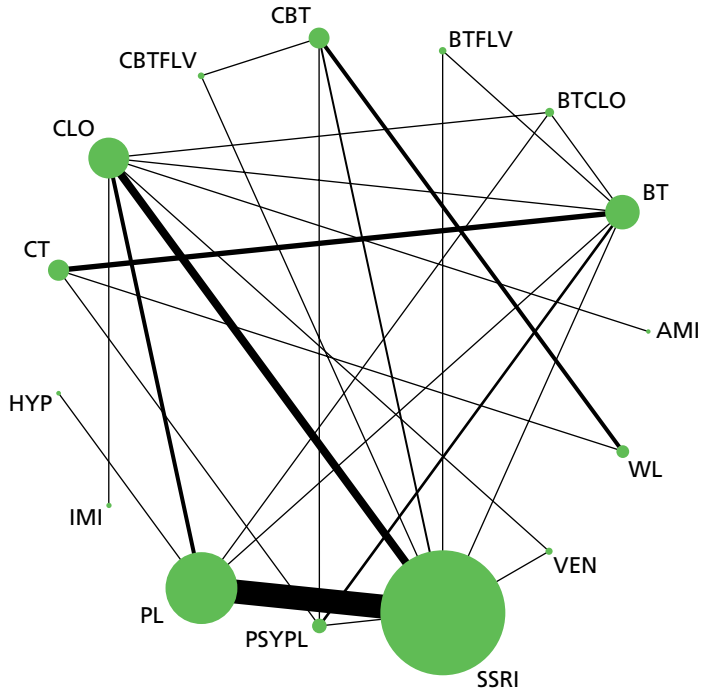


FIGURE 28 Network plot for class effects (the plot for individual effects is included in the main report). AMI, amitriptyline; BTCLO, BT + clomipramine; BTFLV, BT + fluvoxamine; CBTFLV, CBT + fluvoxamine; CLO, clomipramine; HYP, hypericum; IMI, imipramine; PL, placebo; PSYPL, psychological placebo; VEN, venlafaxine; WL, waitlist.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Model fit

TABLE 87 Model fit: adults – consistency model

Model fit								
	Dbar	***Dhat***	***DIC***	***pD***				
r	537.2	464.1	610.3	73.1				
total	537.2	464.1	610.3	73.1				
	Mean	***SD***	***MC_error***	***val2.5pc***	***Median***	***val97.5pc***	***Start***	***Sample***
sd	0.1379	0.08448	0.002286	0.008152	0.1295	0.3204	100,001	200,000
totresdev	118.2	12.81	0.1327	94.43	117.7	144.7	100,001	200,000

TABLE 88 Model fit: adults – inconsistency model

Model fit								
	Dbar	***Dhat***	***DIC***	***pD***				
r	539.3	452.5	626	86.73				
total	539.3	452.5	626	86.73				
	Mean	***SD***	***MC_error***	***val2.5pc***	***Median***	***val97.5pc***	***Start***	***Sample***
SD	0.1304	0.08595	0.001213	0.007238	0.1197	0.3231	100,001	200,000
totresdev	120.3	13.96	0.1046	94.57	119.7	149.3	100,001	200,000

Data synthesis: consistency model (network meta-analysis)

Key: intervention (class)

1. Placebo (1).
2. Waitlist (11).
3. Fluoxetine (3).
4. Fluvoxamine (3).
5. Paroxetine (3).
6. Sertraline (3).
7. Citalopram (3).
8. Venlafaxine (2).
9. Clomipramine (4).
10. BT (5).
11. CBT (6).
12. CT (7).
13. Amitriptyline (10).
14. BT + fluvoxamine (13).
15. CBT + fluvoxamine (9).
16. BT + clomipramine (8).
17. Escitalopram (3).
18. Psychological placebo (12).
19. Hypericum (14).
20. Imipramine (15).

TABLE 89 Data synthesis: adults – class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[1,2]	0.4546	0.2824	0.006189	0.1095	0.3921	1.148	100,001	200,000
OR.D[1,3]	1.087	0.1338	0.002307	0.8511	1.081	1.363	100,001	200,000
OR.D[1,4]	1.539	0.2175	0.004003	1.163	1.521	2.015	100,001	200,000
OR.D[1,5]	1.105	0.411	0.01157	0.5177	1.041	2.085	100,001	200,000
OR.D[1,6]	0.8339	0.3076	0.007419	0.4018	0.7748	1.595	100,001	200,000
OR.D[1,7]	1.103	0.4937	0.01353	0.4341	1.009	2.301	100,001	200,000
OR.D[1,8]	1.383	0.6327	0.01068	0.5262	1.267	2.931	100,001	200,000
OR.D[1,9]	11.39	59.29	1.302	0.04345	2.128	74.15	100,001	200,000
OR.D[1,10]	31.64	294	8.646	0.2991	4.513	138.6	100,001	200,000
OR.D[1,11]	0.5054	0.3846	0.01051	0.09958	0.402	1.502	100,001	200,000
OR.D[1,12]	0.5986	0.3323	0.008996	0.1878	0.5216	1.451	100,001	200,000
OR.D[1,13]	0.7691	0.6121	0.01333	0.1304	0.6073	2.353	100,001	200,000
OR.D[1,14]	1.018	0.6868	0.01217	0.2476	0.8517	2.729	100,001	200,000
OR.D[1,15]	3.486	4.934	0.1183	0.2908	1.965	16.07	100,001	200,000
OR.D[2,3]	3.437	2.555	0.0562	0.9351	2.754	9.894	100,001	200,000
OR.D[2,4]	4.848	3.603	0.0798	1.342	3.893	14.07	100,001	200,000
OR.D[2,5]	3.479	2.973	0.06704	0.7327	2.697	10.99	100,001	200,000
OR.D[2,6]	2.647	2.323	0.05077	0.5758	1.969	8.62	100,001	200,000
OR.D[2,7]	3.461	3.038	0.0705	0.655	2.641	11.18	100,001	200,000
OR.D[2,8]	4.347	3.974	0.07893	0.82	3.254	14.34	100,001	200,000
OR.D[2,9]	35.55	169.6	4.153	0.09668	5.559	245.3	100,001	200,000
OR.D[2,10]	88.25	763.8	19.5	0.6283	11.4	457.7	100,001	200,000
OR.D[2,11]	1.642	2.047	0.05398	0.1755	1.02	6.745	100,001	200,000
OR.D[2,12]	1.875	1.793	0.04252	0.3112	1.352	6.566	100,001	200,000
OR.D[2,13]	2.416	2.889	0.05796	0.2337	1.567	9.449	100,001	200,000
OR.D[2,14]	3.21	4.582	0.06746	0.4138	2.186	11.82	100,001	200,000
OR.D[2,15]	10.94	21.64	0.5357	0.6329	5.165	55.38	100,001	200,000
OR.D[3,4]	1.429	0.2256	0.003166	1.049	1.409	1.92	100,001	200,000
OR.D[3,5]	1.025	0.3859	0.0103	0.4757	0.9626	1.96	100,001	200,000
OR.D[3,6]	0.7713	0.2807	0.006354	0.3736	0.7205	1.458	100,001	200,000
OR.D[3,7]	1.022	0.4608	0.01212	0.398	0.9287	2.164	100,001	200,000
OR.D[3,8]	1.285	0.5984	0.009415	0.482	1.171	2.763	100,001	200,000
OR.D[3,9]	10.52	57.29	1.231	0.04033	1.96	68.64	100,001	200,000
OR.D[3,10]	28.96	266.4	7.609	0.281	4.165	130.1	100,001	200,000
OR.D[3,11]	0.4677	0.3561	0.009647	0.09169	0.3746	1.387	100,001	200,000
OR.D[3,12]	0.5544	0.3075	0.008097	0.1734	0.4835	1.343	100,001	200,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 89 Data synthesis: adults – class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[3,13]	0.7128	0.5665	0.01217	0.1194	0.5624	2.177	100,001	200,000
OR.D[3,14]	0.9489	0.6533	0.01133	0.2263	0.7891	2.598	100,001	200,000
OR.D[3,15]	3.239	4.603	0.1088	0.2702	1.82	15.01	100,001	200,000
OR.D[4,5]	0.725	0.2687	0.007152	0.3367	0.6836	1.365	100,001	200,000
OR.D[4,6]	0.5495	0.2096	0.00475	0.2521	0.5112	1.066	100,001	200,000
OR.D[4,7]	0.7238	0.3236	0.008512	0.279	0.6648	1.517	100,001	200,000
OR.D[4,8]	0.9061	0.4111	0.006424	0.3459	0.8282	1.912	100,001	200,000
OR.D[4,9]	7.599	40.91	0.893	0.02825	1.385	49.55	100,001	200,000
OR.D[4,10]	21.27	209	6.016	0.2031	2.94	90.76	100,001	200,000
OR.D[4,11]	0.3326	0.2554	0.006912	0.06458	0.2654	1.007	100,001	200,000
OR.D[4,12]	0.3925	0.2165	0.005704	0.1237	0.3411	0.9491	100,001	200,000
OR.D[4,13]	0.5061	0.4044	0.008782	0.08497	0.3978	1.579	100,001	200,000
OR.D[4,14]	0.6731	0.4673	0.008039	0.1572	0.5572	1.846	100,001	200,000
OR.D[4,15]	2.256	3.113	0.07227	0.1957	1.294	10.07	100,001	200,000
OR.D[5,6]	0.8443	0.4219	0.01039	0.3086	0.7506	1.904	100,001	200,000
OR.D[5,7]	1.002	0.2496	0.00467	0.598	0.9733	1.573	100,001	200,000
OR.D[5,8]	1.362	0.693	0.01231	0.4607	1.223	3.091	100,001	200,000
OR.D[5,9]	11.3	70.18	1.397	0.04308	2.05	77.11	100,001	200,000
OR.D[5,10]	31.6	283.5	8.307	0.2778	4.329	133.7	100,001	200,000
OR.D[5,11]	0.5049	0.4307	0.01168	0.0914	0.3873	1.65	100,001	200,000
OR.D[5,12]	0.5443	0.2164	0.004716	0.2302	0.506	1.06	100,001	200,000
OR.D[5,13]	0.7347	0.5717	0.01167	0.1261	0.5881	2.234	100,001	200,000
OR.D[5,14]	1.048	0.8506	0.01773	0.1978	0.8174	3.252	100,001	200,000
OR.D[5,15]	3.483	5.141	0.1092	0.2599	1.923	16.52	100,001	200,000
OR.D[6,7]	1.467	0.8041	0.01971	0.4573	1.292	3.472	100,001	200,000
OR.D[6,8]	1.862	1.1	0.0206	0.5442	1.614	4.707	100,001	200,000
OR.D[6,9]	14.49	73.24	1.588	0.05081	2.72	96.33	100,001	200,000
OR.D[6,10]	40.64	335.9	10.24	0.3673	5.493	195.3	100,001	200,000
OR.D[6,11]	0.614	0.4048	0.01061	0.1467	0.526	1.641	100,001	200,000
OR.D[6,12]	0.7916	0.4931	0.01244	0.2065	0.6677	2.035	100,001	200,000
OR.D[6,13]	1.037	0.94	0.02044	0.1448	0.7629	3.418	100,001	200,000
OR.D[6,14]	1.372	1.075	0.01909	0.2664	1.09	4.156	100,001	200,000
OR.D[6,15]	4.731	7.86	0.2071	0.3283	2.57	21.78	100,001	200,000
OR.D[7,8]	1.442	0.8391	0.01591	0.4264	1.251	3.555	100,001	200,000
OR.D[7,9]	11.77	72.72	1.422	0.04379	2.1	80.25	100,001	200,000
OR.D[7,10]	32.96	305.2	8.652	0.2665	4.467	145.6	100,001	200,000
OR.D[7,11]	0.527	0.4687	0.0128	0.09104	0.3952	1.767	100,001	200,000
OR.D[7,12]	0.5707	0.2543	0.005342	0.2155	0.525	1.178	100,001	200,000

TABLE 89 Data synthesis: adults – class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[7,13]	0.7775	0.6611	0.01371	0.1214	0.601	2.464	100,001	200,000
OR.D[7,14]	1.107	0.9609	0.02076	0.1875	0.847	3.562	100,001	200,000
OR.D[7,15]	3.674	5.679	0.1201	0.2566	1.99	17.86	100,001	200,000
OR.D[8,9]	9.921	60.43	1.178	0.03375	1.735	65.2	100,001	200,000
OR.D[8,10]	28.5	317.4	7.988	0.2241	3.573	120	100,001	200,000
OR.D[8,11]	0.4387	0.4185	0.009987	0.06539	0.3156	1.566	100,001	200,000
OR.D[8,12]	0.5026	0.3446	0.006854	0.1265	0.4141	1.405	100,001	200,000
OR.D[8,13]	0.6512	0.6021	0.01046	0.09153	0.4819	2.245	100,001	200,000
OR.D[8,14]	0.894	0.7887	0.01299	0.1541	0.671	2.934	100,001	200,000
OR.D[8,15]	2.957	4.606	0.08921	0.1993	1.574	14.18	100,001	200,000
OR.D[9,10]	59.82	684.1	14.32	0.02385	2.139	291.7	100,001	200,000
OR.D[9,11]	2.12	27.16	0.6386	0.004269	0.1896	11.94	100,001	200,000
OR.D[9,12]	2.971	52.54	1.085	0.006906	0.2424	12.3	100,001	200,000
OR.D[9,13]	3.417	53.45	1.251	0.005859	0.2718	16.1	100,001	200,000
OR.D[9,14]	4.489	62.3	1.452	0.009721	0.3928	23.35	100,001	200,000
OR.D[9,15]	10.21	84.75	1.67	0.01887	1.002	74.09	100,001	200,000
OR.D[10,11]	0.3217	1.189	0.02484	0.002413	0.08551	1.913	100,001	200,000
OR.D[10,12]	0.3608	1.521	0.02863	0.003334	0.117	2.003	100,001	200,000
OR.D[10,13]	0.4583	2.107	0.03533	0.003304	0.1371	2.633	100,001	200,000
OR.D[10,14]	0.6583	3.664	0.05761	0.005043	0.1925	3.699	100,001	200,000
OR.D[10,15]	1.952	8.639	0.1464	0.009582	0.4587	12.83	100,001	200,000
OR.D[11,12]	1.834	1.712	0.04359	0.254	1.325	6.453	100,001	200,000
OR.D[11,13]	2.458	3.08	0.07976	0.2077	1.47	10.96	100,001	200,000
OR.D[11,14]	3.319	4.124	0.09609	0.354	2.132	13.53	100,001	200,000
OR.D[11,15]	11.59	22.71	0.5601	0.4562	4.985	64.95	100,001	200,000
OR.D[12,13]	1.557	1.423	0.02744	0.2142	1.16	5.396	100,001	200,000
OR.D[12,14]	2.248	2.206	0.0467	0.3217	1.628	7.927	100,001	200,000
OR.D[12,15]	7.492	12.33	0.255	0.4661	3.715	38.18	100,001	200,000
OR.D[13,14]	2.288	3.079	0.05419	0.2268	1.417	9.682	100,001	200,000
OR.D[13,15]	7.571	17.92	0.3625	0.3497	3.417	38.12	100,001	200,000
OR.D[14,15]	5.008	9.252	0.2034	0.2605	2.337	26.58	100,001	200,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 90 Data synthesis: adults – individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[1,2]	0.5054	0.3846	0.01051	0.09958	0.402	1.502	100,001	200,000
OR[1,3]	1.146	0.1657	0.00323	0.8801	1.125	1.539	100,001	200,000
OR[1,4]	1.101	0.1416	0.00298	0.852	1.092	1.409	100,001	200,000
OR[1,5]	1.099	0.1324	0.002389	0.8648	1.09	1.385	100,001	200,000
OR[1,6]	1.042	0.1368	0.002443	0.785	1.039	1.326	100,001	200,000
OR[1,7]	1.063	0.1678	0.002733	0.7366	1.059	1.413	100,001	200,000
OR[1,8]	0.4546	0.2824	0.006189	0.1095	0.3921	1.148	100,001	200,000
OR[1,9]	1.539	0.2175	0.004003	1.163	1.521	2.015	100,001	200,000
OR[1,10]	1.105	0.411	0.01157	0.5177	1.041	2.085	100,001	200,000
OR[1,11]	0.8339	0.3076	0.007419	0.4018	0.7748	1.595	100,001	200,000
OR[1,12]	1.103	0.4937	0.01353	0.4341	1.009	2.301	100,001	200,000
OR[1,13]	31.64	294	8.646	0.2991	4.513	138.6	100,001	200,000
OR[1,14]	0.7691	0.6121	0.01333	0.1304	0.6073	2.353	100,001	200,000
OR[1,15]	11.39	59.29	1.302	0.04345	2.128	74.15	100,001	200,000
OR[1,16]	1.383	0.6327	0.01068	0.5262	1.267	2.931	100,001	200,000
OR[1,17]	1.091	0.1666	0.002681	0.7961	1.081	1.461	100,001	200,000
OR[1,18]	0.5986	0.3323	0.008996	0.1878	0.5216	1.451	100,001	200,000
OR[1,19]	1.018	0.6868	0.01217	0.2476	0.8517	2.729	100,001	200,000
OR[1,20]	3.486	4.934	0.1183	0.2908	1.965	16.07	100,001	200,000
OR[2,3]	3.64	2.864	0.07925	0.7702	2.818	11.32	100,001	200,000
OR[2,4]	3.521	2.808	0.07836	0.7258	2.7	10.95	100,001	200,000
OR[2,5]	3.52	2.818	0.07883	0.7285	2.702	11.11	100,001	200,000
OR[2,6]	3.337	2.688	0.07447	0.6859	2.541	10.6	100,001	200,000
OR[2,7]	3.41	2.764	0.07634	0.6762	2.605	10.82	100,001	200,000
OR[2,8]	1.476	1.646	0.03985	0.1483	0.9807	5.698	100,001	200,000
OR[2,9]	4.933	3.982	0.1111	0.9928	3.768	15.49	100,001	200,000
OR[2,10]	3.423	2.827	0.07772	0.6061	2.582	10.94	100,001	200,000
OR[2,11]	2.409	1.719	0.04724	0.6094	1.901	6.815	100,001	200,000
OR[2,12]	3.364	2.856	0.07542	0.566	2.531	10.98	100,001	200,000
OR[2,13]	85.96	665.7	19.86	0.5226	11.69	414.6	100,001	200,000
OR[2,14]	2.458	3.08	0.07976	0.2077	1.47	10.96	100,001	200,000
OR[2,15]	32.47	174.6	3.61	0.08373	5.275	234.4	100,001	200,000
OR[2,16]	4.379	4.156	0.09986	0.6387	3.168	15.29	100,001	200,000
OR[2,17]	3.487	2.807	0.07781	0.7085	2.674	11.01	100,001	200,000
OR[2,18]	1.834	1.712	0.04359	0.254	1.325	6.453	100,001	200,000
OR[2,19]	3.319	4.124	0.09609	0.354	2.132	13.53	100,001	200,000
OR[2,20]	11.59	22.71	0.5601	0.4562	4.985	64.95	100,001	200,000
OR[3,4]	0.9715	0.1316	0.002139	0.6796	0.9855	1.246	100,001	200,000
OR[3,5]	0.9703	0.1269	0.00171	0.6966	0.9837	1.235	100,001	200,000
OR[3,6]	0.9206	0.1304	0.002143	0.6268	0.9486	1.143	100,001	200,000

TABLE 90 Data synthesis: adults – individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[3,7]	0.9392	0.1547	0.002319	0.5827	0.9685	1.229	100,001	200,000
OR[3,8]	0.4023	0.2532	0.00544	0.09534	0.3422	1.015	100,001	200,000
OR[3,9]	1.362	0.2279	0.00366	0.9379	1.35	1.853	100,001	200,000
OR[3,10]	0.9754	0.3665	0.009627	0.4438	0.9183	1.871	100,001	200,000
OR[3,11]	0.7303	0.2527	0.005679	0.36	0.6864	1.332	100,001	200,000
OR[3,12]	0.973	0.4383	0.01139	0.3734	0.8857	2.06	100,001	200,000
OR[3,13]	27.29	237.7	7.204	0.2683	3.99	123.8	100,001	200,000
OR[3,14]	0.6805	0.5435	0.01177	0.111	0.5364	2.114	100,001	200,000
OR[3,15]	10.01	53.13	1.166	0.03831	1.855	65.45	100,001	200,000
OR[3,16]	1.224	0.5745	0.00902	0.4514	1.117	2.648	100,001	200,000
OR[3,17]	0.962	0.1468	0.001912	0.6432	0.9805	1.264	100,001	200,000
OR[3,18]	0.5276	0.2913	0.007611	0.1619	0.4604	1.291	100,001	200,000
OR[3,19]	0.9042	0.6268	0.01106	0.2144	0.7482	2.495	100,001	200,000
OR[3,20]	3.092	4.437	0.1049	0.2544	1.739	14.15	100,001	200,000
OR[4,5]	1.008	0.1307	0.001907	0.7557	1	1.317	100,001	200,000
OR[4,6]	0.9556	0.1308	0.002129	0.6772	0.9749	1.219	100,001	200,000
OR[4,7]	0.9742	0.1561	0.002078	0.6388	0.9871	1.315	100,001	200,000
OR[4,8]	0.4177	0.2622	0.005638	0.09918	0.3575	1.062	100,001	200,000
OR[4,9]	1.412	0.2153	0.00355	1.037	1.393	1.884	100,001	200,000
OR[4,10]	1.01	0.3718	0.009983	0.4754	0.9506	1.922	100,001	200,000
OR[4,11]	0.7633	0.2812	0.006348	0.3663	0.7095	1.458	100,001	200,000
OR[4,12]	1.008	0.4471	0.0118	0.3998	0.9185	2.137	100,001	200,000
OR[4,13]	28.57	260.8	7.54	0.2757	4.066	128.8	100,001	200,000
OR[4,14]	0.7001	0.5479	0.01173	0.1206	0.555	2.117	100,001	200,000
OR[4,15]	10.38	55.63	1.208	0.03995	1.935	66.97	100,001	200,000
OR[4,16]	1.268	0.5865	0.009184	0.4781	1.158	2.714	100,001	200,000
OR[4,17]	0.999	0.1534	0.001928	0.6945	0.9973	1.354	100,001	200,000
OR[4,18]	0.5467	0.3009	0.007949	0.1747	0.4782	1.328	100,001	200,000
OR[4,19]	0.9389	0.6505	0.01133	0.2231	0.7757	2.577	100,001	200,000
OR[4,20]	3.182	4.486	0.1031	0.2699	1.79	14.34	100,001	200,000
OR[5,6]	0.9554	0.1262	0.001717	0.6835	0.9739	1.212	100,001	200,000
OR[5,7]	0.974	0.1515	0.001814	0.6456	0.987	1.296	100,001	200,000
OR[5,8]	0.4147	0.2534	0.005529	0.1012	0.3593	1.029	100,001	200,000
OR[5,9]	1.412	0.2086	0.003072	1.046	1.397	1.868	100,001	200,000
OR[5,10]	1.013	0.3773	0.01014	0.4664	0.9546	1.92	100,001	200,000
OR[5,11]	0.7637	0.2809	0.006426	0.3654	0.7111	1.456	100,001	200,000
OR[5,12]	1.011	0.4524	0.01199	0.3923	0.9218	2.121	100,001	200,000
OR[5,13]	28.58	259.1	7.517	0.2763	4.13	128.4	100,001	200,000
OR[5,14]	0.704	0.5564	0.01195	0.1189	0.5555	2.131	100,001	200,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 90 Data synthesis: adults – individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[5,15]	10.44	56.56	1.22	0.03955	1.935	68.25	100,001	200,000
OR[5,16]	1.269	0.5876	0.009358	0.4772	1.162	2.725	100,001	200,000
OR[5,17]	0.9973	0.1375	0.001376	0.7274	0.9967	1.314	100,001	200,000
OR[5,18]	0.548	0.3014	0.007975	0.1702	0.4789	1.329	100,001	200,000
OR[5,19]	0.9384	0.6472	0.01124	0.2231	0.7797	2.568	100,001	200,000
OR[5,20]	3.203	4.561	0.109	0.2661	1.807	15.02	100,001	200,000
OR[6,7]	1.029	0.1702	0.002173	0.7202	1.007	1.453	100,001	200,000
OR[6,8]	0.4412	0.276	0.005935	0.104	0.3794	1.118	100,001	200,000
OR[6,9]	1.495	0.2482	0.003963	1.081	1.469	2.061	100,001	200,000
OR[6,10]	1.073	0.4116	0.01112	0.4918	1.001	2.077	100,001	200,000
OR[6,11]	0.8072	0.2982	0.006886	0.386	0.7514	1.533	100,001	200,000
OR[6,12]	1.071	0.4889	0.01292	0.412	0.9697	2.306	100,001	200,000
OR[6,13]	30.42	280.2	8.141	0.2922	4.339	135.4	100,001	200,000
OR[6,14]	0.7473	0.5986	0.01322	0.1243	0.5863	2.329	100,001	200,000
OR[6,15]	10.95	59.74	1.273	0.04193	2.042	72.71	100,001	200,000
OR[6,16]	1.344	0.6319	0.01025	0.4972	1.223	2.886	100,001	200,000
OR[6,17]	1.057	0.179	0.002455	0.7688	1.017	1.504	100,001	200,000
OR[6,18]	0.5804	0.3238	0.008627	0.1792	0.5024	1.394	100,001	200,000
OR[6,19]	0.9924	0.6832	0.01197	0.2337	0.8286	2.725	100,001	200,000
OR[6,20]	3.385	4.835	0.1141	0.2827	1.911	15.34	100,001	200,000
OR[7,8]	0.4375	0.2814	0.006025	0.1004	0.3746	1.148	100,001	200,000
OR[7,9]	1.48	0.3017	0.004631	1.012	1.439	2.205	100,001	200,000
OR[7,10]	1.062	0.4309	0.01126	0.4743	0.9828	2.105	100,001	200,000
OR[7,11]	0.7997	0.3172	0.007052	0.3729	0.7357	1.593	100,001	200,000
OR[7,12]	1.059	0.5044	0.01298	0.3995	0.9528	2.318	100,001	200,000
OR[7,13]	29.9	277.2	7.74	0.287	4.276	134.2	100,001	200,000
OR[7,14]	0.7391	0.6056	0.01274	0.1215	0.5756	2.286	100,001	200,000
OR[7,15]	10.8	56.9	1.236	0.04037	2.015	71.57	100,001	200,000
OR[7,16]	1.329	0.6467	0.0102	0.4849	1.199	2.929	100,001	200,000
OR[7,17]	1.044	0.2045	0.002524	0.7223	1.007	1.576	100,001	200,000
OR[7,18]	0.5749	0.3338	0.008727	0.1733	0.4948	1.418	100,001	200,000
OR[7,19]	0.9805	0.688	0.01158	0.229	0.8131	2.729	100,001	200,000
OR[7,20]	3.351	4.772	0.1112	0.2727	1.868	15.43	100,001	200,000
OR[8,9]	4.848	3.603	0.0798	1.342	3.893	14.07	100,001	200,000
OR[8,10]	3.479	2.973	0.06704	0.7327	2.697	10.99	100,001	200,000
OR[8,11]	2.647	2.323	0.05077	0.5758	1.969	8.62	100,001	200,000
OR[8,12]	3.461	3.038	0.0705	0.655	2.641	11.18	100,001	200,000
OR[8,13]	88.25	763.8	19.5	0.6283	11.4	457.7	100,001	200,000
OR[8,14]	2.416	2.889	0.05796	0.2337	1.567	9.449	100,001	200,000
OR[8,15]	35.55	169.6	4.153	0.09668	5.559	245.3	100,001	200,000

TABLE 90 Data synthesis: adults – individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[8,16]	4.347	3.974	0.07893	0.82	3.254	14.34	100,001	200,000
OR[8,17]	3.446	2.587	0.05629	0.9096	2.768	9.988	100,001	200,000
OR[8,18]	1.875	1.793	0.04252	0.3112	1.352	6.566	100,001	200,000
OR[8,19]	3.21	4.582	0.06746	0.4138	2.186	11.82	100,001	200,000
OR[8,20]	10.94	21.64	0.5357	0.6329	5.165	55.38	100,001	200,000
OR[9,10]	0.725	0.2687	0.007152	0.3367	0.6836	1.365	100,001	200,000
OR[9,11]	0.5495	0.2096	0.00475	0.2521	0.5112	1.066	100,001	200,000
OR[9,12]	0.7238	0.3236	0.008512	0.279	0.6648	1.517	100,001	200,000
OR[9,13]	21.27	209	6.016	0.2031	2.94	90.76	100,001	200,000
OR[9,14]	0.5061	0.4044	0.008782	0.08497	0.3978	1.579	100,001	200,000
OR[9,15]	7.599	40.91	0.893	0.02825	1.385	49.55	100,001	200,000
OR[9,16]	0.9061	0.4111	0.006424	0.3459	0.8282	1.912	100,001	200,000
OR[9,17]	0.719	0.1298	0.001756	0.4905	0.7096	1.006	100,001	200,000
OR[9,18]	0.3925	0.2165	0.005704	0.1237	0.3411	0.9491	100,001	200,000
OR[9,19]	0.6731	0.4673	0.008039	0.1572	0.5572	1.846	100,001	200,000
OR[9,20]	2.256	3.113	0.07227	0.1957	1.294	10.07	100,001	200,000
OR[10,11]	0.8443	0.4219	0.01039	0.3086	0.7506	1.904	100,001	200,000
OR[10,12]	1.002	0.2496	0.00467	0.598	0.9733	1.573	100,001	200,000
OR[10,13]	31.6	283.5	8.307	0.2778	4.329	133.7	100,001	200,000
OR[10,14]	0.7347	0.5717	0.01167	0.1261	0.5881	2.234	100,001	200,000
OR[10,15]	11.3	70.18	1.397	0.04308	2.05	77.11	100,001	200,000
OR[10,16]	1.362	0.693	0.01231	0.4607	1.223	3.091	100,001	200,000
OR[10,17]	1.115	0.4284	0.01116	0.4918	1.038	2.147	100,001	200,000
OR[10,18]	0.5443	0.2164	0.004716	0.2302	0.506	1.06	100,001	200,000
OR[10,19]	1.048	0.8506	0.01773	0.1978	0.8174	3.252	100,001	200,000
OR[10,20]	3.483	5.141	0.1092	0.2599	1.923	16.52	100,001	200,000
OR[11,12]	1.467	0.8041	0.01971	0.4573	1.292	3.472	100,001	200,000
OR[11,13]	40.64	335.9	10.24	0.3673	5.493	195.3	100,001	200,000
OR[11,14]	1.037	0.94	0.02044	0.1448	0.7629	3.418	100,001	200,000
OR[11,15]	14.49	73.24	1.588	0.05081	2.72	96.33	100,001	200,000
OR[11,16]	1.862	1.1	0.0206	0.5442	1.614	4.707	100,001	200,000
OR[11,17]	1.468	0.5409	0.01177	0.6645	1.389	2.759	100,001	200,000
OR[11,18]	0.7916	0.4931	0.01244	0.2065	0.6677	2.035	100,001	200,000
OR[11,19]	1.372	1.075	0.01909	0.2664	1.09	4.156	100,001	200,000
OR[11,20]	4.731	7.86	0.2071	0.3283	2.57	21.78	100,001	200,000
OR[12,13]	32.96	305.2	8.652	0.2665	4.467	145.6	100,001	200,000
OR[12,14]	0.7775	0.6611	0.01371	0.1214	0.601	2.464	100,001	200,000
OR[12,15]	11.77	72.72	1.422	0.04379	2.1	80.25	100,001	200,000
OR[12,16]	1.442	0.8391	0.01591	0.4264	1.251	3.555	100,001	200,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 90 Data synthesis: adults – individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[12,17]	1.178	0.5401	0.01398	0.4475	1.076	2.559	100,001	200,000
OR[12,18]	0.5707	0.2543	0.005342	0.2155	0.525	1.178	100,001	200,000
OR[12,19]	1.107	0.9609	0.02076	0.1875	0.847	3.562	100,001	200,000
OR[12,20]	3.674	5.679	0.1201	0.2566	1.99	17.86	100,001	200,000
OR[13,14]	0.4583	2.107	0.03533	0.003304	0.1371	2.633	100,001	200,000
OR[13,15]	5.556	28.5	0.6176	0.003429	0.4675	41.93	100,001	200,000
OR[13,16]	0.8363	3.329	0.06118	0.008335	0.2799	4.463	100,001	200,000
OR[13,17]	0.676	2.681	0.05176	0.007658	0.2391	3.617	100,001	200,000
OR[13,18]	0.3608	1.521	0.02863	0.003334	0.117	2.003	100,001	200,000
OR[13,19]	0.6583	3.664	0.05761	0.005043	0.1925	3.699	100,001	200,000
OR[13,20]	1.952	8.639	0.1464	0.009582	0.4587	12.83	100,001	200,000
OR[14,15]	23.43	123.1	2.653	0.06213	3.679	170.7	100,001	200,000
OR[14,16]	3.005	3.138	0.05922	0.4455	2.075	10.93	100,001	200,000
OR[14,17]	2.437	2.294	0.04934	0.4563	1.778	8.501	100,001	200,000
OR[14,18]	1.247	1.316	0.02774	0.1854	0.8621	4.669	100,001	200,000
OR[14,19]	2.288	3.079	0.05419	0.2268	1.417	9.682	100,001	200,000
OR[14,20]	7.571	17.92	0.3625	0.3497	3.417	38.12	100,001	200,000
OR[15,16]	7.697	133.4	3.041	0.01534	0.5764	29.64	100,001	200,000
OR[15,17]	4.798	59.05	1.332	0.01439	0.509	25.01	100,001	200,000
OR[15,18]	2.971	52.54	1.085	0.006906	0.2424	12.3	100,001	200,000
OR[15,19]	4.489	62.3	1.452	0.009721	0.3928	23.35	100,001	200,000
OR[15,20]	10.21	84.75	1.67	0.01887	1.002	74.09	100,001	200,000
OR[16,17]	0.9526	0.4623	0.007213	0.3544	0.8549	2.11	100,001	200,000
OR[16,18]	0.5026	0.3446	0.006854	0.1265	0.4141	1.405	100,001	200,000
OR[16,19]	0.894	0.7887	0.01299	0.1541	0.671	2.934	100,001	200,000
OR[16,20]	2.957	4.606	0.08921	0.1993	1.574	14.18	100,001	200,000
OR[17,18]	0.557	0.3131	0.008084	0.1705	0.4845	1.358	100,001	200,000
OR[17,19]	0.9535	0.6646	0.01152	0.2234	0.7871	2.615	100,001	200,000
OR[17,20]	3.27	4.723	0.1144	0.267	1.825	15.75	100,001	200,000
OR[18,19]	2.248	2.206	0.0467	0.3217	1.628	7.927	100,001	200,000
OR[18,20]	7.492	12.33	0.255	0.4661	3.715	38.18	100,001	200,000
OR[19,20]	5.008	9.252	0.2034	0.2605	2.337	26.58	100,001	200,000

TABLE 91 Data synthesis: adults – inconsistency model (pairwise comparison)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
or[1,3]	1.293	0.3195	0.003551	0.7902	1.251	2.035	100,001	200,000
or[1,4]	1.422	0.3342	0.00321	0.8762	1.385	2.177	100,001	200,000
or[1,5]	1.097	0.1883	0.001546	0.7836	1.078	1.521	100,001	200,000
or[1,6]	1.009	0.2379	0.001747	0.6274	0.9797	1.549	100,001	200,000
or[1,7]	0.9585	0.3273	0.003297	0.4869	0.9016	1.751	100,001	200,000
or[1,9]	1.267	0.2235	0.001783	0.8794	1.25	1.756	100,001	200,000
or[1,10]	1.406	0.6698	0.005369	0.5194	1.274	3.08	100,001	200,000
or[1,16]	1.371	0.683	0.006053	0.4762	1.23	3.049	100,001	200,000
or[1,17]	1.147	0.3434	0.002527	0.6416	1.092	1.971	100,001	200,000
or[1,19]	1.009	0.6816	0.007816	0.2523	0.8358	2.8	100,001	200,000
or[2,11]	3.016	2.536	0.04166	0.6695	2.329	9.441	100,001	200,000
or[2,12]	7.359	77.39	1.501	0.0235	0.9059	37.32	100,001	200,000
or[3,6]	0.9992	0.4135	0.003322	0.4231	0.9231	1.998	100,001	200,000
or[3,9]	0.9222	0.9469	0.01388	0.1094	0.6574	3.308	100,001	200,000
or[3,11]	0.6126	0.2452	0.001872	0.2643	0.5702	1.209	100,001	200,000
or[4,9]	2.063	0.5714	0.005245	1.177	1.986	3.404	100,001	200,000
or[4,10]	0.8249	0.602	0.007823	0.1737	0.6654	2.401	100,001	200,000
or[4,11]	0.1916	2.693	0.0376	3.22×10^{-29}	3.71×10^{-08}	0.9807	100,001	200,000
or[4,14]	0.6066	0.5124	0.005516	0.093	0.4648	1.954	100,001	200,000
or[4,15]	9.598	112.2	1.093	0.0197	1.011	55.18	100,001	200,000
or[4,18]	2.525	7.221	0.08789	0.02603	0.9102	14.75	100,001	200,000
or[5,8]	0.4725	0.3376	0.003374	0.09511	0.3896	1.333	100,001	200,000
or[5,9]	24.61	164.5	2.297	0.6354	5.26	137.3	100,001	200,000
or[5,17]	Not estimable							
or[6,9]	2.218	0.8519	0.00654	1.009	2.069	4.304	100,001	200,000
or[6,11]	1.593	2.08	0.02623	0.1562	1.01	6.675	100,001	200,000
or[8,9]	34.05	274.8	3.707	0.8065	6.109	186.5	100,001	200,000
or[9,10]	Not estimable							
or[9,13]	37.43	957.5	15.96	0.1695	2.827	106.7	100,001	200,000
or[9,16]	Not estimable							
or[9,20]	2.254	3.057	0.0391	0.1999	1.345	9.741	100,001	200,000
or[10,12]	1.115	0.296	0.003279	0.6476	1.079	1.802	100,001	200,000
or[10,14]	Not estimable							
or[10,16]	Not estimable							
or[10,18]	0.4653	0.2291	0.002258	0.1581	0.4214	1.031	100,001	200,000
or[11,15]	Not estimable							
or[11,18]	0.02907	0.4428	0.00551	5.48×10^{-34}	1.47×10^{-10}	0.2107	100,001	200,000
or[12,18]	1.886	2.371	0.02685	0.2005	1.216	7.628	100,001	200,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 92 Data synthesis: adults – median ranks (class effects)

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	8.085	1.946	0.05168	4	8	12	100,001	200,000
rk.class[2]	3.071	2.329	0.0511	1	2	10	100,001	200,000
rk.class[3]	9.087	1.926	0.0441	5	9	12	100,001	200,000
rk.class[4]	12.04	1.439	0.03463	9	12	14	100,001	200,000
rk.class[5]	8.67	2.485	0.0615	4	9	13	100,001	200,000
rk.class[6]	6.351	2.659	0.0627	2	6	12	100,001	200,000
rk.class[7]	8.397	2.913	0.07246	3	8	14	100,001	200,000
rk.class[8]	10.04	3.093	0.0506	3	11	14	100,001	200,000
rk.class[9]	10.27	5.291	0.1756	1	13	15	100,001	200,000
rk.class[10]	12.73	3.762	0.09555	2	14	15	100,001	200,000
rk.class[11]	3.386	2.829	0.07809	1	2	12	100,001	200,000
rk.class[12]	4.019	2.365	0.05665	1	4	10	100,001	200,000
rk.class[13]	5.306	3.719	0.08131	1	4	14	100,001	200,000
rk.class[14]	7.223	3.919	0.07868	1	7	14	100,001	200,000
rk.class[15]	11.32	3.987	0.08988	2	13	15	100,001	200,000

TABLE 93 Data synthesis: adults – median ranks (individual effects)

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	9.484	2.829	0.06994	5	9	16	100,001	200,000
rk[2]	3.757	3.831	0.1029	1	2	17	100,001	200,000
rk[3]	12.69	2.82	0.04927	7	13	18	100,001	200,000
rk[4]	11.83	2.771	0.04972	6	12	17	100,001	200,000
rk[5]	11.82	2.792	0.05045	6	12	17	100,001	200,000
rk[6]	10.51	2.987	0.05807	5	10	16	100,001	200,000
rk[7]	10.99	3.276	0.05719	5	11	17	100,001	200,000
rk[8]	3.245	2.897	0.05979	1	2	13	100,001	200,000
rk[9]	16.92	1.568	0.03531	13	17	19	100,001	200,000
rk[10]	10.95	4.431	0.1165	4	10	18	100,001	200,000
rk[11]	7.263	4.037	0.09317	2	6	17	100,001	200,000
rk[12]	10.55	4.908	0.1263	3	9	19	100,001	200,000
rk[13]	16.92	5.446	0.1358	2	19	20	100,001	200,000
rk[14]	6.362	5.435	0.1197	1	4	19	100,001	200,000
rk[15]	13.53	7.524	0.2471	1	18	20	100,001	200,000
rk[16]	13.23	5.061	0.08111	4	15	19	100,001	200,000
rk[17]	11.53	3.142	0.05114	5	12	17	100,001	200,000
rk[18]	4.438	3.362	0.08106	1	4	15	100,001	200,000
rk[19]	8.965	5.926	0.1137	1	7	19	100,001	200,000
rk[20]	15.02	5.952	0.1315	2	18	20	100,001	200,000

Children and adolescents/acceptability (total dropouts)

Network geometry

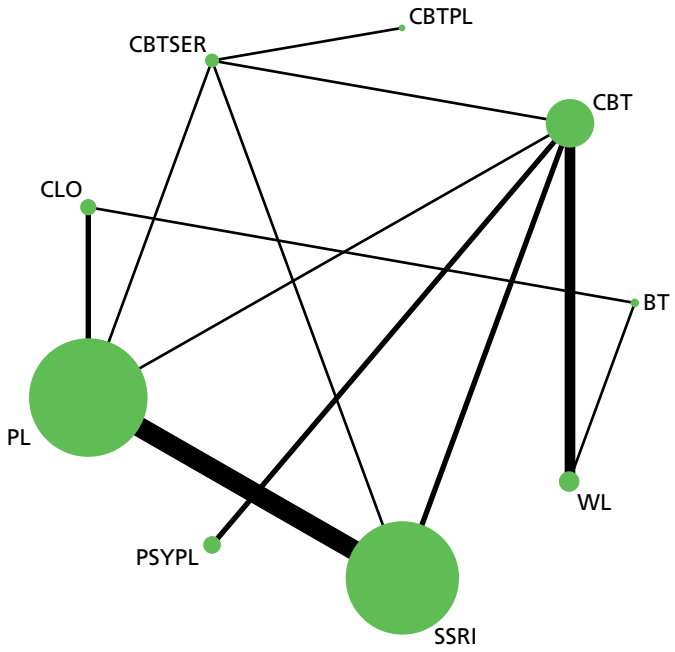


FIGURE 29 Network plot for class effects (the plot for individual effects is included in the main report).
CBTPL, CBT + placebo; CBTSER, CBT + sertraline; CLO, clomipramine; PL, placebo; PSYPL, psychological placebo; WL, waitlist.

Model fit

TABLE 94 Model fit: children and adolescents – consistency model

Model fit								
	Dbar	***Dhat***	***DIC***	***pD***				
r	147.2	116.9	177.5	30.29				
total	147.2	116.9	177.5	30.29				
	Mean	***SD***	***MC_error***	***val2.5pc***	***Median***	***val97.5pc***	***Start***	***Sample***
sd	0.5147	0.3715	0.006303	0.02217	0.4515	1.403	100,001	200,000
totresdev	37.05	8.216	0.06423	22.75	36.44	54.83	100,001	200,000

TABLE 95 Model fit: children and adolescent – inconsistency model

Model fit								
	Dbar	***Dhat***	***DIC***	***pD***				
r	149.1	115.7	182.6	33.43				
total	149.1	115.7	182.6	33.43				
	Mean	***SD***	***MC_error***	***val2.5pc***	***Median***	***val97.5pc***	***Start***	***Sample***
sd	0.8612	0.6323	0.01195	0.04502	0.7421	2.443	70,001	140,000
totresdev	38.99	8.76	0.07706	23.62	38.36	57.84	70,001	140,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Data synthesis: consistency model (network meta-analysis)

Key: intervention (class)

1. Placebo (1).
2. Waitlist (2).
3. Psychological placebo (3).
4. Fluoxetine (4).
5. Fluvoxamine (4).
6. Paroxetine (4).
7. Sertraline (4).
8. Clomipramine (5).
9. BT (6).
10. CBT (7).
11. Sertraline + CBT (8).
12. CBT + placebo (9).

TABLE 96 Data synthesis: children and adolescent – class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[1,2]	0.9559	1.936	0.01895	0.05486	0.5295	4.328	100,001	200,000
OR.D[1,3]	1.033	2.564	0.01631	0.0683	0.5781	4.439	100,001	200,000
OR.D[1,4]	6.742	851.4	1.95	0.227	0.872	2.997	100,001	200,000
OR.D[1,5]	5.094	8.9	0.08637	0.5404	3.061	21.69	100,001	200,000
OR.D[1,6]	107.2	1453	24.67	0.4076	7.645	423.7	100,001	200,000
OR.D[1,7]	0.6919	0.8371	0.008558	0.09176	0.4952	2.415	100,001	200,000
OR.D[1,8]	0.8625	9.133	0.02526	0.07651	0.5374	3.148	100,001	200,000
OR.D[1,9]	0.5534	13.27	0.03814	0.008114	0.1486	2.26	100,001	200,000
OR.D[2,3]	2.018	8.554	0.03339	0.1509	1.081	8.872	100,001	200,000
OR.D[2,4]	17.42	2021	4.562	0.1446	1.628	20.15	100,001	200,000
OR.D[2,5]	18.19	156.2	0.6924	0.4662	5.804	95.46	100,001	200,000
OR.D[2,6]	280.2	4183	76.79	0.8716	14.28	785.2	100,001	200,000
OR.D[2,7]	1.323	1.526	0.0146	0.2087	0.9368	4.786	100,001	200,000
OR.D[2,8]	3.04	106.5	0.2573	0.08032	0.9982	13.51	100,001	200,000
OR.D[2,9]	2.462	174.6	0.4081	0.01024	0.2817	7.587	100,001	200,000
OR.D[3,4]	11.87	1088	2.437	0.1354	1.491	16.49	100,001	200,000
OR.D[3,5]	17.02	193.3	0.6174	0.4127	5.315	85.68	100,001	200,000
OR.D[3,6]	258.7	3404	54.9	0.5696	13.49	922	100,001	200,000
OR.D[3,7]	1.087	1.212	0.006656	0.2347	0.8582	3.236	100,001	200,000
OR.D[3,8]	2.277	15.15	0.05515	0.07783	0.9071	11.15	100,001	200,000
OR.D[3,9]	1.817	122.3	0.2775	0.009615	0.257	6.481	100,001	200,000
OR.D[4,5]	76.63	12,040	26.87	0.4338	3.553	38.72	100,001	200,000
OR.D[4,6]	554.3	89,330	205.4	0.374	8.929	635.8	100,001	200,000

TABLE 96 Data synthesis: children and adolescent – class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[4,7]	10.86	2349	5.272	0.07641	0.5772	4.21	100,001	200,000
OR.D[4,8]	15.5	3969	8.915	0.06728	0.6203	5.557	100,001	200,000
OR.D[4,9]	9.836	2643	5.916	0.007736	0.1714	3.576	100,001	200,000
OR.D[5,6]	31.56	471.1	7.974	0.1311	2.483	114.1	100,001	200,000
OR.D[5,7]	0.315	0.9211	0.006088	0.01411	0.163	1.498	100,001	200,000
OR.D[5,8]	0.5014	23.49	0.0536	0.01133	0.172	2.019	100,001	200,000
OR.D[5,9]	0.3448	22.67	0.06146	0.001491	0.04777	1.189	100,001	200,000
OR.D[6,7]	0.2088	3.232	0.009925	0.001165	0.06527	1.222	100,001	200,000
OR.D[6,8]	0.543	86.68	0.195	9.79×10^{-04}	0.06738	1.925	100,001	200,000
OR.D[6,9]	0.6371	137.2	0.42	1.67×10^{-04}	0.01871	1.026	100,001	200,000
OR.D[7,8]	2.104	52.45	0.124	0.1312	1.076	8.83	100,001	200,000
OR.D[7,9]	1.357	36.53	0.1004	0.01429	0.3014	5.617	100,001	200,000
OR.D[8,9]	0.5331	6.051	0.01487	0.0303	0.284	2.25	100,001	200,000

TABLE 97 Data synthesis: children and adolescent – individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[1,2]	0.9559	1.936	0.01895	0.05486	0.5295	4.328	100,001	200,000
OR[1,3]	1.033	2.564	0.01631	0.0683	0.5781	4.439	100,001	200,000
OR[1,4]	0.794	0.4219	0.0038	0.2479	0.7371	1.685	100,001	200,000
OR[1,5]	0.8868	1.63	0.005053	0.2456	0.7863	2.068	100,001	200,000
OR[1,6]	1.33	1.974	0.006881	0.3738	1.118	3.416	100,001	200,000
OR[1,7]	0.9712	0.6798	0.004586	0.3211	0.8925	2.069	100,001	200,000
OR[1,8]	5.094	8.9	0.08637	0.5404	3.061	21.69	100,001	200,000
OR[1,9]	107.2	1453	24.67	0.4076	7.645	423.7	100,001	200,000
OR[1,10]	0.6919	0.8371	0.008558	0.09176	0.4952	2.415	100,001	200,000
OR[1,11]	0.8625	9.133	0.02526	0.07651	0.5374	3.148	100,001	200,000
OR[1,12]	0.5534	13.27	0.03814	0.008114	0.1486	2.26	100,001	200,000
OR[2,3]	2.018	8.554	0.03339	0.1509	1.081	8.872	100,001	200,000
OR[2,4]	3.042	18.91	0.1008	0.1342	1.361	14.35	100,001	200,000
OR[2,5]	3.507	39.05	0.1307	0.1436	1.457	16.19	100,001	200,000
OR[2,6]	5.1	30.22	0.1806	0.2113	2.137	24.52	100,001	200,000
OR[2,7]	3.307	10.22	0.07605	0.1953	1.669	15.4	100,001	200,000
OR[2,8]	18.19	156.2	0.6924	0.4662	5.804	95.46	100,001	200,000
OR[2,9]	280.2	4183	76.79	0.8716	14.28	785.2	100,001	200,000
OR[2,10]	1.323	1.526	0.0146	0.2087	0.9368	4.786	100,001	200,000
OR[2,11]	3.04	106.5	0.2573	0.08032	0.9982	13.51	100,001	200,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 97 Data synthesis: children and adolescent – individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[2,12]	2.462	174.6	0.4081	0.01024	0.2817	7.587	100,001	200,000
OR[3,4]	2.608	11.99	0.06187	0.1282	1.249	11.67	100,001	200,000
OR[3,5]	3.004	34.47	0.1066	0.1356	1.335	13.25	100,001	200,000
OR[3,6]	4.512	42.92	0.1743	0.1992	1.953	20.02	100,001	200,000
OR[3,7]	2.829	9.741	0.05322	0.1882	1.533	12.37	100,001	200,000
OR[3,8]	17.02	193.3	0.6174	0.4127	5.315	85.68	100,001	200,000
OR[3,9]	258.7	3404	54.9	0.5696	13.49	922	100,001	200,000
OR[3,10]	1.087	1.212	0.006656	0.2347	0.8582	3.236	100,001	200,000
OR[3,11]	2.277	15.15	0.05515	0.07783	0.9071	11.15	100,001	200,000
OR[3,12]	1.817	122.3	0.2775	0.009615	0.257	6.481	100,001	200,000
OR[4,5]	1.35	3.422	0.01122	0.3257	1.03	3.962	100,001	200,000
OR[4,6]	2.156	10.46	0.03006	0.5414	1.398	7.302	100,001	200,000
OR[4,7]	1.495	2.231	0.01093	0.4176	1.127	4.38	100,001	200,000
OR[4,8]	8.423	26.44	0.1767	0.6242	4.257	39.7	100,001	200,000
OR[4,9]	181.7	3674	42.78	0.5159	10.75	682.9	100,001	200,000
OR[4,10]	1.104	2.866	0.01676	0.1108	0.6883	4.419	100,001	200,000
OR[4,11]	1.452	21.8	0.05584	0.09549	0.7402	5.771	100,001	200,000
OR[4,12]	1.014	51.89	0.1321	0.01033	0.2054	3.781	100,001	200,000
OR[5,6]	2.072	13.12	0.03253	0.4542	1.306	6.815	100,001	200,000
OR[5,7]	1.471	19.68	0.04918	0.3417	1.074	4.143	100,001	200,000
OR[5,8]	8.204	37.83	0.179	0.5597	3.976	37.72	100,001	200,000
OR[5,9]	1076	402,800	920.1	0.4583	10.06	630.1	100,001	200,000
OR[5,10]	1.17	37.78	0.09073	0.09699	0.6418	4.208	100,001	200,000
OR[5,11]	1.425	23.22	0.0606	0.08489	0.6927	5.429	100,001	200,000
OR[5,12]	3.115	968.3	2.163	0.009302	0.1932	3.573	100,001	200,000
OR[6,7]	0.9465	3.136	0.008293	0.1962	0.8573	2.296	100,001	200,000
OR[6,8]	6.161	239.5	0.5562	0.3643	2.717	26.15	100,001	200,000
OR[6,9]	142.6	12,870	38.12	0.3133	6.805	423.3	100,001	200,000
OR[6,10]	0.7211	2.777	0.01193	0.06349	0.4408	2.793	100,001	200,000
OR[6,11]	0.9726	17.57	0.05602	0.05624	0.4719	3.725	100,001	200,000
OR[6,12]	0.8511	65.25	0.1538	0.006448	0.1303	2.479	100,001	200,000
OR[7,8]	6.738	28.23	0.1415	0.5278	3.444	31.11	100,001	200,000
OR[7,9]	136.3	3712	24.62	0.4528	8.661	528.2	100,001	200,000
OR[7,10]	0.7998	1.026	0.008957	0.1085	0.5644	2.844	100,001	200,000

TABLE 97 Data synthesis: children and adolescent – individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[7,11]	1.013	8.437	0.0233	0.09035	0.6052	3.916	100,001	200,000
OR[7,12]	0.769	46.44	0.1119	0.00959	0.1673	2.794	100,001	200,000
OR[8,9]	31.56	471.1	7.974	0.1311	2.483	114.1	100,001	200,000
OR[8,10]	0.315	0.9211	0.006088	0.01411	0.163	1.498	100,001	200,000
OR[8,11]	0.5014	23.49	0.0536	0.01133	0.172	2.019	100,001	200,000
OR[8,12]	0.3448	22.67	0.06146	0.001491	0.04777	1.189	100,001	200,000
OR[9,10]	0.2088	3.232	0.009925	0.001165	0.06527	1.222	100,001	200,000
OR[9,11]	0.543	86.68	0.195	9.79×10^{-4}	0.06738	1.925	100,001	200,000
OR[9,12]	0.6371	137.2	0.42	1.67×10^{-4}	0.01871	1.026	100,001	200,000
OR[10,11]	2.104	52.45	0.124	0.1312	1.076	8.83	100,001	200,000
OR[10,12]	1.357	36.53	0.1004	0.01429	0.3014	5.617	100,001	200,000
OR[11,12]	0.5331	6.051	0.01487	0.0303	0.284	2.25	100,001	200,000

TABLE 98 Data synthesis: children and adolescent – inconsistency model (pairwise comparison)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
or[1,4]	0.8024	4.62	0.01388	0.0948	0.5591	2.567	70,001	140,000
or[1,5]	4.409	395.2	1.456	0.06265	0.6615	6.949	70,001	140,000
or[1,6]	17.57	1645	4.528	0.1618	1.59	16.65	70,001	140,000
or[1,7]	1.265	19.6	0.06121	0.1058	0.807	3.784	70,001	140,000
or[1,8]	10.7	484.8	1.345	0.415	3.437	41.35	70,001	140,000
or[1,10]	4.49	505.5	1.392	0.02441	0.441	5.079	70,001	140,000
or[1,11]	2.774	246.6	0.6614	0.02385	0.4328	4.915	70,001	140,000
or[2,9]	78,230	1.39E+07	60,100	0.2729	12.92	9205	70,001	140,000
or[2,10]	1.948	9.336	0.03735	0.1654	1.04	7.907	70,001	140,000
or[3,10]	1.549	12.69	0.04082	0.1434	0.8612	5.475	70,001	140,000
or[7,10]	4.438	634.4	1.722	2.25×10^{-4}	0.1758	10.21	70,001	140,000
or[7,11]	Not estimable							
or[8,9]	6840	643,600	2588	0.06813	4.448	2504	70,001	140,000
or[10,11]	Not estimable							
or[11,12]	16.02	3927	10.53	0.01717	0.2818	4.169	70,001	140,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 99 Data synthesis: children and adolescents – median ranks (class effects)

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	5.769	1.498	0.0213	2	6	8	100,001	200,000
rk.class[2]	4.003	2.107	0.02918	1	4	8	100,001	200,000
rk.class[3]	4.27	2.069	0.02356	1	4	8	100,001	200,000
rk.class[4]	5.184	1.858	0.01989	1	5	8	100,001	200,000
rk.class[5]	7.725	1.361	0.01701	3	8	9	100,001	200,000
rk.class[6]	8.35	1.377	0.0248	4	9	9	100,001	200,000
rk.class[7]	3.678	1.502	0.01782	1	4	7	100,001	200,000
rk.class[8]	4.059	1.958	0.02073	1	4	8	100,001	200,000
rk.class[9]	1.961	1.752	0.01679	1	1	7	100,001	200,000

TABLE 100 Data synthesis: children and adolescents – median ranks (individual effects)

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	7.652	1.96	0.02736	3	8	11	100,001	200,000
rk[2]	4.993	3.158	0.04543	1	4	11	100,001	200,000
rk[3]	5.321	3.121	0.0377	1	5	11	100,001	200,000
rk[4]	5.741	2.404	0.02741	1	6	10	100,001	200,000
rk[5]	6.099	2.48	0.02415	1	6	11	100,001	200,000
rk[6]	8.067	2.388	0.02601	3	9	12	100,001	200,000
rk[7]	6.873	2.174	0.02246	2	7	11	100,001	200,000
rk[8]	10.43	1.945	0.02452	4	11	12	100,001	200,000
rk[9]	11.11	2.012	0.03567	4	12	12	100,001	200,000
rk[10]	4.467	2.351	0.0305	1	4	10	100,001	200,000
rk[11]	4.97	2.906	0.02952	1	4	11	100,001	200,000
rk[12]	2.283	2.458	0.02273	1	1	10	100,001	200,000

Complete data for rank probabilities by type of intervention

TABLE 101 Data used to draw the absolute rankograms that appear in the main text of the report

		Rank (YBOCS: 17 treatments; dropouts: 20 treatments)																				
Adults		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	Sum
YBOCS	Placebo	0	0	0	0	0	0	0	0	0	1.00×10^{-5}	5.00×10^{-5}	5.50×10^{-4}	0.00586	0.07351	0.4772	0.4383	0.00453				1
Dropout	Placebo	0.00	0.00	0.00	0.02	0.04	0.08	0.12	0.14	0.14	0.13	0.10	0.08	0.06	0.04	0.03	0.02	0.01	0.00	0.00	0.00	1
YBOCS	Waitlist	0	0	0	0	0	1.00×10^{-5}	3.00×10^{-5}	1.00×10^{-5}	2.00×10^{-5}	0	1.00×10^{-5}	4.00×10^{-5}	1.30×10^{-4}	0.00135	0.0063	0.09427	0.8978				1
Dropout	Waitlist	0.29	0.21	0.15	0.10	0.06	0.04	0.03	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00	1
YBOCS	Fluoxetine	0	0	8.00×10^{-5}	0.00223	0.01146	0.03125	0.06575	0.1076	0.1323	0.1413	0.146	0.1426	0.1258	0.07633	0.01688	3.30×10^{-4}	0				1
Dropout	Fluoxetine	0.00	0.00	0.00	0.00	0.00	0.01	0.02	0.04	0.06	0.08	0.10	0.13	0.13	0.13	0.12	0.09	0.05	0.02	0.01	0.00	1
YBOCS	Fluvoxamine	0	0	0	0.00166	0.01125	0.0377	0.08082	0.1311	0.1591	0.1571	0.1451	0.1246	0.09534	0.04741	0.00875	2.00×10^{-5}	0				1
Dropout	Fluvoxamine	0.00	0.00	0.00	0.00	0.01	0.02	0.04	0.06	0.08	0.11	0.13	0.13	0.13	0.11	0.09	0.06	0.03	0.01	0.00	0.00	1
YBOCS	Paroxetine	0	0	1.00×10^{-5}	0.00139	0.00764	0.02466	0.05581	0.09689	0.1297	0.1461	0.1559	0.1563	0.1355	0.07485	0.01502	1.20×10^{-4}	0				1
Dropout	Paroxetine	0.00	0.00	0.00	0.00	0.01	0.02	0.04	0.06	0.09	0.11	0.12	0.13	0.13	0.11	0.09	0.06	0.03	0.01	0.00	0.00	1
YBOCS	Sertraline	0	0	6.00×10^{-5}	0.00275	0.01315	0.03431	0.06953	0.1118	0.137	0.1448	0.1448	0.1386	0.116	0.07135	0.01556	2.60×10^{-4}	0				1
Dropout	Sertraline	0.00	0.00	0.00	0.01	0.03	0.05	0.07	0.10	0.11	0.12	0.12	0.11	0.09	0.07	0.05	0.03	0.01	0.00	0.00	0.00	1
YBOCS	Citalopram	0	1.00×10^{-5}	2.10×10^{-4}	0.00634	0.02091	0.04177	0.07302	0.1076	0.125	0.129	0.132	0.133	0.1248	0.08273	0.02196	0.00169	7.00×10^{-5}				1
Dropout	Citalopram	0.00	0.00	0.01	0.01	0.03	0.05	0.06	0.08	0.10	0.11	0.11	0.11	0.10	0.09	0.07	0.05	0.03	0.01	0.00	0.00	1
YBOCS	Venlafaxine	2.00×10^{-4}	5.90×10^{-4}	0.00452	0.05998	0.09522	0.08724	0.08047	0.06269	0.03474	0.03017	0.03238	0.0416	0.07623	0.199	0.1285	0.06263	0.00382				1
Dropout	Venlafaxine	0.28	0.25	0.16	0.11	0.07	0.04	0.03	0.02	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	1
YBOCS	Clomipramine	0	0	8.60×10^{-4}	0.06048	0.1751	0.2376	0.2215	0.1153	0.05586	0.03749	0.02873	0.02559	0.02463	0.01445	0.00242	1.00×10^{-5}	0				1
Dropout	Clomipramine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02	0.04	0.08	0.17	0.28	0.26	0.11	0.02	1
YBOCS	BT	5.11×10^{-1}	0.3972	0.08817	0.00367	3.00×10^{-5}	0	0	0	0	0	0	0	0	0	0	0	0				1
Dropout	BT	0.00	0.00	0.01	0.03	0.06	0.10	0.11	0.09	0.06	0.04	0.04	0.04	0.05	0.08	0.09	0.08	0.07	0.04	0.02	0.00	1
YBOCS	CBT	0	6.00×10^{-5}	0.00445	0.1258	0.33	0.1982	0.1035	0.05264	0.03062	0.02482	0.02428	0.03059	0.03744	0.02797	0.00867	9.80×10^{-4}	0				1
Dropout	CBT	0.00	0.03	0.09	0.15	0.16	0.14	0.10	0.07	0.05	0.03	0.03	0.02	0.02	0.02	0.03	0.03	0.02	0.01	0.00	0.00	1
YBOCS	CT	0.1726	0.4096	0.3718	0.04326	0.0021	3.70×10^{-4}	1.00×10^{-4}	7.00×10^{-5}	2.00×10^{-5}	2.00×10^{-5}	1.00×10^{-5}	1.00×10^{-5}	2.00×10^{-5}	0	0	0	0				1
Dropout	CT	0.00	0.01	0.02	0.06	0.09	0.11	0.10	0.07	0.05	0.04	0.03	0.03	0.04	0.05	0.07	0.08	0.08	0.05	0.03	0.00	1
YBOCS	Hypericum	3.10×10^{-4}	7.10×10^{-4}	0.00299	0.02795	0.03718	0.03148	0.02984	0.02298	0.0172	0.01398	0.01413	0.01878	0.03187	0.08821	0.196	0.3728	0.09357				1

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 101 Data used to draw the absolute rankograms that appear in the main text of the report (*continued*)

		Rank (YBOCS: 17 treatments; dropouts: 20 treatments)																				
Adults		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	Sum
Dropout	Hypericum	0.04	0.07	0.10	0.10	0.09	0.08	0.06	0.04	0.03	0.02	0.02	0.02	0.02	0.03	0.04	0.05	0.06	0.07	0.05	0.01	1
YBOCS	CBT + fluvoxamine	0.0151	0.02434	0.09851	0.5006	0.1236	0.06653	0.03564	0.01945	0.01279	0.01009	0.0107	0.01376	0.02199	0.02712	0.01438	0.00538	1.10×10^{-4}				1
Dropout	CBT + fluvoxamine	0.12	0.05	0.04	0.03	0.03	0.02	0.02	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.03	0.09	0.20	0.27	1
YBOCS	BT + clomipramine	0.3009	0.1674	0.4262	0.08548	0.01209	0.00361	0.00154	6.30×10^{-4}	3.60×10^{-4}	3.40×10^{-4}	3.00×10^{-4}	4.20×10^{-4}	3.40×10^{-4}	3.10×10^{-4}	1.10×10^{-4}	1.00×10^{-5}	0				1
Dropout	BT + clomipramine	0.00	0.01	0.02	0.03	0.05	0.05	0.05	0.05	0.04	0.03	0.03	0.03	0.03	0.04	0.07	0.10	0.14	0.14	0.08	0.02	1
YBOCS	Escitalopram	0	2.00×10^{-5}	2.40×10^{-4}	0.00669	0.02092	0.04178	0.07282	0.1064	0.1263	0.1309	0.1329	0.1308	0.1215	0.08387	0.02289	0.00203	2.00×10^{-5}				1
Dropout	Escitalopram	0.00	0.00	0.00	0.01	0.02	0.03	0.05	0.07	0.09	0.10	0.12	0.11	0.11	0.10	0.08	0.06	0.03	0.01	0.00	0.00	1
YBOCS	Psychological placebo	0	0	0.00195	0.07178	0.1394	0.1635	0.1096	0.06475	0.03905	0.03389	0.03261	0.04278	0.08253	0.1316	0.06533	0.02116	5.00×10^{-5}				1
Dropout	Psychological placebo	0.09	0.19	0.21	0.17	0.12	0.06	0.04	0.03	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00	0.00	0.00	1
Dropout	Amitriptyline	0.02	0.02	0.02	0.02	0.02	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.03	0.07	0.20	0.49	1
Dropout	BT + fluvoxamine	0.13	0.14	0.14	0.12	0.09	0.06	0.04	0.03	0.02	0.01	0.01	0.01	0.02	0.02	0.03	0.03	0.03	0.04	0.02	0.01	1
Dropout	Imipramine	0.02	0.02	0.03	0.03	0.03	0.03	0.03	0.02	0.02	0.01	0.01	0.01	0.01	0.02	0.02	0.04	0.06	0.15	0.27	0.17	1

		Rank (CYBOCS: 12 treatments; dropouts: 12 treatments)												
Children and adolescents		1	2	3	4	5	6	7	8	9	10	11	12	Sum
CYBOCS	Placebo	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.04	0.14	0.69	0.12	1.00
Dropout	Placebo	0.00	0.01	0.02	0.04	0.08	0.12	0.16	0.20	0.20	0.14	0.03	0.00	1.00
CYBOCS	Waitlist	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.02	0.04	0.10	0.82	1.00
Dropout	Waitlist	0.12	0.16	0.14	0.11	0.10	0.06	0.05	0.05	0.06	0.10	0.04	0.00	1.00
CYBOCS	Psychological placebo	0.02	0.03	0.06	0.11	0.17	0.16	0.12	0.08	0.08	0.11	0.05	0.00	1.00
Dropout	Psychological placebo	0.08	0.14	0.14	0.13	0.10	0.06	0.05	0.06	0.07	0.09	0.05	0.02	1.00
CYBOCS	Fluoxetine	0.00	0.00	0.01	0.02	0.05	0.10	0.17	0.23	0.22	0.17	0.02	0.00	1.00
Dropout	Fluoxetine	0.03	0.07	0.10	0.11	0.13	0.16	0.14	0.10	0.08	0.05	0.01	0.00	1.00
CYBOCS	Fluvoxamine	0.00	0.00	0.01	0.02	0.04	0.08	0.14	0.21	0.24	0.21	0.04	0.01	1.00
Dropout	Fluvoxamine	0.03	0.06	0.09	0.10	0.12	0.15	0.14	0.12	0.09	0.06	0.02	0.01	1.00
Dropout	Paroxetine	0.01	0.02	0.03	0.04	0.06	0.09	0.11	0.13	0.16	0.22	0.10	0.03	1.00
CYBOCS	Sertraline	0.00	0.00	0.01	0.02	0.06	0.12	0.21	0.25	0.20	0.11	0.01	0.00	1.00
Dropout	Sertraline	0.01	0.02	0.05	0.07	0.11	0.16	0.17	0.16	0.13	0.09	0.03	0.00	1.00
CYBOCS	Clomipramine	0.02	0.04	0.08	0.12	0.17	0.18	0.13	0.08	0.07	0.08	0.02	0.01	1.00
Dropout	Clomipramine	0.00	0.01	0.01	0.01	0.01	0.02	0.02	0.03	0.05	0.10	0.51	0.23	1.00
CYBOCS	BT	0.19	0.14	0.15	0.15	0.13	0.08	0.05	0.03	0.03	0.03	0.01	0.00	1.00
Dropout	BT	0.01	0.01	0.01	0.01	0.01	0.02	0.01	0.02	0.02	0.04	0.16	0.69	1.00
CYBOCS	CBT	0.09	0.17	0.26	0.24	0.13	0.06	0.02	0.01	0.01	0.00	0.00	0.00	1.00
Dropout	CBT	0.04	0.15	0.23	0.19	0.11	0.07	0.06	0.06	0.05	0.03	0.01	0.00	1.00
CYBOCS	CBT + sertraline	0.24	0.35	0.19	0.11	0.06	0.03	0.01	0.00	0.00	0.00	0.00	0.00	1.00
Dropout	CBT + sertraline	0.03	0.25	0.12	0.12	0.12	0.07	0.06	0.05	0.06	0.07	0.03	0.01	1.00
CYBOCS	CBT + placebo	0.36	0.18	0.12	0.10	0.07	0.05	0.03	0.02	0.02	0.02	0.01	0.01	1.00
Dropout	CBT + placebo	0.66	0.10	0.06	0.05	0.03	0.02	0.02	0.02	0.02	0.02	0.01	0.01	1.00
CYBOCS	BT + fluvoxamine	0.08	0.08	0.11	0.11	0.12	0.13	0.10	0.06	0.07	0.08	0.04	0.03	1.00

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

WinBUGs code

```
#Y-BOC random effects analysis
# Code adapted from Program 5(a)
#http://www.nicedsu.org.uk/TSD2%20General%20meta%20analysis%20corrected%2015Ap
ril2014.pdf

model{
for (i in 1:complete){ #loop through studies reporting SD
      for(z in 1:na[i]){
            sd1[i,z]<-sd[i,z]
#calculate the mean and precision of the reported SDs
            sd1[i,z]~dnorm(mu.sd[out[i]],prec.sd[out[i]])
            }     }

for (i in complete+1:ns){#loop through remaining studies (not report SD)
      for (z in 1:na[i]){
            sd1[i,z]~dnorm(mu.sd[out[i]],prec.sd[out[i]])
#SD is equal to estimated SD only for studies that did not report uncertainty
                  sd[i,z]<- cut(sd1[i,z])
            }     }

      for (i in 1:ns){ #loop through all studies converting SDs to SEs
            for (z in 1:na[i]){
                  se[i,z]<-sd[i,z]/sqrt(n[i,z])
                  prec[i,z]<-pow(se[i,z],-2)
            }     }

#TSD code
for(i in 1:ns){ # LOOP THROUGH STUDIES
      w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
      delta[i,1] <- 0 # treatment effect is zero for control arm
      mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
      for (k in 1:na[i]) { # LOOP THROUGH ARMS
                  y[i,k] ~ dnorm(theta[i,k],prec[i,k]) # normal likelihood
                  theta[i,k] <- mu[i] + delta[i,k] # model for linear
predictor
                  dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-
theta[i,k])*prec[i,k]
            }

resdev[i] <- sum(dev[i,1:na[i]]) # summed deviance contribution

for (k in 2:na[i]) { # LOOP THROUGH ARMS
            delta[i,k] ~ dnorm(md[i,k],taud[i,k]) # trial-specific LOR
distributions
            md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k] # mean of treat effect
distributions (with multi-arm trial correction)
            taud[i,k] <- tau *2*(k-1)/k # precision of treat effects
distributions
            w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]]) # adjustment for
multi-arm
            sw[i,k] <- sum(w[i,1:k-1])/(k-1) # cumulative adjustment for
multi-arm
            }
      }

totresdev <- sum(resdev[1:complete]) #Total Residual Deviance
d[1]<-0 # treatment effect is zero for reference treatment
```

```
D[1]<-0

for (i in 1:n.j1){      #vague prior for trt effects only 1 treatment per
"class"
      d[j1[i]]~dnorm(0,.0001)
      D[class[j1[i]]]<-d[j1[i]]
}

for (i in 1:n.jclass){  #trt effects when multiple treatments form a 'class'
      d[jclass[i]]~dnorm(D[class[jclass[i]]],Prec3[class[jclass[i]]])
}


D[3]~dnorm(0, 0.0001)   #vague prior for 'class' effect

Prec3[3]<- 1/(SD3*SD3)
SD3~dunif(0,10)


      # vague priors for treatment effects
      sdev ~ dunif(0,10) # vague prior for between-trial SD.
      tau <- pow(sdev,-2) # between-trial precision = (1/between-trial
variance)

for (i  in 1:2){
      mu.sd[i]~dnorm(0,.0001)I(0,)
      }
      for (i  in 1:2){
            prec.sd[i]~dgamma(.01,.01)
            }

# Ranking and probabilities for treatment and class level effects
for(k in 1:nt){
      rk[k]<-rank(d[],k)
      best[k]<-equals(rk[k],1)
            for (h in 1:nt){  prob[h,k]<-equals(rk[k],h)}  }

for (q in 1:nclass){
      rk.class[q]<-rank(D[],q)
      best.class[q]<-equals(rk.class[q],1)
            for (x in 1:nclass){
                  prob.class[x,q]<-equals(rk.class[x],q)
}     }

      # all MDs for each treatment level comparison
for (c in 1:(nt-1)) {
      for (k in (c+1):nt) {
            treat.mean.diff[c,k] <- (d[k]-d[c])  } }

# all MDs for each class level comparison
for (f in 1:(nclass-1)) {
      for (q in (f+1):nclass) {
            class.mean.diff[f,q] <- (D[q]-D[f])  } }

}

*****************************************************************************
```

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

```
#Drop outs (tolerability) consistency model
#Random effects model for multi-arm trials. Binomial link

model{ #
for(i in 1:ns){
 w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
 delta[i,1] <- 0 # treatment effect is zero for control arm
 mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines

 for (k in 1:na[i]) { # LOOP THROUGH ARMS
 r[i,k] ~ dbin(p[i,k],n[i,k]) # binomial likelihood
 logit(p[i,k]) <- mu[i] + delta[i,k] # model for linear predictor
 rhat[i,k] <- p[i,k] * n[i,k] # expected value of the numerators
 dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k])) #Deviance contribution
 + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
 }

 resdev[i] <- sum(dev[i,1:na[i]]) # summed res.dev contribution per trial

 for (k in 2:na[i]) { # LOOP THROUGH ARMS
 delta[i,k] ~ dnorm(md[i,k],taud[i,k]) # trial-specific LOR distributions
 md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k] # mean of LOR distributions
 taud[i,k] <- tau *2*(k-1)/k # precision of LOR distributions
 w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]]) # adjustment for multi-arm
RCTs
 sw[i,k] <- sum(w[i,1:k-1])/(k-1) # cumulative adjustment for multi-arm trials
 }
 }

totresdev <- sum(resdev[]) #Total Residual Deviance
d[1] <- 0 # treatment effect is zero for reference treatment
D[1]<-0


for (i in 1:n.j1){
      d[j1[i]]~dnorm(0,.0001)
      D[class[j1[i]]]<-d[j1[i]]   }


for (i in 1:n.jclass){
      d[jclass[i]]~dnorm(D[class[jclass[i]]],Prec3[class[jclass[i]]])   }


D[3]~dnorm(0, 0.0001)
Prec3[3]<- 1/(SD3*SD3)
SD3~dunif(0,10)
sd ~ dunif(0,5) # vague prior for between-trialSD
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)


# Ranking and probabilities for treatment and class level effects
for(k in 1:20){
      rk[k]<-rank(d[],k)
      best[k]<-equals(rk[k],1)
            for (h in 1:20){  prob[h,k]<-equals(rk[k],h)}  }
for (q in 1:15){
      rk.class[q]<-rank(D[],q)
      best.class[q]<-equals(rk.class[q],1)
            for (x in 1:15){
```

```
                    prob.class[x,q]<-equals(rk.class[x],q)
}      }


#Pairwise ORs for treatment level analysis
for (f in 1:14)
          {  for (q in (f+1):15)
                {  lor.D[f,q] <- D[q] - D[f]
                  OR.D[f,q]<-exp(lor.D[f,q])
                 }}

#Pairwise ORs for class level analyis
for (c in 1:19)  {
for (k in (c+1):20) {
     lor[c,k] <- d[k] - d[c]
     OR[c,k]<-exp(lor[c,k])}   }

   }}}
```

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 9 Detailed results of the sensitivity analyses

Adults

Adults: clinical effectiveness (YBOCS) – sensitivity analysis 1 (low overall attrition)

See *Table 21* for a summary.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 102 Raw data used

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
Albert *et al.*, 2002[155]	18.36	25	7.11	17.3	40	6.15	NA	NA	NA	NA	NA	NA	2	2	8	9	NA	NA
Anderson and Rees, 2007[157]	23.5	14	6.4	16.7	17	6.8	NA	NA	NA	NA	NA	NA	2	2	2	11	NA	NA
Andersson *et al.*, 2012[158]	12.94	49	6.26	18.88	51	4.18	NA	NA	NA	NA	NA	NA	2	2	11	17	NA	NA
Belloch *et al.*, 2008[159]	8.31	13	8.75	6.8	16	3.55	NA	NA	NA	NA	NA	NA	2	2	10	12	NA	NA
CCSG1, 1991[154]	25.11	108	6.34	16.23	102	7.37	NA	NA	NA	NA	NA	NA	2	2	1	9	NA	NA
CCSG2, 1991[154]	25.59	119	5.78	14.7	120	7.45	NA	NA	NA	NA	NA	NA	2	2	1	9	NA	NA
Chouinard *et al.*, 1990[163]	–1.48	44	NA	–3.79	43	NA	NA	NA	NA	NA	NA	NA	2	1	1	6	NA	NA
Cordioli *et al.*, 2003[164]	23.2	24	5.5	15.1	23	7.8	NA	NA	NA	NA	NA	NA	2	2	2	11	NA	NA
Cottraux *et al.*, 2001[166]	–12.1	30	7.8	–12.5	30	8.2	NA	NA	NA	NA	NA	NA	2	1	10	12	NA	NA
Denys *et al.*, 2003[167]	–7.8	72	5.4	–7.2	73	7.5	NA	NA	NA	NA	NA	NA	2	1	5	8	NA	NA
Fals-Stewart *et al.*, 1993[170]	–8.1	31	NA	–1.8	32	NA	NA	NA	NA	NA	NA	NA	2	1	10	17	NA	NA
GlaxoSmithKline, 2005[175]	–14.26	72	6.33	–13.19	69	6.48	NA	NA	NA	NA	NA	NA	2	1	5	9	NA	NA
Greist *et al.*, 2002[178]	17.6	55	6.2	24.1	66	6.7	NA	NA	NA	NA	NA	NA	2	2	10	17	NA	NA
Hollander *et al.*, 2003[181]	–3.33	89	NA	–4.14	88	NA	–6.35	86	NA	–7.34	85	NA	4	1	1	5	5	5
Jaurrieta *et al.*, 2008[182]	24.6	19	8.9	17.8	19	8.4	NA	NA	NA	NA	NA	NA	2	2	2	11	NA	NA
Jenike *et al.*, 1990[183]	22.3	9	7.8	20.6	10	9.2	NA	NA	NA	NA	NA	NA	2	2	1	6	NA	NA
Jenike *et al.*, 1990[184]	21.8	20	7.6	18.8	18	4	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
Jenike *et al.*, 1997[185]	18.7	18	6.1	16.2	19	6.3	NA	NA	NA	NA	NA	NA	2	2	1	3	NA	NA
Kamijima *et al.*, 2004[187]	20.3	94	7.38	15.8	94	8.09	NA	NA	NA	NA	NA	NA	2	2	1	5	NA	NA
Lindsay *et al.*, 1997[192]	11	9	3.81	25.89	9	5.8	NA	NA	NA	NA	NA	NA	2	2	10	17	NA	NA
López-Ibor *et al.*, 1996[193]	–7.5	30	9.29	–8.9	24	7.13	NA	NA	NA	NA	NA	NA	2	1	3	9	NA	NA

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
Milanfranchi *et al.*, 1997[196]	18.4	13	9.2	16.5	12	11	NA	NA	NA	NA	NA	NA	2	2	4	9	NA	NA
Montgomery *et al.*, 2001[198]	–5.6	101	6.9	–8.4	102	7.3	–8.9	98	7	–10.4	100	6.9	4	1	1	7	7	7
Mundo *et al.*, 1997[199]	16.2	10	8.9	21.6	9	7.6	19.8	11	10.1	NA	NA	NA	3	2	4	5	7	NA
Mundo *et al.*, 2001[200]	–12.2	115	NA	–12	112	NA	NA	NA	NA	NA	NA	NA	2	1	4	9	NA	NA
Nakatani *et al.*, 2005[202]	20.2	10	9.4	12.9	10	4.9	28.4	8	5.5	NA	NA	NA	3	2	4	10	17	NA
O'Connor *et al.*, 1999[203]	17.5	6	4	13.3	6	8.6	NA	NA	NA	NA	NA	NA	2	2	2	11	NA	NA
Shareh *et al.*, 2010[206]	16.66	6	3.2	7	7	2.38	8.5	6	2.42	NA	NA	NA	3	2	4	11	14	NA
Sousa *et al.*, 2006[207]	–7.36	25	NA	–10.8	25	NA	NA	NA	NA	NA	NA	NA	2	1	6	11	NA	NA
Stein *et al.*, 2007[124]	–8.46	113	8.08	–11.67	116	8.40	–11.43	112	8.25	–12.14	114	8.22	4	1	1	5	16	16
Tollefson *et al.*, 1994[127]	–0.8	89	5.66	–5.44	266	7.88	NA	NA	NA	NA	NA	NA	2	1	1	3	NA	NA
Van Oppen *et al.*, 1995[209]	17.9	29	9	13.4	28	9.4	NA	NA	NA	NA	NA	NA	2	2	10	12	NA	NA
Whittal *et al.*, 2010[212]	6.43	37	4.77	9.1	30	6.48	NA	NA	NA	NA	NA	NA	2	2	12	17	NA	NA

CCSG, Clomipramine Collaborative Study Group; NA, not applicable.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Key: intervention (class)

1. Placebo (1).
2. Waitlist (2).
3. Fluoxetine(3).
4. Fluvoxamine(3).
5. Paroxetine (3).
6. Sertraline (3).
7. Citalopram (3).
8. Venlafaxine (4).
9. Clomipramine(5).
10. BT (6).
11. CBT (7).
12. CT (8).
13. CBT + fluvoxamine (9).
14. Escitalopram (3).
15. Psychological placebo (10).

TABLE 103 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[1,2]	–3.317	2.875	0.03854	–8.983	–3.324	2.38	50,001	100,000
class.mean.diff[1,3]	–4.091	1.005	0.0165	–6.066	–4.092	–2.061	50,001	100,000
class.mean.diff[1,4]	–4.319	2.234	0.01698	–8.719	–4.321	0.1204	50,001	100,000
class.mean.diff[1,5]	–6.419	1.284	0.01173	–8.932	–6.435	–3.852	50,001	100,000
class.mean.diff[1,6]	–11.04	2.971	0.0506	–16.84	–11.04	–5.186	50,001	100,000
class.mean.diff[1,7]	–10.13	2.241	0.03435	–14.52	–10.15	–5.687	50,001	100,000
class.mean.diff[1,8]	–10.63	3.282	0.05325	–17.08	–10.62	–4.16	50,001	100,000
class.mean.diff[1,9]	–10.31	2.939	0.0301	–16.14	–10.31	–4.521	50,001	100,000
class.mean.diff[1,10]	–2.851	2.811	0.04821	–8.334	–2.868	2.771	50,001	100,000
class.mean.diff[2,3]	–0.7743	2.771	0.03045	–6.23	–0.776	4.688	50,001	100,000
class.mean.diff[2,4]	–1.002	3.487	0.03399	–7.916	–0.9951	5.826	50,001	100,000
class.mean.diff[2,5]	–3.102	2.984	0.03305	–9.001	–3.116	2.781	50,001	100,000
class.mean.diff[2,6]	–7.725	3.195	0.0332	–13.98	–7.734	–1.385	50,001	100,000
class.mean.diff[2,7]	–6.816	1.816	0.01158	–10.38	–6.819	–3.22	50,001	100,000
class.mean.diff[2,8]	–7.31	3.461	0.03576	–14.15	–7.299	–0.5329	50,001	100,000
class.mean.diff[2,9]	–6.996	3.24	0.01976	–13.41	–6.997	–0.6501	50,001	100,000
class.mean.diff[2,10]	0.466	2.969	0.03005	–5.327	0.4427	6.392	50,001	100,000
class.mean.diff[3,4]	–0.2282	2.198	0.011	–4.59	–0.2308	4.143	50,001	100,000
class.mean.diff[3,5]	–2.328	1.324	0.009057	–4.944	–2.333	0.2878	50,001	100,000
class.mean.diff[3,6]	–6.951	2.883	0.04368	–12.63	–6.943	–1.295	50,001	100,000
class.mean.diff[3,7]	–6.042	2.109	0.02551	–10.19	–6.048	–1.89	50,001	100,000
class.mean.diff[3,8]	–6.535	3.202	0.04661	–12.84	–6.513	–0.2369	50,001	100,000
class.mean.diff[3,9]	–6.222	2.844	0.02163	–11.91	–6.212	–0.651	50,001	100,000

TABLE 103 Class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[3,10]	1.24	2.713	0.04085	–4.066	1.227	6.595	50,001	100,000
class.mean.diff[4,5]	–2.1	2.15	0.01099	–6.334	–2.103	2.167	50,001	100,000
class.mean.diff[4,6]	–6.723	3.562	0.04667	–13.7	–6.73	0.3361	50,001	100,000
class.mean.diff[4,7]	–5.814	2.977	0.02942	–11.63	–5.837	0.1271	50,001	100,000
class.mean.diff[4,8]	–6.307	3.83	0.04946	–13.81	–6.314	1.295	50,001	100,000
class.mean.diff[4,9]	–5.994	3.524	0.02539	–12.98	–5.999	0.9386	50,001	100,000
class.mean.diff[4,10]	1.468	3.43	0.04404	–5.222	1.436	8.318	50,001	100,000
class.mean.diff[5,6]	–4.623	3.072	0.04576	–10.65	–4.629	1.457	50,001	100,000
class.mean.diff[5,7]	–3.714	2.374	0.02835	–8.372	–3.718	0.9799	50,001	100,000
class.mean.diff[5,8]	–4.207	3.377	0.04856	–10.86	–4.196	2.451	50,001	100,000
class.mean.diff[5,9]	–3.894	3.039	0.02453	–9.925	–3.889	2.079	50,001	100,000
class.mean.diff[5,10]	3.568	2.914	0.04304	–2.132	3.547	9.364	50,001	100,000
class.mean.diff[6,7]	0.909	2.631	0.02946	–4.294	0.9241	6.055	50,001	100,000
class.mean.diff[6,8]	0.4155	1.699	0.01145	–2.946	0.4231	3.735	50,001	100,000
class.mean.diff[6,9]	0.7288	3.549	0.03566	–6.29	0.7441	7.672	50,001	100,000
class.mean.diff[6,10]	8.191	1.441	0.007783	5.408	8.173	11.1	50,001	100,000
class.mean.diff[7,8]	–0.4935	2.951	0.0326	–6.361	–0.4901	5.267	50,001	100,000
class.mean.diff[7,9]	–0.1802	2.679	0.01381	–5.513	–0.1689	5.036	50,001	100,000
class.mean.diff[7,10]	7.282	2.346	0.02592	2.708	7.252	12	50,001	100,000
class.mean.diff[8,9]	0.3133	3.799	0.03858	–7.207	0.3088	7.792	50,001	100,000
class.mean.diff[8,10]	7.776	1.919	0.0128	4.082	7.744	11.64	50,001	100,000
class.mean.diff[9,10]	7.462	3.377	0.03274	0.9321	7.425	14.23	50,001	100,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 104 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[1,2]	–3.317	2.875	0.03854	–8.983	–3.324	2.38	50,001	100,000
treat.mean.diff[1,3]	–4.103	1.11	0.01554	–6.307	–4.106	–1.837	50,001	100,000
treat.mean.diff[1,4]	–4.259	1.141	0.0184	–6.642	–4.224	–1.997	50,001	100,000
treat.mean.diff[1,5]	–4.096	0.9845	0.01555	–6.032	–4.098	–2.095	50,001	100,000
treat.mean.diff[1,6]	–4.048	1.193	0.01704	–6.413	–4.065	–1.62	50,001	100,000
treat.mean.diff[1,7]	–4.009	1.149	0.01604	–6.247	–4.031	–1.633	50,001	100,000
treat.mean.diff[1,8]	–4.319	2.234	0.01698	–8.719	–4.321	0.1204	50,001	100,000
treat.mean.diff[1,9]	–6.419	1.284	0.01173	–8.932	–6.435	–3.852	50,001	100,000
treat.mean.diff[1,10]	–11.04	2.971	0.0506	–16.84	–11.04	–5.186	50,001	100,000
treat.mean.diff[1,11]	–10.13	2.241	0.03435	–14.52	–10.15	–5.687	50,001	100,000
treat.mean.diff[1,12]	–10.63	3.282	0.05325	–17.08	–10.62	–4.16	50,001	100,000
treat.mean.diff[1,13]	–10.31	2.939	0.0301	–16.14	–10.31	–4.521	50,001	100,000
treat.mean.diff[1,14]	–4.031	1.169	0.01598	–6.304	–4.05	–1.609	50,001	100,000
treat.mean.diff[1,15]	–2.851	2.811	0.04821	–8.334	–2.868	2.771	50,001	100,000
treat.mean.diff[2,3]	–0.7862	2.858	0.0316	–6.418	–0.7947	4.886	50,001	100,000
treat.mean.diff[2,4]	–0.9422	2.714	0.02867	–6.295	–0.9318	4.388	50,001	100,000
treat.mean.diff[2,5]	–0.7796	2.819	0.03121	–6.333	–0.7792	4.795	50,001	100,000
treat.mean.diff[2,6]	–0.7312	2.776	0.02917	–6.191	–0.7352	4.749	50,001	100,000
treat.mean.diff[2,7]	–0.6924	2.87	0.03127	–6.315	–0.6962	4.98	50,001	100,000
treat.mean.diff[2,8]	–1.002	3.487	0.03399	–7.916	–0.9951	5.826	50,001	100,000
treat.mean.diff[2,9]	–3.102	2.984	0.03305	–9.001	–3.116	2.781	50,001	100,000
treat.mean.diff[2,10]	–7.725	3.195	0.0332	–13.98	–7.734	–1.385	50,001	100,000
treat.mean.diff[2,11]	–6.816	1.816	0.01158	–10.38	–6.819	–3.22	50,001	100,000
treat.mean.diff[2,12]	–7.31	3.461	0.03576	–14.15	–7.299	–0.5329	50,001	100,000
treat.mean.diff[2,13]	–6.996	3.24	0.01976	–13.41	–6.997	–0.6501	50,001	100,000
treat.mean.diff[2,14]	–0.7137	2.869	0.03115	–6.355	–0.721	4.963	50,001	100,000
treat.mean.diff[2,15]	0.466	2.969	0.03005	–5.327	0.4427	6.392	50,001	100,000
treat.mean.diff[3,4]	–0.156	1.103	0.007438	–2.735	–0.04447	2.038	50,001	100,000
treat.mean.diff[3,5]	0.006609	1.008	0.004452	–2.178	0.001402	2.213	50,001	100,000
treat.mean.diff[3,6]	0.05504	1.172	0.005662	–2.451	0.01024	2.699	50,001	100,000
treat.mean.diff[3,7]	0.09385	1.146	0.005167	–2.324	0.02365	2.704	50,001	100,000
treat.mean.diff[3,8]	–0.2163	2.266	0.01135	–4.703	–0.2168	4.258	50,001	100,000
treat.mean.diff[3,9]	–2.316	1.4	0.008942	–5.099	–2.322	0.4748	50,001	100,000
treat.mean.diff[3,10]	–6.939	2.965	0.04455	–12.8	–6.929	–1.119	50,001	100,000
treat.mean.diff[3,11]	–6.03	2.224	0.02668	–10.45	–6.035	–1.652	50,001	100,000
treat.mean.diff[3,12]	–6.524	3.276	0.04749	–13	–6.5	–0.07921	50,001	100,000
treat.mean.diff[3,13]	–6.21	2.931	0.02268	–12.05	–6.2	–0.4791	50,001	100,000

TABLE 104 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[3,14]	0.0725	1.149	0.004902	–2.351	0.01609	2.679	50,001	100,000
treat.mean.diff[3,15]	1.252	2.802	0.04176	–4.238	1.242	6.796	50,001	100,000
treat.mean.diff[4,5]	0.1626	0.9883	0.007063	–1.784	0.05258	2.498	50,001	100,000
treat.mean.diff[4,6]	0.211	1.126	0.006667	–1.972	0.06478	2.911	50,001	100,000
treat.mean.diff[4,7]	0.2498	1.135	0.00808	–1.907	0.082	2.999	50,001	100,000
treat.mean.diff[4,8]	–0.06028	2.248	0.01251	–4.467	–0.07289	4.436	50,001	100,000
treat.mean.diff[4,9]	–2.16	1.354	0.01034	–4.79	–2.18	0.5713	50,001	100,000
treat.mean.diff[4,10]	–6.783	2.794	0.04167	–12.26	–6.785	–1.267	50,001	100,000
treat.mean.diff[4,11]	–5.874	2.03	0.02349	–9.855	–5.887	–1.842	50,001	100,000
treat.mean.diff[4,12]	–6.368	3.122	0.04471	–12.5	–6.361	–0.2322	50,001	100,000
treat.mean.diff[4,13]	–6.054	2.75	0.01995	–11.5	–6.054	–0.6226	50,001	100,000
treat.mean.diff[4,14]	0.2285	1.147	0.007522	–1.963	0.06855	3.003	50,001	100,000
treat.mean.diff[4,15]	1.408	2.624	0.0388	–3.693	1.395	6.616	50,001	100,000
treat.mean.diff[5,6]	0.04843	1.075	0.005323	–2.252	0.01349	2.452	50,001	100,000
treat.mean.diff[5,7]	0.08724	1.032	0.004494	–2.071	0.02513	2.433	50,001	100,000
treat.mean.diff[5,8]	–0.2229	2.108	0.009994	–4.415	–0.2219	3.938	50,001	100,000
treat.mean.diff[5,9]	–2.323	1.29	0.008259	–4.891	–2.327	0.2327	50,001	100,000
treat.mean.diff[5,10]	–6.946	2.924	0.04461	–12.71	–6.928	–1.22	50,001	100,000
treat.mean.diff[5,11]	–6.037	2.17	0.02639	–10.31	–6.04	–1.745	50,001	100,000
treat.mean.diff[5,12]	–6.53	3.238	0.04748	–12.91	–6.51	–0.1723	50,001	100,000
treat.mean.diff[5,13]	–6.217	2.888	0.02244	–11.99	–6.207	–0.5708	50,001	100,000
treat.mean.diff[5,14]	0.06589	0.9877	0.003986	–1.993	0.01554	2.29	50,001	100,000
treat.mean.diff[5,15]	1.246	2.755	0.04179	–4.146	1.231	6.695	50,001	100,000
treat.mean.diff[6,7]	0.03881	1.182	0.005654	–2.523	0.008911	2.675	50,001	100,000
treat.mean.diff[6,8]	–0.2713	2.316	0.01176	–4.882	–0.2655	4.303	50,001	100,000
treat.mean.diff[6,9]	–2.371	1.494	0.009976	–5.379	–2.368	0.5962	50,001	100,000
treat.mean.diff[6,10]	–6.994	2.914	0.0427	–12.72	–6.991	–1.266	50,001	100,000
treat.mean.diff[6,11]	–6.085	2.115	0.02415	–10.27	–6.088	–1.935	50,001	100,000
treat.mean.diff[6,12]	–6.579	3.23	0.04573	–12.97	–6.57	–0.2254	50,001	100,000
treat.mean.diff[6,13]	–6.265	2.887	0.02079	–12.02	–6.243	–0.6345	50,001	100,000
treat.mean.diff[6,14]	0.01746	1.187	0.005286	–2.536	0.001934	2.635	50,001	100,000
treat.mean.diff[6,15]	1.197	2.741	0.03985	–4.157	1.18	6.626	50,001	100,000
treat.mean.diff[7,8]	–0.3101	2.3	0.01147	–4.911	–0.3019	4.232	50,001	100,000
treat.mean.diff[7,9]	–2.41	1.48	0.009452	–5.408	–2.4	0.4917	50,001	100,000
treat.mean.diff[7,10]	–7.033	2.977	0.04466	–12.92	–7.021	–1.186	50,001	100,000
treat.mean.diff[7,11]	–6.124	2.235	0.02647	–10.56	–6.122	–1.743	50,001	100,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 104 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[7,12]	–6.617	3.285	0.04754	–13.1	–6.593	–0.1509	50,001	100,000
treat.mean.diff[7,13]	–6.304	2.939	0.02248	–12.17	–6.28	–0.5407	50,001	100,000
treat.mean.diff[7,14]	–0.02135	1.154	0.004668	–2.562	–0.00565	2.516	50,001	100,000
treat.mean.diff[7,15]	1.158	2.811	0.04188	–4.36	1.148	6.676	50,001	100,000
treat.mean.diff[8,9]	–2.1	2.15	0.01099	–6.334	–2.103	2.167	50,001	100,000
treat.mean.diff[8,10]	–6.723	3.562	0.04667	–13.7	–6.73	0.3361	50,001	100,000
treat.mean.diff[8,11]	–5.814	2.977	0.02942	–11.63	–5.837	0.1271	50,001	100,000
treat.mean.diff[8,12]	–6.307	3.83	0.04946	–13.81	–6.314	1.295	50,001	100,000
treat.mean.diff[8,13]	–5.994	3.524	0.02539	–12.98	–5.999	0.9386	50,001	100,000
treat.mean.diff[8,14]	0.2888	2.288	0.01111	–4.217	0.2814	4.854	50,001	100,000
treat.mean.diff[8,15]	1.468	3.43	0.04404	–5.222	1.436	8.318	50,001	100,000
treat.mean.diff[9,10]	–4.623	3.072	0.04576	–10.65	–4.629	1.457	50,001	100,000
treat.mean.diff[9,11]	–3.714	2.374	0.02835	–8.372	–3.718	0.9799	50,001	100,000
treat.mean.diff[9,12]	–4.207	3.377	0.04856	–10.86	–4.196	2.451	50,001	100,000
treat.mean.diff[9,13]	–3.894	3.039	0.02453	–9.925	–3.889	2.079	50,001	100,000
treat.mean.diff[9,14]	2.389	1.476	0.009127	–0.5044	2.379	5.359	50,001	100,000
treat.mean.diff[9,15]	3.568	2.914	0.04304	–2.132	3.547	9.364	50,001	100,000
treat.mean.diff[10,11]	0.909	2.631	0.02946	–4.294	0.9241	6.055	50,001	100,000
treat.mean.diff[10,12]	0.4155	1.699	0.01145	–2.946	0.4231	3.735	50,001	100,000
treat.mean.diff[10,13]	0.7288	3.549	0.03566	–6.29	0.7441	7.672	50,001	100,000
treat.mean.diff[10,14]	7.012	2.978	0.04446	1.171	6.995	12.9	50,001	100,000
treat.mean.diff[10,15]	8.191	1.441	0.007783	5.408	8.173	11.1	50,001	100,000
treat.mean.diff[11,12]	–0.4935	2.951	0.0326	–6.361	–0.4901	5.267	50,001	100,000
treat.mean.diff[11,13]	–0.1802	2.679	0.01381	–5.513	–0.1689	5.036	50,001	100,000
treat.mean.diff[11,14]	6.103	2.241	0.02636	1.693	6.095	10.55	50,001	100,000
treat.mean.diff[11,15]	7.282	2.346	0.02592	2.708	7.252	12	50,001	100,000
treat.mean.diff[12,13]	0.3133	3.799	0.03858	–7.207	0.3088	7.792	50,001	100,000
treat.mean.diff[12,14]	6.596	3.285	0.04743	0.1353	6.576	13.06	50,001	100,000
treat.mean.diff[12,15]	7.776	1.919	0.0128	4.082	7.744	11.64	50,001	100,000
treat.mean.diff[13,14]	6.283	2.939	0.02256	0.5358	6.257	12.18	50,001	100,000
treat.mean.diff[13,15]	7.462	3.377	0.03274	0.9321	7.425	14.23	50,001	100,000
treat.mean.diff[14,15]	1.18	2.812	0.04166	–4.332	1.171	6.716	50,001	100,000

Median ranks

TABLE 105 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[2]	7.601	1.575	0.01425	5	8	10	50,001	100,000
rk.class[3]	7.167	1.017	0.01022	5	7	9	50,001	100,000
rk.class[4]	6.893	1.61	0.01281	3	7	9	50,001	100,000
rk.class[5]	5.127	1.116	0.01217	2	5	7	50,001	100,000
rk.class[6]	2.287	1.195	0.0116	1	2	5	50,001	100,000
rk.class[7]	2.823	1.135	0.008796	1	3	5	50,001	100,000
rk.class[8]	2.695	1.437	0.0147	1	2	6	50,001	100,000
rk.class[9]	2.778	1.518	0.009753	1	3	6	50,001	100,000
rk.class[10]	7.933	1.469	0.02014	5	8	10	50,001	100,000

TABLE 106 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	14.69	0.6014	0.007856	13	15	15	50,001	100,000
rk[2]	10.65	3.606	0.03481	5	12	15	50,001	100,000
rk[3]	9.634	2.297	0.01488	6	10	14	50,001	100,000
rk[4]	9.255	2.115	0.01239	6	9	13	50,001	100,000
rk[5]	9.658	2.098	0.0142	6	10	13	50,001	100,000
rk[6]	9.753	2.28	0.01095	6	10	14	50,001	100,000
rk[7]	9.853	2.321	0.01454	6	10	14	50,001	100,000
rk[8]	9.188	3.559	0.02113	3	9	14	50,001	100,000
rk[9]	5.38	1.585	0.01406	3	5	10	50,001	100,000
rk[10]	2.335	1.398	0.01375	1	2	5	50,001	100,000
rk[11]	2.844	1.207	0.009126	1	3	5	50,001	100,000
rk[12]	2.807	1.829	0.0191	1	2	7	50,001	100,000
rk[13]	2.86	1.799	0.0103	1	3	7	50,001	100,000
rk[14]	9.787	2.316	0.01366	6	10	14	50,001	100,000
rk[15]	11.31	3.409	0.04808	5	13	15	50,001	100,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Adults: clinical effectiveness (Yale–Brown Obsessive–Compulsive Scale) – sensitivity analysis 2 (incomplete outcome data)

See *Table 22* for a summary.

TABLE 107 Raw data used

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
Anderson and Rees, 2007[157]	23.5	14	6.4	16.7	17	6.8	NA	NA	NA	NA	NA	NA	2	2	2	11	NA	NA
Andersson *et al.*, 2012[158]	12.94	49	6.26	18.88	51	4.18	NA	NA	NA	NA	NA	NA	2	2	11	15	NA	NA
Belotto-Silva *et al.*, 2012[160]	20.29	88	8.05	19.97	70	8.48	NA	NA	NA	NA	NA	NA	2	2	3	11	NA	NA
Bergeron *et al.*, 2002[161]	–9.7	72	7.7	–9.6	76	7.9	NA	NA	NA	NA	NA	NA	2	1	3	6	NA	NA
Bisserbe *et al.*, 1997[162]	–14.3	86	NA	–11.71	81	NA	NA	NA	NA	NA	NA	NA	2	1	6	9	NA	NA
Chouinard *et al.*, 1990[163]	–1.48	44	NA	–3.79	43	NA	NA	NA	NA	NA	NA	NA	2	1	1	6	NA	NA
Cordioli *et al.*, 2003[164]	23.2	24	5.5	15.1	23	7.8	NA	NA	NA	NA	NA	NA	2	2	2	11	NA	NA
Denys *et al.*, 2003[167]	–7.8	72	5.4	–7.2	73	7.5	NA	NA	NA	NA	NA	NA	2	1	5	8	NA	NA
Foa *et al.*, 2005[171]	22.2	26	6.4	18.2	36	7.8	11	29	7.9	10.5	31	8.2	4	2	1	9	10	13
Freeman *et al.*, 1994[172]	–8.6	28	NA	–7.8	19	NA	NA	NA	NA	NA	NA	NA	2	1	4	9	NA	NA
Freeston *et al.*, 1997[173]	22	14	6	12.2	15	9.6	NA	NA	NA	NA	NA	NA	2	2	2	11	NA	NA
GlaxoSmithKline, 2005[174]	–4.61	75	7.53	–5.61	79	7.47	–7.73	78	7.42	NA	NA	NA	3	1	1	5	9	NA
Goodman *et al.*, 1989[176]	28	21	7	19.4	21	7	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
Goodman *et al.*, 1996[177]	–1.71	78	4.88	–3.95	78	6.28	NA	NA	NA	NA	NA	NA	2	1	1	4	NA	NA
Greist *et al.*, 2002[178]	17.6	55	6.2	24.1	66	6.7	NA	NA	NA	NA	NA	NA	2	2	10	15	NA	NA
Hollander *et al.*, 2003[180]	–5.6	120	7.67	–8.5	117	7.57	NA	NA	NA	NA	NA	NA	2	1	1	4	NA	NA
Hollander *et al.*, 2003[181]	–3.33	89	NA	–4.14	88	NA	–6.35	86	NA	–7.34	85	NA	4	1	1	5	5	5
Jaurrieta *et al.*, 2008[182]	24.6	19	8.9	17.8	19	8.4	NA	NA	NA	NA	NA	NA	2	2	2	11	NA	NA

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
Jenike *et al.*, 1990[183]	22.3	9	7.8	20.6	10	9.2	NA	NA	NA	NA	NA	NA	2	2	1	6	NA	NA
Jenike *et al.*, 1997[185]	18.7	18	6.1	16.2	19	6.3	NA	NA	NA	NA	NA	NA	2	2	1	3	NA	NA
Kamijima *et al.*, 2004[187]	20.3	94	7.38	15.8	94	8.09	NA	NA	NA	NA	NA	NA	2	2	1	5	NA	NA
Kobak *et al.*,[189]	19.87	30	7.46	19.75	30	7.46	NA	NA	NA	NA	NA	NA	2	2	1	12	NA	NA
Koran *et al.*, 1996[190]	17.8	34	7.7	17	39	8.55	NA	NA	NA	NA	NA	NA	2	2	4	9	NA	NA
Kronig *et al.*, 1999[191]	–4.14	79	NA	–8.5	85	NA	NA	NA	NA	NA	NA	NA	2	1	1	6	NA	NA
López-Ibor *et al.*, 1996[193]	–7.5	30	9.29	–8.9	24	7.13	NA	NA	NA	NA	NA	NA	2	1	3	9	NA	NA
Montgomery *et al.*, 1993[197]	–3.7	56	5.98	–5.13	52	6.41	–4.76	52	6.89	–6.07	54	6.92	4	1	1	3	3	3
Montgomery *et al.*, 2001[198]	–5.6	101	6.9	–8.4	102	7.3	–8.9	98	7	–10.4	100	6.9	4	1	1	7	7	7
Mundo *et al.*, 1997[199]	16.2	10	8.9	21.6	9	7.6	19.8	11	10.1	NA	NA	NA	3	2	4	5	7	NA
Mundo *et al.*, 2001[200]	–12.2	115	NA	–12	112	NA	NA	NA	NA	NA	NA	NA	2	1	4	9	NA	NA
Nakajima *et al.*, 1996[201]	–1.9	33	7.2	–7.1	60	7.03	NA	NA	NA	NA	NA	NA	2	1	1	4	NA	NA
Sousa *et al.*, 2006[207]	–7.36	25	NA	–10.8	25	NA	NA	NA	NA	NA	NA	NA	2	1	6	11	NA	NA
Stein *et al.*, 2007[124]	–8.46	113	8.08	–11.67	116	8.40	–11.43	112	8.25	–12.14	114	8.22	4	1	1	5	14	14
Tollefson *et al.*, 1994[127]	–0.8	89	5.66	–5.44	266	7.88	NA	NA	NA	NA	NA	NA	2	1	1	3	NA	NA
Zohar and Judge, 1996[213]	–4.2	99	7.2	–6.4	201	7.1	–7	99	6.8	NA	NA	NA	3	1	1	5	9	NA

NA, not applicable.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Key: intervention (class)

1. Placebo (1).
2. Waitlist (2).
3. Fluoxetine (3).
4. Fluvoxamine (3).
5. Paroxetine (3).
6. Sertraline (3).
7. Citalopram (3).
8. Venlafaxine (4).
9. Clomipramine (5).
10. BT (6).
11. CBT (7).
12. Hypericum (8).
13. BT + clomipramine (9).
14. Escitalopram (3).
15. Psychological placebo (10).

TABLE 108 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[1,2]	2.063	1.806	0.03318	–1.509	2.067	5.611	50,001	100,000
class.mean.diff[1,3]	–3.332	0.4591	0.006652	–4.25	–3.329	–2.456	50,001	100,000
class.mean.diff[1,4]	–2.458	1.533	0.01317	–5.492	–2.461	0.5665	50,001	100,000
class.mean.diff[1,5]	–3.156	0.6228	0.008235	–4.392	–3.151	–1.95	50,001	100,000
class.mean.diff[1,6]	–8.7	1.541	0.02275	–11.78	–8.686	–5.747	50,001	100,000
class.mean.diff[1,7]	–5.758	1.254	0.02213	–8.232	–5.744	–3.314	50,001	100,000
class.mean.diff[1,8]	–0.103	2.164	0.02634	–4.344	–0.1013	4.112	50,001	100,000
class.mean.diff[1,9]	–10.67	1.916	0.02438	–14.42	–10.68	–6.9	50,001	100,000
class.mean.diff[1,10]	–0.9254	1.563	0.02449	–4.097	–0.8947	2.087	50,001	100,000
class.mean.diff[2,3]	–5.395	1.808	0.03138	–8.945	–5.391	–1.829	50,001	100,000
class.mean.diff[2,4]	–4.52	2.351	0.03469	–9.157	–4.511	0.08525	50,001	100,000
class.mean.diff[2,5]	–5.219	1.856	0.0317	–8.904	–5.21	–1.566	50,001	100,000
class.mean.diff[2,6]	–10.76	2.04	0.0285	–14.87	–10.74	–6.858	50,001	100,000
class.mean.diff[2,7]	–7.821	1.32	0.01947	–10.41	–7.816	–5.23	50,001	100,000
class.mean.diff[2,8]	–2.166	2.825	0.04148	–7.694	–2.138	3.396	50,001	100,000
class.mean.diff[2,9]	–12.73	2.55	0.03768	–17.77	–12.72	–7.707	50,001	100,000
class.mean.diff[2,10]	–2.988	1.838	0.02496	–6.636	–2.964	0.5565	50,001	100,000
class.mean.diff[3,4]	0.8747	1.533	0.0124	–2.121	0.8695	3.917	50,001	100,000
class.mean.diff[3,5]	0.1763	0.6482	0.005658	–1.104	0.1775	1.444	50,001	100,000
class.mean.diff[3,6]	–5.368	1.564	0.02109	–8.483	–5.36	–2.357	50,001	100,000
class.mean.diff[3,7]	–2.425	1.253	0.02014	–4.891	–2.417	0.03083	50,001	100,000
class.mean.diff[3,8]	3.229	2.214	0.02709	–1.126	3.233	7.557	50,001	100,000
class.mean.diff[3,9]	–7.339	1.948	0.02407	–11.16	–7.34	–3.519	50,001	100,000
class.mean.diff[3,10]	2.407	1.569	0.02221	–0.7641	2.435	5.452	50,001	100,000
class.mean.diff[4,5]	–0.6984	1.605	0.01404	–3.883	–0.6939	2.453	50,001	100,000
class.mean.diff[4,6]	–6.242	2.159	0.02455	–10.57	–6.21	–2.064	50,001	100,000
class.mean.diff[4,7]	–3.3	1.947	0.0237	–7.165	–3.296	0.5222	50,001	100,000

TABLE 108 Class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[4,8]	2.354	2.654	0.03049	–2.853	2.366	7.492	50,001	100,000
class.mean.diff[4,9]	–8.214	2.448	0.02614	–13.03	–8.188	–3.395	50,001	100,000
class.mean.diff[4,10]	1.532	2.161	0.02547	–2.839	1.562	5.704	50,001	100,000
class.mean.diff[5,6]	–5.544	1.569	0.02063	–8.669	–5.542	–2.494	50,001	100,000
class.mean.diff[5,7]	–2.602	1.326	0.02093	–5.179	–2.603	0.01789	50,001	100,000
class.mean.diff[5,8]	3.053	2.244	0.0267	–1.368	3.063	7.418	50,001	100,000
class.mean.diff[5,9]	–7.516	1.923	0.02344	–11.28	–7.513	–3.713	50,001	100,000
class.mean.diff[5,10]	2.231	1.604	0.02237	–0.9882	2.245	5.346	50,001	100,000
class.mean.diff[6,7]	2.942	1.563	0.01848	–0.05385	2.929	6.044	50,001	100,000
class.mean.diff[6,8]	8.597	2.65	0.03238	3.396	8.619	13.8	50,001	100,000
class.mean.diff[6,9]	–1.971	2.152	0.02598	–6.188	–1.968	2.292	50,001	100,000
class.mean.diff[6,10]	7.775	1.342	0.01406	5.142	7.772	10.43	50,001	100,000
class.mean.diff[7,8]	5.655	2.499	0.03332	0.7631	5.664	10.58	50,001	100,000
class.mean.diff[7,9]	–4.914	2.18	0.02919	–9.214	–4.906	–0.6075	50,001	100,000
class.mean.diff[7,10]	4.832	1.278	0.01355	2.256	4.847	7.284	50,001	100,000
class.mean.diff[8,9]	–10.57	2.89	0.03667	–16.23	–10.58	–4.859	50,001	100,000
class.mean.diff[8,10]	–0.8223	2.675	0.0347	–6.086	–0.8262	4.44	50,001	100,000
class.mean.diff[9,10]	9.746	2.279	0.02926	5.261	9.76	14.22	50,001	100,000

TABLE 109 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[1,2]	2.063	1.806	0.03318	–1.509	2.067	5.611	50,001	100,000
treat.mean.diff[1,3]	–3.374	0.4854	0.007081	–4.367	–3.369	–2.426	50,001	100,000
treat.mean.diff[1,4]	–3.44	0.4873	0.007192	–4.479	–3.422	–2.535	50,001	100,000
treat.mean.diff[1,5]	–3.038	0.4909	0.007551	–3.924	–3.067	–1.993	50,001	100,000
treat.mean.diff[1,6]	–3.486	0.5394	0.007976	–4.662	–3.455	–2.499	50,001	100,000
treat.mean.diff[1,7]	–3.366	0.5748	0.006907	–4.579	–3.357	–2.24	50,001	100,000
treat.mean.diff[1,8]	–2.458	1.533	0.01317	–5.492	–2.461	0.5665	50,001	100,000
treat.mean.diff[1,9]	–3.156	0.6228	0.008235	–4.392	–3.151	–1.95	50,001	100,000
treat.mean.diff[1,10]	–8.7	1.541	0.02275	–11.78	–8.686	–5.747	50,001	100,000
treat.mean.diff[1,11]	–5.758	1.254	0.02213	–8.232	–5.744	–3.314	50,001	100,000
treat.mean.diff[1,12]	–0.103	2.164	0.02634	–4.344	–0.1013	4.112	50,001	100,000
treat.mean.diff[1,13]	–10.67	1.916	0.02438	–14.42	–10.68	–6.9	50,001	100,000
treat.mean.diff[1,14]	–3.289	0.583	0.007209	–4.447	–3.3	–2.07	50,001	100,000
treat.mean.diff[1,15]	–0.9254	1.563	0.02449	–4.097	–0.8947	2.087	50,001	100,000
treat.mean.diff[2,3]	–5.437	1.783	0.03076	–8.956	–5.432	–1.929	50,001	100,000
treat.mean.diff[2,4]	–5.503	1.822	0.03167	–9.106	–5.493	–1.918	50,001	100,000
treat.mean.diff[2,5]	–5.101	1.841	0.03199	–8.726	–5.093	–1.483	50,001	100,000
treat.mean.diff[2,6]	–5.549	1.804	0.03141	–9.099	–5.545	–2	50,001	100,000
treat.mean.diff[2,7]	–5.429	1.854	0.03184	–9.071	–5.426	–1.759	50,001	100,000
treat.mean.diff[2,8]	–4.52	2.351	0.03469	–9.157	–4.511	0.08525	50,001	100,000
treat.mean.diff[2,9]	–5.219	1.856	0.0317	–8.904	–5.21	–1.566	50,001	100,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 109 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[2,10]	–10.76	2.04	0.0285	–14.87	–10.74	–6.858	50,001	100,000
treat.mean.diff[2,11]	–7.821	1.32	0.01947	–10.41	–7.816	–5.23	50,001	100,000
treat.mean.diff[2,12]	–2.166	2.825	0.04148	–7.694	–2.138	3.396	50,001	100,000
treat.mean.diff[2,13]	–12.73	2.55	0.03768	–17.77	–12.72	–7.707	50,001	100,000
treat.mean.diff[2,14]	–5.352	1.854	0.0316	–8.987	–5.35	–1.699	50,001	100,000
treat.mean.diff[2,15]	–2.988	1.838	0.02496	–6.636	–2.964	0.5565	50,001	100,000
treat.mean.diff[3,4]	–0.06626	0.535	0.004969	–1.276	–0.02218	1.039	50,001	100,000
treat.mean.diff[3,5]	0.3363	0.5731	0.006438	–0.5877	0.1992	1.711	50,001	100,000
treat.mean.diff[3,6]	–0.1113	0.5238	0.004289	–1.318	–0.04389	0.9157	50,001	100,000
treat.mean.diff[3,7]	0.007895	0.6048	0.004594	–1.315	0.001216	1.316	50,001	100,000
treat.mean.diff[3,8]	0.9167	1.561	0.01295	–2.149	0.9082	3.996	50,001	100,000
treat.mean.diff[3,9]	0.2183	0.682	0.006852	–1.122	0.2135	1.565	50,001	100,000
treat.mean.diff[3,10]	–5.326	1.561	0.02122	–8.441	–5.316	–2.31	50,001	100,000
treat.mean.diff[3,11]	–2.383	1.218	0.01932	–4.777	–2.374	0.0129	50,001	100,000
treat.mean.diff[3,12]	3.271	2.216	0.02696	–1.086	3.276	7.605	50,001	100,000
treat.mean.diff[3,13]	–7.297	1.954	0.02443	–11.13	–7.303	–3.467	50,001	100,000
treat.mean.diff[3,14]	0.08549	0.6104	0.004855	–1.127	0.02296	1.507	50,001	100,000
treat.mean.diff[3,15]	2.449	1.553	0.02204	–0.6869	2.479	5.475	50,001	100,000
treat.mean.diff[4,5]	0.4026	0.5837	0.006677	–0.4634	0.2551	1.823	50,001	100,000
treat.mean.diff[4,6]	–0.04508	0.5522	0.004903	–1.264	–0.01395	1.109	50,001	100,000
treat.mean.diff[4,7]	0.07415	0.6022	0.004913	–1.168	0.02271	1.449	50,001	100,000
treat.mean.diff[4,8]	0.9829	1.567	0.01313	–2.052	0.9648	4.119	50,001	100,000
treat.mean.diff[4,9]	0.2846	0.632	0.006125	–0.9381	0.274	1.548	50,001	100,000
treat.mean.diff[4,10]	–5.26	1.56	0.02093	–8.352	–5.257	–2.247	50,001	100,000
treat.mean.diff[4,11]	–2.317	1.273	0.02044	–4.816	–2.322	0.2033	50,001	100,000
treat.mean.diff[4,12]	3.337	2.225	0.02755	–1.029	3.333	7.673	50,001	100,000
treat.mean.diff[4,13]	–7.231	1.944	0.02369	–11.05	–7.235	–3.392	50,001	100,000
treat.mean.diff[4,14]	0.1518	0.6232	0.005332	–1.029	0.05458	1.642	50,001	100,000
treat.mean.diff[4,15]	2.515	1.571	0.02206	–0.6391	2.533	5.588	50,001	100,000
treat.mean.diff[5,6]	–0.4477	0.638	0.007698	–2.005	–0.2799	0.4829	50,001	100,000
treat.mean.diff[5,7]	–0.3284	0.632	0.006024	–1.869	–0.1792	0.7137	50,001	100,000
treat.mean.diff[5,8]	0.5804	1.459	0.0117	–2.292	0.5793	3.454	50,001	100,000
treat.mean.diff[5,9]	–0.118	0.67	0.006758	–1.489	–0.101	1.153	50,001	100,000
treat.mean.diff[5,10]	–5.662	1.586	0.02154	–8.832	–5.647	–2.628	50,001	100,000
treat.mean.diff[5,11]	–2.72	1.301	0.02126	–5.327	–2.709	–0.195	50,001	100,000
treat.mean.diff[5,12]	2.935	2.222	0.02774	–1.443	2.948	7.263	50,001	100,000
treat.mean.diff[5,13]	–7.634	1.961	0.02443	–11.48	–7.632	–3.774	50,001	100,000
treat.mean.diff[5,14]	–0.2508	0.5732	0.004741	–1.606	–0.1365	0.7843	50,001	100,000
treat.mean.diff[5,15]	2.113	1.601	0.02298	–1.129	2.149	5.188	50,001	100,000
treat.mean.diff[6,7]	0.1192	0.6287	0.005016	–1.128	0.04269	1.588	50,001	100,000
treat.mean.diff[6,8]	1.028	1.588	0.01362	–2.061	1.012	4.194	50,001	100,000
treat.mean.diff[6,9]	0.3296	0.6914	0.006814	–1.012	0.3196	1.732	50,001	100,000
treat.mean.diff[6,10]	–5.214	1.573	0.02119	–8.353	–5.202	–2.172	50,001	100,000
treat.mean.diff[6,11]	–2.272	1.245	0.01989	–4.715	–2.262	0.1749	50,001	100,000

TABLE 109 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[6,12]	3.383	2.232	0.02709	–0.9925	3.391	7.727	50,001	100,000
treat.mean.diff[6,13]	–7.186	1.961	0.02443	–11.03	–7.189	–3.335	50,001	100,000
treat.mean.diff[6,14]	0.1968	0.6542	0.005736	–0.9927	0.07337	1.795	50,001	100,000
treat.mean.diff[6,15]	2.56	1.568	0.02219	–0.6208	2.576	5.595	50,001	100,000
treat.mean.diff[7,8]	0.9088	1.587	0.01318	–2.186	0.898	4.079	50,001	100,000
treat.mean.diff[7,9]	0.2104	0.7561	0.006955	–1.273	0.2016	1.732	50,001	100,000
treat.mean.diff[7,10]	–5.334	1.615	0.02169	–8.531	–5.319	–2.209	50,001	100,000
treat.mean.diff[7,11]	–2.391	1.321	0.02061	–4.996	–2.384	0.1972	50,001	100,000
treat.mean.diff[7,12]	3.263	2.24	0.02707	–1.131	3.268	7.622	50,001	100,000
treat.mean.diff[7,13]	–7.305	1.986	0.02454	–11.2	–7.309	–3.41	50,001	100,000
treat.mean.diff[7,14]	0.0776	0.6677	0.004748	–1.278	0.01998	1.616	50,001	100,000
treat.mean.diff[7,15]	2.441	1.624	0.02278	–0.8331	2.466	5.593	50,001	100,000
treat.mean.diff[8,9]	–0.6984	1.605	0.01404	–3.883	–0.6939	2.453	50,001	100,000
treat.mean.diff[8,10]	–6.242	2.159	0.02455	–10.57	–6.21	–2.064	50,001	100,000
treat.mean.diff[8,11]	–3.3	1.947	0.0237	–7.165	–3.296	0.5222	50,001	100,000
treat.mean.diff[8,12]	2.354	2.654	0.03049	–2.853	2.366	7.492	50,001	100,000
treat.mean.diff[8,13]	–8.214	2.448	0.02614	–13.03	–8.188	–3.395	50,001	100,000
treat.mean.diff[8,14]	–0.8312	1.566	0.01265	–3.945	–0.8274	2.228	50,001	100,000
treat.mean.diff[8,15]	1.532	2.161	0.02547	–2.839	1.562	5.704	50,001	100,000
treat.mean.diff[9,10]	–5.544	1.569	0.02063	–8.669	–5.542	–2.494	50,001	100,000
treat.mean.diff[9,11]	–2.602	1.326	0.02093	–5.179	–2.603	0.01789	50,001	100,000
treat.mean.diff[9,12]	3.053	2.244	0.0267	–1.368	3.063	7.418	50,001	100,000
treat.mean.diff[9,13]	–7.516	1.923	0.02344	–11.28	–7.513	–3.713	50,001	100,000
treat.mean.diff[9,14]	–0.1328	0.7567	0.006481	–1.614	–0.1446	1.413	50,001	100,000
treat.mean.diff[9,15]	2.231	1.604	0.02237	–0.9882	2.245	5.346	50,001	100,000
treat.mean.diff[10,11]	2.942	1.563	0.01848	–0.05385	2.929	6.044	50,001	100,000
treat.mean.diff[10,12]	8.597	2.65	0.03238	3.396	8.619	13.8	50,001	100,000
treat.mean.diff[10,13]	–1.971	2.152	0.02598	–6.188	–1.968	2.292	50,001	100,000
treat.mean.diff[10,14]	5.411	1.614	0.02145	2.293	5.403	8.617	50,001	100,000
treat.mean.diff[10,15]	7.775	1.342	0.01406	5.142	7.772	10.43	50,001	100,000
treat.mean.diff[11,12]	5.655	2.499	0.03332	0.7631	5.664	10.58	50,001	100,000
treat.mean.diff[11,13]	–4.914	2.18	0.02919	–9.214	–4.906	–0.6075	50,001	100,000
treat.mean.diff[11,14]	2.469	1.322	0.02055	–0.08331	2.457	5.096	50,001	100,000
treat.mean.diff[11,15]	4.832	1.278	0.01355	2.256	4.847	7.284	50,001	100,000
treat.mean.diff[12,13]	–10.57	2.89	0.03667	–16.23	–10.58	–4.859	50,001	100,000
treat.mean.diff[12,14]	–3.186	2.244	0.02729	–7.572	–3.188	1.22	50,001	100,000
treat.mean.diff[12,15]	–0.8223	2.675	0.0347	–6.086	–0.8262	4.44	50,001	100,000
treat.mean.diff[13,14]	7.383	1.987	0.02431	3.48	7.389	11.3	50,001	100,000
treat.mean.diff[13,15]	9.746	2.279	0.02926	5.261	9.76	14.22	50,001	100,000
treat.mean.diff[14,15]	2.363	1.623	0.02262	–0.9254	2.397	5.517	50,001	100,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Median ranks

TABLE 110 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	8.313	0.814	0.01061	7	8	10	50,001	100,000
rk.class[2]	9.576	0.7913	0.01062	7	10	10	50,001	100,000
rk.class[3]	4.78	0.8116	0.006447	4	5	6	50,001	100,000
rk.class[4]	5.846	1.456	0.01269	3	6	9	50,001	100,000
rk.class[5]	5.085	0.9136	0.007409	4	5	7	50,001	100,000
rk.class[6]	1.853	0.4327	0.003828	1	2	3	50,001	100,000
rk.class[7]	3.069	0.4784	0.004582	2	3	4	50,001	100,000
rk.class[8]	7.963	1.677	0.01967	4	8	10	50,001	100,000
rk.class[9]	1.191	0.4275	0.004097	1	1	2	50,001	100,000
rk.class[10]	7.323	1.297	0.01672	4	7	9	50,001	100,000

TABLE 111 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	13.31	0.814	0.0106	12	13	15	50,001	100,000
rk[2]	14.57	0.8591	0.01129	12	15	15	50,001	100,000
rk[3]	7.109	2.014	0.01435	4	7	11	50,001	100,000
rk[4]	6.782	1.983	0.01532	4	7	11	50,001	100,000
rk[5]	8.675	1.881	0.01767	5	9	12	50,001	100,000
rk[6]	6.617	2.041	0.01592	4	6	11	50,001	100,000
rk[7]	7.154	2.19	0.01599	4	7	11	50,001	100,000
rk[8]	9.42	3.3	0.02823	3	11	14	50,001	100,000
rk[9]	8.087	2.534	0.0223	4	9	12	50,001	100,000
rk[10]	1.856	0.4524	0.003938	1	2	3	50,001	100,000
rk[11]	3.219	1.074	0.01102	2	3	7	50,001	100,000
rk[12]	12.59	2.633	0.02894	4	13	15	50,001	100,000
rk[13]	1.192	0.4339	0.00412	1	1	2	50,001	100,000
rk[14]	7.441	2.19	0.01384	4	7	11	50,001	100,000
rk[15]	11.98	2.151	0.02675	4	12	14	50,001	100,000

Adults: clinical effectiveness (Yale–Brown Obsessive–Compulsive Scale) – sensitivity analysis 3 (blinding)

See *Table 23* for a summary.

TABLE 112 Raw data used

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
Albert *et al.*, 2002[155]	18.36	25	7.11	17.3	40	6.15	NA	NA	NA	NA	NA	NA	2	2	8	9	NA	NA
Andersson *et al.*, 2012[158]	12.94	49	6.26	18.88	51	4.18	NA	NA	NA	NA	NA	NA	2	2	11	15	NA	NA
Belloch *et al.*, 2008[159]	8.31	13	8.75	6.8	16	3.55	NA	NA	NA	NA	NA	NA	2	2	10	12	NA	NA
Belotto-Silva *et al.*, 2012[160]	20.29	88	8.05	19.97	70	8.48	NA	NA	NA	NA	NA	NA	2	2	3	11	NA	NA
Cordioli *et al.*, 2003[164]	23.2	24	5.5	15.1	23	7.8	NA	NA	NA	NA	NA	NA	2	2	2	11	NA	NA
Cottraux *et al.*, 2001[166]	–12.1	30	7.8	–12.5	30	8.2	NA	NA	NA	NA	NA	NA	2	1	10	12	NA	NA
Denys *et al.*, 2003[167]	–7.8	72	5.4	–7.2	73	7.5	NA	NA	NA	NA	NA	NA	2	1	5	8	NA	NA
Foa *et al.*, 2005[171]	22.2	26	6.4	18.2	36	7.8	11	29	7.9	10.5	31	8.2	4	2	1	9	10	13
Goodman *et al.*, 1989[176]	28	21	7	19.4	21	7	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
Jenike *et al.*, 1990[184]	21.8	20	7.6	18.8	18	4	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
Mundo *et al.*, 1997[199]	16.2	10	8.9	21.6	9	7.6	19.8	11	10.1	NA	NA	NA	3	2	4	5	7	NA
Nakatani *et al.*, 2005[202]	20.2	10	9.4	12.9	10	4.9	28.4	8	5.5	NA	NA	NA	3	2	4	10	15	NA
O'Connor *et al.*, 1999[203]	17.5	6	4	13.3	6	8.6	NA	NA	NA	NA	NA	NA	2	2	2	11	NA	NA
O'Connor *et al.*, 2006[204]	25.4	10	3.5	24	11	4.7	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
Sousa *et al.*, 2006[207]	–7.36	25	NA	–10.8	25	NA	NA	NA	NA	NA	NA	NA	2	1	6	11	NA	NA
Stein *et al.*, 2007[124]	–8.46	113	8.08	–11.67	116	8.40	–11.43	112	8.25	–12.14	114	8.22	4	1	1	5	14	14
Whittal *et al.*, 2005[211]	10.41	29	7.6	10.6	30	7.1	NA	NA	NA	NA	NA	NA	2	2	10	12	NA	NA

NA, not available.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Key

1. Placebo (1).
2. Waitlist (2).
3. Fluoxetine (3).
4. Fluvoxamine (3).
5. Paroxetine (3).
6. Sertraline (3).
7. Citalopram (3).
8. Venlafaxine (4).
9. Clomipramine (5).
10. BT (6).
11. CBT (7).
12. CT (8).
13. BT + clomipramine (9).
14. Escitalopram (3).
15. Psychological placebo (10).

TABLE 113 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[1,2]	3.235	2.714	0.06924	–2.16	3.238	8.44	50,001	100,000
class.mean.diff[1,3]	–3.305	1.234	0.02794	–5.59	–3.349	–0.6521	50,001	100,000
class.mean.diff[1,4]	–2.728	1.632	0.0314	–5.968	–2.7	0.4702	50,001	100,000
class.mean.diff[1,5]	–4.046	1.674	0.03403	–7.303	–4.023	–0.73	50,001	100,000
class.mean.diff[1,6]	–11.79	1.762	0.04753	–15.17	–11.81	–8.279	50,001	100,000
class.mean.diff[1,7]	–4.112	1.842	0.04886	–7.631	–4.125	–0.3389	50,001	100,000
class.mean.diff[1,8]	–12.23	2.231	0.05662	–16.66	–12.24	–7.796	50,001	100,000
class.mean.diff[1,9]	–11.85	2.064	0.03817	–16.07	–11.85	–7.821	50,001	100,000
class.mean.diff[1,10]	2.328	1.991	0.0483	–1.486	2.28	6.364	50,001	100,000
class.mean.diff[2,3]	–6.539	2.542	0.05609	–11.41	–6.547	–1.448	50,001	100,000
class.mean.diff[2,4]	–5.963	2.911	0.06212	–11.5	–5.948	–0.1066	50,001	100,000
class.mean.diff[2,5]	–7.28	2.983	0.06417	–12.95	–7.338	–1.344	50,001	100,000
class.mean.diff[2,6]	–15.02	2.918	0.06588	–20.59	–15.07	–9.151	50,001	100,000
class.mean.diff[2,7]	–7.347	1.969	0.04063	–11.07	–7.404	–3.352	50,001	100,000
class.mean.diff[2,8]	–15.47	3.237	0.07454	–21.74	–15.48	–9.029	50,001	100,000
class.mean.diff[2,9]	–15.09	3.247	0.06687	–21.38	–15.13	–8.626	50,001	100,000
class.mean.diff[2,10]	–0.9071	2.429	0.04743	–5.577	–0.9553	4.094	50,001	100,000
class.mean.diff[3,4]	0.5765	1.669	0.02399	–2.802	0.5924	3.827	50,001	100,000
class.mean.diff[3,5]	–0.7409	1.845	0.03034	–4.413	–0.7264	2.846	50,001	100,000
class.mean.diff[3,6]	–8.486	1.902	0.04269	–12.2	–8.487	–4.694	50,001	100,000
class.mean.diff[3,7]	–0.8074	1.611	0.03221	–3.942	–0.8267	2.399	50,001	100,000
class.mean.diff[3,8]	–8.929	2.349	0.05339	–13.58	–8.912	–4.286	50,001	100,000
class.mean.diff[3,9]	–8.55	2.272	0.03812	–13.14	–8.521	–4.061	50,001	100,000

TABLE 113 Class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[3,10]	5.632	1.883	0.03501	1.957	5.593	9.45	50,001	100,000
class.mean.diff[4,5]	–1.317	1.645	0.02532	–4.541	–1.319	1.944	50,001	100,000
class.mean.diff[4,6]	–9.062	2.129	0.04457	–13.15	–9.064	–4.827	50,001	100,000
class.mean.diff[4,7]	–1.384	2.151	0.03957	–5.588	–1.387	2.924	50,001	100,000
class.mean.diff[4,8]	–9.506	2.52	0.0536	–14.52	–9.486	–4.519	50,001	100,000
class.mean.diff[4,9]	–9.126	2.363	0.03643	–13.85	–9.098	–4.476	50,001	100,000
class.mean.diff[4,10]	5.056	2.304	0.0404	0.6046	5.021	9.779	50,001	100,000
class.mean.diff[5,6]	–7.745	1.937	0.03849	–11.47	–7.768	–3.863	50,001	100,000
class.mean.diff[5,7]	–0.06652	2.247	0.04401	–4.412	–0.07668	4.391	50,001	100,000
class.mean.diff[5,8]	–8.188	2.369	0.04925	–12.86	–8.214	–3.489	50,001	100,000
class.mean.diff[5,9]	–7.809	2.119	0.03235	–12.02	–7.798	–3.656	50,001	100,000
class.mean.diff[5,10]	6.373	2.334	0.04407	1.879	6.35	11.12	50,001	100,000
class.mean.diff[6,7]	7.678	2.142	0.04823	3.483	7.676	11.91	50,001	100,000
class.mean.diff[6,8]	–0.4437	1.39	0.02557	–3.137	–0.472	2.314	50,001	100,000
class.mean.diff[6,9]	–0.0644	2.231	0.04198	–4.457	–0.09329	4.256	50,001	100,000
class.mean.diff[6,10]	14.12	2.108	0.04427	10.07	14.1	18.22	50,001	100,000
class.mean.diff[7,8]	–8.122	2.542	0.05765	–13.14	–8.119	–3.13	50,001	100,000
class.mean.diff[7,9]	–7.743	2.583	0.04772	–12.93	–7.699	–2.677	50,001	100,000
class.mean.diff[7,10]	6.44	1.4	0.01987	3.792	6.404	9.349	50,001	100,000
class.mean.diff[8,9]	0.3793	2.612	0.05047	–4.818	0.3555	5.518	50,001	100,000
class.mean.diff[8,10]	14.56	2.518	0.05403	9.674	14.52	19.51	50,001	100,000
class.mean.diff[9,10]	14.18	2.643	0.04615	9.044	14.14	19.53	50,001	100,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 114 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[1,2]	3.235	2.714	0.06924	–2.16	3.238	8.44	50,001	100,000
treat.mean.diff[1,3]	–3.416	1.611	0.03769	–6.618	–3.456	0.06601	50,001	100,000
treat.mean.diff[1,4]	–3.849	1.018	0.02311	–5.988	–3.813	–1.948	50,001	100,000
treat.mean.diff[1,5]	–3.203	1.103	0.02543	–5.291	–3.238	–0.8988	50,001	100,000
treat.mean.diff[1,6]	–2.713	1.897	0.04831	–5.647	–3.041	2.035	50,001	100,000
treat.mean.diff[1,7]	–3.272	1.64	0.03575	–6.501	–3.333	0.4173	50,001	100,000
treat.mean.diff[1,8]	–2.728	1.632	0.0314	–5.968	–2.7	0.4702	50,001	100,000
treat.mean.diff[1,9]	–4.046	1.674	0.03403	–7.303	–4.023	–0.73	50,001	100,000
treat.mean.diff[1,10]	–11.79	1.762	0.04753	–15.17	–11.81	–8.279	50,001	100,000
treat.mean.diff[1,11]	–4.112	1.842	0.04886	–7.631	–4.125	–0.3389	50,001	100,000
treat.mean.diff[1,12]	–12.23	2.231	0.05662	–16.66	–12.24	–7.796	50,001	100,000
treat.mean.diff[1,13]	–11.85	2.064	0.03817	–16.07	–11.85	–7.821	50,001	100,000
treat.mean.diff[1,14]	–3.356	1.058	0.02341	–5.376	–3.374	–1.212	50,001	100,000
treat.mean.diff[1,15]	2.328	1.991	0.0483	–1.486	2.28	6.364	50,001	100,000
treat.mean.diff[2,3]	–6.65	2.408	0.05065	–11.19	–6.696	–1.818	50,001	100,000
treat.mean.diff[2,4]	–7.084	2.684	0.06565	–12.27	–7.059	–1.813	50,001	100,000
treat.mean.diff[2,5]	–6.437	2.643	0.06003	–11.49	–6.466	–1.121	50,001	100,000
treat.mean.diff[2,6]	–5.948	2.585	0.05411	–10.79	–5.974	–0.701	50,001	100,000
treat.mean.diff[2,7]	–6.507	2.826	0.06123	–11.91	–6.538	–0.7908	50,001	100,000
treat.mean.diff[2,8]	–5.963	2.911	0.06212	–11.5	–5.948	–0.1066	50,001	100,000
treat.mean.diff[2,9]	–7.28	2.983	0.06417	–12.95	–7.338	–1.344	50,001	100,000
treat.mean.diff[2,10]	–15.02	2.918	0.06588	–20.59	–15.07	–9.151	50,001	100,000
treat.mean.diff[2,11]	–7.347	1.969	0.04063	–11.07	–7.404	–3.352	50,001	100,000
treat.mean.diff[2,12]	–15.47	3.237	0.07454	–21.74	–15.48	–9.029	50,001	100,000
treat.mean.diff[2,13]	–15.09	3.247	0.06687	–21.38	–15.13	–8.626	50,001	100,000
treat.mean.diff[2,14]	–6.591	2.672	0.0623	–11.7	–6.581	–1.299	50,001	100,000
treat.mean.diff[2,15]	–0.9071	2.429	0.04743	–5.577	–0.9553	4.094	50,001	100,000
treat.mean.diff[3,4]	–0.4335	1.539	0.03259	–4.176	–0.1464	2.393	50,001	100,000
treat.mean.diff[3,5]	0.213	1.507	0.02551	–2.921	0.07384	3.508	50,001	100,000
treat.mean.diff[3,6]	0.7025	1.613	0.02607	–1.828	0.274	4.886	50,001	100,000
treat.mean.diff[3,7]	0.1434	1.802	0.02922	–3.65	0.03283	4.281	50,001	100,000
treat.mean.diff[3,8]	0.6875	1.981	0.032	–3.29	0.6776	4.713	50,001	100,000
treat.mean.diff[3,9]	–0.6299	2.107	0.03662	–4.804	–0.6254	3.512	50,001	100,000
treat.mean.diff[3,10]	–8.375	2.085	0.04425	–12.47	–8.381	–4.207	50,001	100,000
treat.mean.diff[3,11]	–0.6964	1.413	0.025	–3.48	–0.6962	2.101	50,001	100,000
treat.mean.diff[3,12]	–8.818	2.498	0.05483	–13.73	–8.806	–3.848	50,001	100,000

TABLE 114 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[3,13]	–8.439	2.477	0.04285	–13.47	–8.4	–3.502	50,001	100,000
treat.mean.diff[3,14]	0.05968	1.528	0.0269	–3.238	0.01872	3.303	50,001	100,000
treat.mean.diff[3,15]	5.743	1.812	0.02962	2.273	5.698	9.405	50,001	100,000
treat.mean.diff[4,5]	0.6465	1.14	0.02204	–1.226	0.3928	3.394	50,001	100,000
treat.mean.diff[4,6]	1.136	1.944	0.04714	–1.374	0.5156	6.365	50,001	100,000
treat.mean.diff[4,7]	0.5769	1.558	0.03087	–2.189	0.24	4.473	50,001	100,000
treat.mean.diff[4,8]	1.121	1.692	0.02782	–2.14	1.081	4.632	50,001	100,000
treat.mean.diff[4,9]	–0.1964	1.813	0.03407	–3.689	–0.2383	3.494	50,001	100,000
treat.mean.diff[4,10]	–7.941	1.858	0.04794	–11.5	–7.995	–4.206	50,001	100,000
treat.mean.diff[4,11]	–0.2629	1.804	0.04362	–3.538	–0.3853	3.639	50,001	100,000
treat.mean.diff[4,12]	–8.385	2.298	0.05613	–12.94	–8.403	–3.759	50,001	100,000
treat.mean.diff[4,13]	–8.005	2.195	0.0387	–12.36	–7.983	–3.628	50,001	100,000
treat.mean.diff[4,14]	0.4932	1.107	0.02017	–1.358	0.2504	3.153	50,001	100,000
treat.mean.diff[4,15]	6.177	1.97	0.04435	2.515	6.081	10.36	50,001	100,000
treat.mean.diff[5,6]	0.4895	1.708	0.03427	–2.301	0.1156	5.021	50,001	100,000
treat.mean.diff[5,7]	–0.06957	1.463	0.02327	–3.284	–0.02529	3.131	50,001	100,000
treat.mean.diff[5,8]	0.4744	1.39	0.01956	–2.333	0.4868	3.177	50,001	100,000
treat.mean.diff[5,9]	–0.8429	1.7	0.02827	–4.188	–0.834	2.518	50,001	100,000
treat.mean.diff[5,10]	–8.588	1.872	0.04338	–12.34	–8.598	–4.862	50,001	100,000
treat.mean.diff[5,11]	–0.9094	1.761	0.0377	–4.336	–0.9386	2.646	50,001	100,000
treat.mean.diff[5,12]	–9.031	2.325	0.05383	–13.77	–9.029	–4.414	50,001	100,000
treat.mean.diff[5,13]	–8.652	2.21	0.03778	–13.1	–8.625	–4.289	50,001	100,000
treat.mean.diff[5,14]	–0.1533	0.8776	0.01126	–2.036	–0.06866	1.617	50,001	100,000
treat.mean.diff[5,15]	5.53	1.963	0.03868	1.663	5.47	9.495	50,001	100,000
treat.mean.diff[6,7]	–0.559	1.947	0.03412	–5.537	–0.1474	2.741	50,001	100,000
treat.mean.diff[6,8]	–0.01503	2.163	0.04166	–4.997	0.178	3.768	50,001	100,000
treat.mean.diff[6,9]	–1.332	2.291	0.04468	–6.485	–1.177	2.757	50,001	100,000
treat.mean.diff[6,10]	–9.077	2.281	0.05002	–13.99	–8.955	–4.8	50,001	100,000
treat.mean.diff[6,11]	–1.399	1.721	0.03463	–5.105	–1.283	1.726	50,001	100,000
treat.mean.diff[6,12]	–9.521	2.677	0.0606	–15.06	–9.402	–4.468	50,001	100,000
treat.mean.diff[6,13]	–9.141	2.662	0.05178	–14.85	–9.002	–4.184	50,001	100,000
treat.mean.diff[6,14]	–0.6428	1.768	0.03724	–5.344	–0.2007	2.104	50,001	100,000
treat.mean.diff[6,15]	5.041	2.089	0.03947	0.7185	5.109	8.958	50,001	100,000
treat.mean.diff[7,8]	0.544	1.983	0.03284	–3.508	0.5492	4.486	50,001	100,000
treat.mean.diff[7,9]	–0.7733	2.131	0.03768	–5.113	–0.7453	3.389	50,001	100,000
treat.mean.diff[7,10]	–8.518	2.207	0.05009	–12.94	–8.523	–4.154	50,001	100,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 114 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[7,11]	–0.8399	2.024	0.0397	–4.941	–0.8563	3.252	50,001	100,000
treat.mean.diff[7,12]	–8.962	2.606	0.05965	–14.2	–8.937	–3.861	50,001	100,000
treat.mean.diff[7,13]	–8.582	2.506	0.04391	–13.64	–8.573	–3.58	50,001	100,000
treat.mean.diff[7,14]	–0.08376	1.496	0.02316	–3.474	–0.01512	3.063	50,001	100,000
treat.mean.diff[7,15]	5.6	2.232	0.04279	1.03	5.56	10.09	50,001	100,000
treat.mean.diff[8,9]	–1.317	1.645	0.02532	–4.541	–1.319	1.944	50,001	100,000
treat.mean.diff[8,10]	–9.062	2.129	0.04457	–13.15	–9.064	–4.827	50,001	100,000
treat.mean.diff[8,11]	–1.384	2.151	0.03957	–5.588	–1.387	2.924	50,001	100,000
treat.mean.diff[8,12]	–9.506	2.52	0.0536	–14.52	–9.486	–4.519	50,001	100,000
treat.mean.diff[8,13]	–9.126	2.363	0.03643	–13.85	–9.098	–4.476	50,001	100,000
treat.mean.diff[8,14]	–0.6278	1.588	0.0237	–3.819	–0.6289	2.551	50,001	100,000
treat.mean.diff[8,15]	5.056	2.304	0.0404	0.6046	5.021	9.779	50,001	100,000
treat.mean.diff[9,10]	–7.745	1.937	0.03849	–11.47	–7.768	–3.863	50,001	100,000
treat.mean.diff[9,11]	–0.06652	2.247	0.04401	–4.412	–0.07668	4.391	50,001	100,000
treat.mean.diff[9,12]	–8.188	2.369	0.04925	–12.86	–8.214	–3.489	50,001	100,000
treat.mean.diff[9,13]	–7.809	2.119	0.03235	–12.02	–7.798	–3.656	50,001	100,000
treat.mean.diff[9,14]	0.6896	1.772	0.02976	–2.805	0.6723	4.18	50,001	100,000
treat.mean.diff[9,15]	6.373	2.334	0.04407	1.879	6.35	11.12	50,001	100,000
treat.mean.diff[10,11]	7.678	2.142	0.04823	3.483	7.676	11.91	50,001	100,000
treat.mean.diff[10,12]	–0.4437	1.39	0.02557	–3.137	–0.472	2.314	50,001	100,000
treat.mean.diff[10,13]	–0.0644	2.231	0.04198	–4.457	–0.09329	4.256	50,001	100,000
treat.mean.diff[10,14]	8.434	1.879	0.04381	4.725	8.445	12.12	50,001	100,000
treat.mean.diff[10,15]	14.12	2.108	0.04427	10.07	14.1	18.22	50,001	100,000
treat.mean.diff[11,12]	–8.122	2.542	0.05765	–13.14	–8.119	–3.13	50,001	100,000
treat.mean.diff[11,13]	–7.743	2.583	0.04772	–12.93	–7.699	–2.677	50,001	100,000
treat.mean.diff[11,14]	0.7561	1.794	0.04019	–2.931	0.7941	4.193	50,001	100,000
treat.mean.diff[11,15]	6.44	1.4	0.01987	3.792	6.404	9.349	50,001	100,000
treat.mean.diff[12,13]	0.3793	2.612	0.05047	–4.818	0.3555	5.518	50,001	100,000
treat.mean.diff[12,14]	8.878	2.324	0.05373	4.27	8.853	13.55	50,001	100,000
treat.mean.diff[12,15]	14.56	2.518	0.05403	9.674	14.52	19.51	50,001	100,000
treat.mean.diff[13,14]	8.499	2.213	0.03778	4.126	8.485	12.94	50,001	100,000
treat.mean.diff[13,15]	14.18	2.643	0.04615	9.044	14.14	19.53	50,001	100,000
treat.mean.diff[14,15]	5.684	1.997	0.04124	1.801	5.616	9.757	50,001	100,000

Median ranks

TABLE 115 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	8.137	0.6112	0.01187	7	8	10	50,001	100,000
rk.class[2]	9.508	0.7976	0.01363	8	10	10	50,001	100,000
rk.class[3]	5.739	0.9598	0.01586	4	6	7	50,001	100,000
rk.class[4]	6.292	1.061	0.01519	4	7	8	50,001	100,000
rk.class[5]	5.078	1.096	0.01975	4	5	7	50,001	100,000
rk.class[6]	2.151	0.6964	0.01172	1	2	3	50,001	100,000
rk.class[7]	5.029	1.128	0.02361	4	5	7	50,001	100,000
rk.class[8]	1.817	0.8127	0.01454	1	2	3	50,001	100,000
rk.class[9]	2.042	0.9115	0.01683	1	2	3	50,001	100,000
rk.class[10]	9.207	0.6445	0.009085	8	9	10	50,001	100,000

TABLE 116 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	13	0.8523	0.01843	11	13	15	50,001	100,000
rk[2]	14.45	1.038	0.01616	12	15	15	50,001	100,000
rk[3]	8.025	2.379	0.03519	4	8	12	50,001	100,000
rk[4]	7.033	2.123	0.042	4	7	11	50,001	100,000
rk[5]	8.577	1.988	0.02899	5	9	12	50,001	100,000
rk[6]	9.308	2.443	0.04107	5	10	13	50,001	100,000
rk[7]	8.341	2.554	0.04085	4	8	13	50,001	100,000
rk[8]	9.542	2.724	0.04309	4	10	13	50,001	100,000
rk[9]	6.822	2.859	0.05316	4	6	12	50,001	100,000
rk[10]	2.153	0.7003	0.01172	1	2	3	50,001	100,000
rk[11]	6.548	2.704	0.06183	4	5	12	50,001	100,000
rk[12]	1.82	0.8264	0.01462	1	2	3	50,001	100,000
rk[13]	2.047	0.9274	0.01687	1	2	3	50,001	100,000
rk[14]	8.16	2.132	0.03462	4	8	12	50,001	100,000
rk[15]	14.17	0.7426	0.01001	13	14	15	50,001	100,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Adults: clinical effectiveness (Yale–Brown Obsessive–Compulsive Scale) – sensitivity analysis 4 (post hoc), excluding studies that have used a waitlist as control

This is a post-hoc analysis.

TABLE 117 Raw data used

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
Albert *et al.*, 2002[155]	18.36	25	7.11	17.3	40	6.15	NA	NA	NA	NA	NA	NA	2	2	7	8	NA	NA
Andersson *et al.*, 2012[158]	12.94	49	6.26	18.88	51	4.18	NA	NA	NA	NA	NA	NA	2	2	10	16	NA	NA
Bisserbe *et al.*, 1997[162]	–14.3	86	NA	–11.71	81	NA	NA	NA	NA	NA	NA	NA	2	1	5	8	NA	NA
Belloch *et al.*, 2008[159]	8.31	13	8.75	6.8	16	3.55	NA	NA	NA	NA	NA	NA	2	2	9	11	NA	NA
Belotto-Silva *et al.*, 2012[160]	20.29	88	8.05	19.97	70	8.48	NA	NA	NA	NA	NA	NA	2	2	2	10	NA	NA
Bergeron *et al.*, 2002[161]	–9.7	72	7.7	–9.6	76	7.9	NA	NA	NA	NA	NA	NA	2	1	2	5	NA	NA
CCSG1, 1991[154]	25.11	108	6.34	16.23	102	7.37	NA	NA	NA	NA	NA	NA	2	2	1	8	NA	NA
CCSG2, 1991[154]	25.59	119	5.78	14.7	120	7.45	NA	NA	NA	NA	NA	NA	2	2	1	8	NA	NA
Chouinard *et al.*, 1990[163]	–1.48	44	NA	–3.79	43	NA	NA	NA	NA	NA	NA	NA	2	1	1	5	NA	NA
Cottraux *et al.*, 2001[166]	–12.1	30	7.8	–12.5	30	8.2	NA	NA	NA	NA	NA	NA	2	1	9	11	NA	NA
Denys *et al.*, 2003[167]	–7.8	72	5.4	–7.2	73	7.5	NA	NA	NA	NA	NA	NA	2	1	4	7	NA	NA
Fals-Stewart *et al.*, 1993[170]	–8.1	31	NA	–1.8	32	NA	NA	NA	NA	NA	NA	NA	2	1	9	16	NA	NA
Foa *et al.*, 2005[171]	22.2	26	6.4	18.2	36	7.8	11	29	7.9	10.5	31	8.2	4	2	1	8	9	14
Freeman *et al.*, 1994[172]	–8.6	28	NA	–7.8	19	NA	NA	NA	NA	NA	NA	NA	2	1	3	8	NA	NA
GlaxoSmithKline, 2005[174]	–4.61	75	7.53	–5.61	79	7.47	–7.73	78	7.42	NA	NA	NA	3	1	1	4	8	NA
GlaxoSmithKline, 2005[175]	–14.26	72	6.33	–13.19	69	6.48	NA	NA	NA	NA	NA	NA	2	1	4	8	NA	NA
Goodman *et al.*, 1989[176]	28	21	7	19.4	21	7	NA	NA	NA	NA	NA	NA	2	2	1	3	NA	NA

TABLE 117 Raw data used (*continued*)

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
Goodman *et al.*, 1996[177]	–1.71	78	4.88	–3.95	78	6.28	NA	NA	NA	NA	NA	NA	2	1	1	3	NA	NA
Greist *et al.*, 1995[126]	–3.41	84	6.19	–5.57	240	6.19	NA	NA	NA	NA	NA	NA	2	1	1	5	NA	NA
Greist *et al.*, 2002[178]	17.6	55	6.2	24.1	66	6.7	NA	NA	NA	NA	NA	NA	2	2	9	16	NA	NA
Hollander *et al.*, 2003[180]	–5.6	120	7.67	–8.5	117	7.57	NA	NA	NA	NA	NA	NA	2	1	1	3	NA	NA
Hollander *et al.*, 2003[181]	–3.33	89	NA	–4.14	88	NA	–6.35	86	NA	–7.34	85	NA	4	1	1	4	4	4
Jenike *et al.*, 1990[183]	22.3	9	7.8	20.6	10	9.2	NA	NA	NA	NA	NA	NA	2	2	1	5	NA	NA
Jenike *et al.*, 1990[184]	21.8	20	7.6	18.8	18	4	NA	NA	NA	NA	NA	NA	2	2	1	3	NA	NA
Jenike *et al.*, 1997[185]	18.7	18	6.1	16.2	19	6.3	NA	NA	NA	NA	NA	NA	2	2	1	2	NA	NA
Kamijima *et al.*, 2004[187]	20.3	94	7.38	15.8	94	8.09	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
Kobak *et al.*, 2005[189]	19.87	30	7.46	19.75	30	7.46	NA	NA	NA	NA	NA	NA	2	2	1	12	NA	NA
Koran *et al.*, 1996[190]	17.8	34	7.7	17	39	8.55	NA	NA	NA	NA	NA	NA	2	2	3	8	NA	NA
Kronig *et al.*, 1999[191]	–4.14	79	NA	–8.5	85	NA	NA	NA	NA	NA	NA	NA	2	1	1	5	NA	NA
Lindsay *et al.*, 1997[192]	11	9	3.81	25.89	9	5.8	NA	NA	NA	NA	NA	NA	2	2	9	16	NA	NA
López-Ibor *et al.*, 1996[193]	–7.5	30	9.29	–8.9	24	7.13	NA	NA	NA	NA	NA	NA	2	1	2	8	NA	NA
McLean *et al.*, 2001[195]	16.1	31	6.7	13.2	32	7.2	NA	NA	NA	NA	NA	NA	2	2	11	9	NA	NA
Milanfranchi *et al.*, 1997[196]	18.4	13	9.2	16.5	12	11	NA	NA	NA	NA	NA	NA	2	2	3	8	NA	NA
Montgomery *et al.*, 1993[197]	–3.7	56	5.98	–5.13	52	6.41	–4.76	52	6.89	–6.07	54	6.92	4	1	1	2	2	2
Montgomery *et al.*, 2001[198]	–5.6	101	6.9	–8.4	102	7.3	–8.9	98	7	–10.4	100	6.9	4	1	1	6	6	6
Mundo *et al.*, 1997[199]	16.2	10	8.9	21.6	9	7.6	19.8	11	10.1	NA	NA	NA	3	2	3	4	6	NA
Mundo *et al.*, 2001[200]	–12.2	115	NA	–12	112	NA	NA	NA	NA	NA	NA	NA	2	1	3	8	NA	NA
Nakajima *et al.*, 1996[201]	–1.9	33	7.2	–7.1	60	7.03	NA	NA	NA	NA	NA	NA	2	1	1	3	NA	NA
Nakatani *et al.*, 2005[202]	20.2	10	9.4	12.9	10	4.9	28.4	8	5.5	NA	NA	NA	3	2	3	9	16	NA
O'Connor *et al.*, 2006[203]	25.4	10	3.5	24	11	4.7	NA	NA	NA	NA	NA	NA	2	2	1	3	NA	NA

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 117 Raw data used (*continued*)

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
Shareh *et al.*, 2010[206]	16.66	6	3.2	7	7	2.38	8.5	6	2.42	NA	NA	NA	3	2	3	10	13	NA
Sousa *et al.*, 2006[207]	–7.36	25	NA	–10.8	25	NA	NA	NA	NA	NA	NA	NA	2	1	5	10	NA	NA
Stein *et al.*, 2007[124]	–8.46	113	8.08	–11.67	116	8.40	–11.43	112	8.25	–12.14	114	8.22	4	1	1	4	15	15
Tollefson *et al.*, 1994[127]	–0.8	89	5.66	–5.44	266	7.88	NA	NA	NA	NA	NA	NA	2	1	1	2	NA	NA
Van Oppen *et al.*, 1995[209]	17.9	29	9	13.4	28	9.4	NA	NA	NA	NA	NA	NA	2	2	9	11	NA	NA
Whittal *et al.*, 2005[211]	10.41	29	7.6	10.6	30	7.1	NA	NA	NA	NA	NA	NA	2	2	9	11	NA	NA
Whittal *et al.*, 2010[212]	6.43	37	4.77	9.1	30	6.48	NA	NA	NA	NA	NA	NA	2	2	11	16	NA	NA
Zohar and Judge, 1996[213]	–4.2	99	7.2	–6.4	201	7.1	–7	99	6.8	NA	NA	NA	3	1	1	4	8	NA

CCSG, Clomipramine Collaborative Study Group; NA, not applicable.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

Key

1. Placebo (1).
2. Fluoxetine (2).
3. Fluvoxamine (2).
4. Paroxetine (2).
5. Sertraline (2).
6. Citalopram (2).
7. Venlafaxine (3).
8. Clomipramine (4).
9. BT (5).
10. CBT (6).
11. CT (7).
12. Hypericum (8).
13. Fluvoxamine + CBT (9).
14. BT + clomipramine (10).
15. Escitalopram (2).
16. Psychological placebo (11).

TABLE 118 Class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
D[2]	–3.619	0.6562	0.008122	–4.889	–3.616	–2.341	72,201	140,000
D[3]	–3.211	1.965	0.01096	–7.068	–3.222	0.6873	72,201	140,000
D[4]	–4.665	0.8162	0.00625	–6.264	–4.668	–3.046	72,201	140,000
D[5]	–10.41	1.854	0.02225	–14.04	–10.41	–6.774	72,201	140,000
D[6]	–7.981	1.544	0.01264	–11.02	–7.982	–4.93	72,201	140,000
D[7]	–9.452	2.179	0.02475	–13.76	–9.447	–5.195	72,201	140,000
D[8]	–0.1281	2.957	0.01417	–5.932	–0.125	5.678	72,201	140,000
D[9]	–8.808	2.5	0.01532	–13.75	–8.8	–3.879	72,201	140,000
D[10]	–11.68	2.565	0.01434	–16.73	–11.68	–6.655	72,201	140,000
D[11]	–1.896	1.923	0.02168	–5.621	–1.901	1.908	72,201	140,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 119 Individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
d[2]	–3.668	0.7231	0.008129	–5.126	–3.655	–2.26	72,201	140,000
d[3]	–3.658	0.6577	0.007807	–4.964	–3.648	–2.375	72,201	140,000
d[4]	–3.513	0.6774	0.007931	–4.809	–3.528	–2.137	72,201	140,000
d[5]	–3.684	0.717	0.007973	–5.141	–3.67	–2.296	72,201	140,000
d[6]	–3.602	0.83	0.008281	–5.251	–3.606	–1.906	72,201	140,000
d[7]	–3.211	1.965	0.01096	–7.068	–3.222	0.6873	72,201	140,000
d[8]	–4.665	0.8162	0.00625	–6.264	–4.668	–3.046	72,201	140,000
d[9]	–10.41	1.854	0.02225	–14.04	–10.41	–6.774	72,201	140,000
d[10]	–7.981	1.544	0.01264	–11.02	–7.982	–4.93	72,201	140,000
d[11]	–9.452	2.179	0.02475	–13.76	–9.447	–5.195	72,201	140,000
d[12]	–0.1281	2.957	0.01417	–5.932	–0.125	5.678	72,201	140,000
d[13]	–8.808	2.5	0.01532	–13.75	–8.8	–3.879	72,201	140,000
d[14]	–11.68	2.565	0.01434	–16.73	–11.68	–6.655	72,201	140,000
d[15]	–3.593	0.8384	0.008388	–5.247	–3.598	–1.861	72,201	140,000
d[16]	–1.896	1.923	0.02168	–5.621	–1.901	1.908	72,201	140,000

Please note that these figures can be directly compared with those in *Table 20* using the correct key for the treatment. For example, the posterior MD for BT (treatment #9 in this table) is –10.41 (95% CrI –14.04 to –6.77) and this compares with a MD of –14.48 (95% CrI –18.61 to –10.23) in *Table 20*.

Median ranks

TABLE 120 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	10.31	0.661	0.003972	9	10	11	72,201	140,000
rk.class[2]	7.593	0.8419	0.004448	6	8	9	72,201	140,000
rk.class[3]	7.828	1.488	0.007127	5	8	11	72,201	140,000
rk.class[4]	6.379	0.7793	0.003608	5	6	8	72,201	140,000
rk.class[5]	2.299	0.959	0.00593	1	2	4	72,201	140,000
rk.class[6]	4.237	1.006	0.004598	2	4	6	72,201	140,000
rk.class[7]	3.263	1.244	0.008831	1	3	5	72,201	140,000
rk.class[8]	9.763	1.565	0.007451	6	10	11	72,201	140,000
rk.class[9]	3.587	1.605	0.007865	1	4	7	72,201	140,000
rk.class[10]	1.861	1.25	0.005406	1	1	5	72,201	140,000
rk.class[11]	8.882	1.297	0.01203	6	9	11	72,201	140,000

TABLE 121 Individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	15.31	0.6624	0.003989	14	15	16	72,201	140,000
rk[2]	9.917	2.111	0.007922	6	10	14	72,201	140,000
rk[3]	9.955	2.012	0.007881	6	10	14	72,201	140,000
rk[4]	10.49	1.975	0.007702	7	11	14	72,201	140,000
rk[5]	9.856	2.095	0.007831	6	10	14	72,201	140,000
rk[6]	10.12	2.242	0.008465	6	10	14	72,201	140,000
rk[7]	10.74	3.543	0.01511	5	12	16	72,201	140,000
rk[8]	6.998	1.73	0.007727	5	6	12	72,201	140,000
rk[9]	2.301	0.9668	0.006013	1	2	4	72,201	140,000
rk[10]	4.254	1.063	0.004597	2	4	6	72,201	140,000
rk[11]	3.288	1.35	0.00982	1	3	6	72,201	140,000
rk[12]	14.14	2.944	0.01332	6	15	16	72,201	140,000
rk[13]	3.684	1.935	0.008808	1	4	8	72,201	140,000
rk[14]	1.868	1.287	0.00547	1	1	5	72,201	140,000
rk[15]	10.14	2.236	0.008085	6	10	14	72,201	140,000
rk[16]	12.94	2.84	0.02645	6	14	16	72,201	140,000

Please note these figures can be directly compared with those in *Table 20* using the correct key for the treatment.
For example, the posterior median rank for BT (treatment #9 in this table) is 2 (95% CrI 1 to 4) and this compares with a median rank of 1 (95% CrI 1 to 3) in *Table 20*.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Adults: acceptability (dropouts) – sensitivity analysis 1 (low overall attrition)

See *Table 28* for a summary.

TABLE 122 Raw data used

Study	r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	r[,4]	n[,4]	na[]	t[,1]	t[,2]	t[,3]	t[,4]
Ananth *et al.* 1981[156]	1	10	2	10	NA	NA	NA	NA	2	9	13	NA	NA
Anderson and Rees, 2007[157]	3	17	4	21	NA	NA	NA	NA	2	2	11	NA	NA
Andersson *et al.*, 2012[158]	2	50	0	51	NA	NA	NA	NA	2	11	16	NA	NA
Belloch *et al.*, 2008[159]	2	15	2	18	NA	NA	NA	NA	2	10	12	NA	NA
Belotto-Silva *et al.*, 2012[160]	33	88	18	70	NA	NA	NA	NA	2	3	11	NA	NA
CCSG1, 1991[154]	13	121	17	118	NA	NA	NA	NA	2	1	9	NA	NA
CCSG2, 1991[154]	12	139	14	142	NA	NA	NA	NA	2	1	9	NA	NA
Chouinard *et al.*, 1990[163]	4	44	6	43	NA	NA	NA	NA	2	1	6	NA	NA
Cordioli *et al.*, 2003[164]	1	24	1	23	NA	NA	NA	NA	2	2	11	NA	NA
Cottraux *et al.*, 2001[166]	3	33	2	32	NA	NA	NA	NA	2	10	12	NA	NA
Denys *et al.*, 2003[167]	9	75	4	75	NA	NA	NA	NA	2	5	8	NA	NA
Emmelkamp *et al.*, 1988[169]	1	10	1	10	NA	NA	NA	NA	2	10	12	NA	NA
Fals-Stewart *et al.*, 1993[170]	3	34	0	32	NA	NA	NA	NA	2	10	16	NA	NA
Freeston *et al.*, 1997[173]	0	14	3	15	NA	NA	NA	NA	2	2	11	NA	NA
GlaxoSmithKline, 2005[175]	1	73	4	73	NA	NA	NA	NA	2	5	9	NA	NA
Goodman *et al.*, 1996[177]	17	80	23	80	NA	NA	NA	NA	2	1	4	NA	NA
Greist *et al.*, 2002[178]	14	69	9	75	NA	NA	NA	NA	2	10	16	NA	NA
Hollander *et al.*, 2003[180]	31	126	43	127	NA	NA	NA	NA	2	1	4	NA	NA
Hollander *et al.*, 2003[181]	15	89	14	88	20	86	19	85	4	1	5	5	5
Jenike *et al.*, 1990[184]	0	20	2	20	NA	NA	NA	NA	2	1	4	NA	NA
Jenike *et al.*, 1997[185]	3	21	4	23	NA	NA	NA	NA	2	1	3	NA	NA
Jones and Menzies, 1998[186]	1	11	1	12	NA	NA	NA	NA	2	2	12	NA	NA
Kobak *et al.*, 2005[189]	9	30	8	30	NA	NA	NA	NA	2	1	17	NA	NA

TABLE 122 Raw data used (*continued*)

Study	r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	r[,4]	n[,4]	na[]	t[,1]	t[,2]	t[,3]	t[,4]
López-Ibor *et al.*, 1996[193]	5	30	3	25	NA	NA	NA	NA	2	3	9	NA	NA
McLean *et al.*, 2001[195]	12	44	18	49	NA	NA	NA	NA	2	10	12	NA	NA
Milanfranchi *et al.*, 1997[196]	0	13	1	13	NA	NA	NA	NA	2	4	9	NA	NA
Montgomery *et al.*, 1993[197]	15	57	14	53	13	52	14	55	4	1	3	3	3
Montgomery *et al.*, 2001[198]	17	101	15	100	15	98	16	102	4	1	7	7	7
Mundo *et al.*, 2001[200]	19	115	26	112	NA	NA	NA	NA	2	4	9	NA	NA
Nakatani *et al.*, 2005[202]	1	11	1	11	1	9	NA	NA	3	4	10	16	NA
O'Connor *et al.*, 1999[203]	0	6	1	7	NA	NA	NA	NA	2	2	11	NA	NA
Perse *et al.*, 1987[205]	2	10	2	10	NA	NA	NA	NA	2	1	4	NA	NA
Shareh *et al.*, 2010[206]	1	7	0	7	1	7	NA	NA	3	4	11	14	NA
Sousa *et al.*, 2006[207]	3	28	3	28	NA	NA	NA	NA	2	6	11	NA	NA
Stein *et al.*, 2007[124]	16	115	29	119	24	116	21	116	4	1	5	15	15
Tollefson *et al.*, 1994[127]	13	89	12	87	22	89	22	90	4	1	3	3	3
Van Oppen *et al.*, 1995[209]	7	36	7	35	NA	NA	NA	NA	2	10	12	NA	NA
Volavka *et al.*, 1985[210]	3	11	4	12	NA	NA	NA	NA	2	9	18	NA	NA
Whittal *et al.*, 2005[211]	13	42	11	41	NA	NA	NA	NA	2	10	12	NA	NA
Whittal *et al.*, 2010[212]	3	40	3	33	NA	NA	NA	NA	2	12	16	NA	NA

CCSG, Clomipramine Collaborative Study Group; NA, not available.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Key: intervention

1. Placebo (1).
2. Waitlist (2).
3. Fluoxetine (3).
4. Fluvoxamine (3).
5. Paroxetine (3).
6. Sertraline (3).
7. Citalopram (3).
8. Venlafaxine (4).
9. Clomipramine (5).
10. BT (6).
11. CBT (7).
12. CT (8).
13. Amitriptyline (9).
14. CBT + fluvoxamine (10).
15. Escitalopram (3).
16. Psychological placebo (11).
17. Hypericum (12).
18. Imipramine (13).

TABLE 123 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[1,2]	0.4606	0.3501	0.01443	0.08904	0.3605	1.427	60,001	120,000
OR.D[1,3]	1.302	0.5778	0.005701	0.9421	1.284	1.726	60,001	120,000
OR.D[1,4]	0.6364	0.4778	0.01466	0.1053	0.5162	1.844	60,001	120,000
OR.D[1,5]	1.639	0.389	0.0117	1.039	1.584	2.588	60,001	120,000
OR.D[1,6]	0.6941	0.7862	0.03535	0.04697	0.441	2.772	60,001	120,000
OR.D[1,7]	0.8902	0.3111	0.0109	0.4249	0.8389	1.623	60,001	120,000
OR.D[1,8]	0.6763	0.773	0.03433	0.05704	0.4481	2.699	60,001	120,000
OR.D[1,9]	21.37	93.67	2.768	0.2314	3.94	162.7	60,001	120,000
OR.D[1,10]	13.73	153.6	3.737	0.06158	1.936	79.68	60,001	120,000
OR.D[1,11]	0.371	0.4034	0.01803	0.02338	0.244	1.463	60,001	120,000
OR.D[1,12]	1.001	0.6832	0.01939	0.2341	0.825	2.914	60,001	120,000
OR.D[1,13]	3.569	4.944	0.1543	0.2675	2.05	15.9	60,001	120,000
OR.D[2,3]	4.455	4.03	0.1474	0.9014	3.545	14.27	60,001	120,000
OR.D[2,4]	2.197	2.781	0.08812	0.1703	1.383	9.484	60,001	120,000
OR.D[2,5]	5.704	5.164	0.2038	1.073	4.326	18.4	60,001	120,000
OR.D[2,6]	2.033	2.669	0.1063	0.1405	1.197	8.662	60,001	120,000
OR.D[2,7]	2.756	1.927	0.07397	0.7092	2.258	8.006	60,001	120,000
OR.D[2,8]	1.982	2.625	0.1042	0.1675	1.155	8.94	60,001	120,000

TABLE 123 Class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[2,9]	63.9	294.6	7.505	0.4477	11.69	446.1	60,001	120,000
OR.D[2,10]	57.78	656.4	18.21	0.1507	5.399	223.4	60,001	120,000
OR.D[2,11]	1.086	1.332	0.05339	0.07371	0.6644	4.877	60,001	120,000
OR.D[2,12]	3.482	4.569	0.1517	0.4019	2.181	14.26	60,001	120,000
OR.D[2,13]	12.08	19.77	0.6272	0.5223	5.667	66.09	60,001	120,000
OR.D[3,4]	0.4951	0.3906	0.0112	0.08368	0.4031	1.472	60,001	120,000
OR.D[3,5]	1.287	0.4541	0.01003	0.7809	1.23	2.132	60,001	120,000
OR.D[3,6]	0.5391	0.6117	0.02709	0.0379	0.3446	2.155	60,001	120,000
OR.D[3,7]	0.6934	0.2743	0.007734	0.3377	0.6553	1.251	60,001	120,000
OR.D[3,8]	0.5248	0.6027	0.02624	0.04514	0.3496	2.17	60,001	120,000
OR.D[3,9]	16.58	71.88	2.044	0.1758	3.1	132.5	60,001	120,000
OR.D[3,10]	10.97	124.1	3.095	0.04991	1.508	62.93	60,001	120,000
OR.D[3,11]	0.2879	0.3122	0.01373	0.01926	0.1913	1.117	60,001	120,000
OR.D[3,12]	0.7896	0.567	0.01591	0.1776	0.6382	2.362	60,001	120,000
OR.D[3,13]	2.803	4.134	0.1232	0.2114	1.603	12.64	60,001	120,000
OR.D[4,5]	4.285	4.116	0.13	0.8094	3.101	15.29	60,001	120,000
OR.D[4,6]	1.825	2.953	0.1114	0.06651	0.8913	9.311	60,001	120,000
OR.D[4,7]	2.344	2.488	0.07862	0.3828	1.623	8.663	60,001	120,000
OR.D[4,8]	1.778	2.949	0.1098	0.06723	0.8737	9.341	60,001	120,000
OR.D[4,9]	54.1	250	7.15	0.3928	7.709	437.8	60,001	120,000
OR.D[4,10]	38.58	467.8	10.23	0.1029	3.557	226.3	60,001	120,000
OR.D[4,11]	0.9715	1.567	0.05868	0.03401	0.4878	4.693	60,001	120,000
OR.D[4,12]	2.707	3.643	0.1184	0.2615	1.635	12.61	60,001	120,000
OR.D[4,13]	9.49	19.25	0.6017	0.3936	4.032	53.97	60,001	120,000
OR.D[5,6]	0.4444	0.5035	0.02233	0.02804	0.2835	1.882	60,001	120,000
OR.D[5,7]	0.5686	0.2302	0.007678	0.239	0.5306	1.114	60,001	120,000
OR.D[5,8]	0.4333	0.5018	0.02191	0.03094	0.2805	1.759	60,001	120,000
OR.D[5,9]	13.6	61.38	1.756	0.1445	2.417	105.6	60,001	120,000
OR.D[5,10]	8.955	98.02	2.421	0.03736	1.17	54.48	60,001	120,000
OR.D[5,11]	0.2376	0.2609	0.01146	0.01275	0.1516	0.9647	60,001	120,000
OR.D[5,12]	0.6426	0.4697	0.01298	0.1333	0.5216	1.873	60,001	120,000
OR.D[5,13]	2.139	2.853	0.08707	0.1799	1.305	9.181	60,001	120,000
OR.D[6,7]	3.074	4.322	0.2128	0.3113	1.847	14.04	60,001	120,000
OR.D[6,8]	1.008	0.276	0.008877	0.5775	0.9644	1.685	60,001	120,000
OR.D[6,9]	55.97	262	7.207	0.3638	8.582	383.7	60,001	120,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 123 Class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[6,10]	37.52	470.2	11.27	0.09105	4.489	194	60,001	120,000
OR.D[6,11]	0.5831	0.2309	0.007426	0.2459	0.5486	1.149	60,001	120,000
OR.D[6,12]	3.557	6.237	0.2474	0.1934	1.878	17.05	60,001	120,000
OR.D[6,13]	16.09	45.9	2.105	0.3054	4.402	121.9	60,001	120,000
OR.D[7,8]	0.7888	0.9077	0.03755	0.0783	0.5294	2.995	60,001	120,000
OR.D[7,9]	26.38	112.3	3.388	0.2515	4.747	189.2	60,001	120,000
OR.D[7,10]	17.54	206.1	4.953	0.07379	2.26	92.65	60,001	120,000
OR.D[7,11]	0.4352	0.478	0.02037	0.03298	0.2954	1.739	60,001	120,000
OR.D[7,12]	1.259	1.006	0.02827	0.2463	0.969	3.995	60,001	120,000
OR.D[7,13]	4.393	6.19	0.1776	0.2817	2.437	20.19	60,001	120,000
OR.D[8,9]	58.61	362.6	8.542	0.3793	9.009	409.6	60,001	120,000
OR.D[8,10]	40.73	655.4	14.48	0.09474	4.631	193	60,001	120,000
OR.D[8,11]	0.6139	0.2895	0.009711	0.235	0.5527	1.364	60,001	120,000
OR.D[8,12]	3.634	6.27	0.2406	0.2045	1.937	16.93	60,001	120,000
OR.D[8,13]	15.06	36.71	1.509	0.3086	4.474	119.3	60,001	120,000
OR.D[9,10]	5.53	39.52	0.9571	0.003667	0.4567	44.15	60,001	120,000
OR.D[9,11]	0.2245	0.5699	0.02051	0.001242	0.06062	1.593	60,001	120,000
OR.D[9,12]	0.7359	2.279	0.08093	0.005101	0.1999	4.611	60,001	120,000
OR.D[9,13]	2.564	9.984	0.3729	0.01042	0.4719	17.31	60,001	120,000
OR.D[10,11]	0.8251	3.825	0.1046	0.00282	0.1198	5.837	60,001	120,000
OR.D[10,12]	3.228	37.11	0.9332	0.01088	0.4266	14.55	60,001	120,000
OR.D[10,13]	11.66	192.3	3.894	0.01944	1.045	59.85	60,001	120,000
OR.D[11,12]	6.769	12	0.4891	0.3975	3.357	35.34	60,001	120,000
OR.D[11,13]	29.51	82.34	3.567	0.5747	7.942	243.2	60,001	120,000
OR.D[12,13]	5.49	10.53	0.3723	0.2458	2.469	32.39	60,001	120,000

TABLE 124 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[1,2]	0.4606	0.3501	0.01443	0.08904	0.3605	1.427	60,001	120,000
OR[1,3]	1.338	0.23	0.007745	0.9537	1.316	1.874	60,001	120,000
OR[1,4]	1.325	0.2049	0.006246	0.9793	1.309	1.76	60,001	120,000
OR[1,5]	1.361	0.2378	0.006944	0.9756	1.336	1.901	60,001	120,000
OR[1,6]	1.31	0.2954	0.007809	0.8018	1.279	1.972	60,001	120,000
OR[1,7]	1.222	0.2357	0.006839	0.7468	1.224	1.672	60,001	120,000
OR[1,8]	0.6364	0.4778	0.01466	0.1053	0.5162	1.844	60,001	120,000
OR[1,9]	1.639	0.389	0.0117	1.039	1.584	2.588	60,001	120,000
OR[1,10]	0.6941	0.7862	0.03535	0.04697	0.441	2.772	60,001	120,000
OR[1,11]	0.8902	0.3111	0.0109	0.4249	0.8389	1.623	60,001	120,000
OR[1,12]	0.6763	0.773	0.03433	0.05704	0.4481	2.699	60,001	120,000
OR[1,13]	21.37	93.67	2.768	0.2314	3.94	162.7	60,001	120,000
OR[1,14]	13.73	153.6	3.737	0.06158	1.936	79.68	60,001	120,000
OR[1,15]	1.281	0.2332	0.006379	0.878	1.265	1.795	60,001	120,000
OR[1,16]	0.371	0.4034	0.01803	0.02338	0.244	1.463	60,001	120,000
OR[1,17]	1.001	0.6832	0.01939	0.2341	0.825	2.914	60,001	120,000
OR[1,18]	3.569	4.944	0.1543	0.2675	2.05	15.9	60,001	120,000
OR[2,3]	4.535	3.746	0.1472	0.9427	3.642	14.33	60,001	120,000
OR[2,4]	4.557	3.911	0.1555	0.9225	3.604	14.98	60,001	120,000
OR[2,5]	4.672	4.012	0.157	0.9489	3.659	15.04	60,001	120,000
OR[2,6]	4.503	4.001	0.1537	0.8925	3.537	15.34	60,001	120,000
OR[2,7]	4.175	3.561	0.1368	0.8044	3.323	13.4	60,001	120,000
OR[2,8]	2.197	2.781	0.08812	0.1703	1.383	9.484	60,001	120,000
OR[2,9]	5.704	5.164	0.2038	1.073	4.326	18.4	60,001	120,000
OR[2,10]	2.033	2.669	0.1063	0.1405	1.197	8.662	60,001	120,000
OR[2,11]	2.756	1.927	0.07397	0.7092	2.258	8.006	60,001	120,000
OR[2,12]	1.982	2.625	0.1042	0.1675	1.155	8.94	60,001	120,000
OR[2,13]	63.9	294.6	7.505	0.4477	11.69	446.1	60,001	120,000
OR[2,14]	57.78	656.4	18.21	0.1507	5.399	223.4	60,001	120,000
OR[2,15]	4.389	3.735	0.1444	0.8639	3.497	14.32	60,001	120,000
OR[2,16]	1.086	1.332	0.05339	0.07371	0.6644	4.877	60,001	120,000
OR[2,17]	3.482	4.569	0.1517	0.4019	2.181	14.26	60,001	120,000
OR[2,18]	12.08	19.77	0.6272	0.5223	5.667	66.09	60,001	120,000
OR[3,4]	1.007	0.1715	0.004519	0.6857	0.9984	1.409	60,001	120,000
OR[3,5]	1.034	0.195	0.005247	0.6817	1.006	1.522	60,001	120,000
OR[3,6]	0.9938	0.2267	0.005706	0.5629	0.993	1.539	60,001	120,000
OR[3,7]	0.9296	0.191	0.005216	0.4989	0.9628	1.292	60,001	120,000
OR[3,8]	0.481	0.3614	0.01066	0.08211	0.3942	1.418	60,001	120,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 124 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[3,9]	1.253	0.3481	0.01095	0.7396	1.207	2.032	60,001	120,000
OR[3,10]	0.5243	0.5968	0.02639	0.03664	0.3399	2.07	60,001	120,000
OR[3,11]	0.6685	0.2146	0.006749	0.3502	0.6374	1.17	60,001	120,000
OR[3,12]	0.5101	0.5863	0.02546	0.04024	0.343	2.073	60,001	120,000
OR[3,13]	16.42	72.74	2.059	0.1734	2.999	133.2	60,001	120,000
OR[3,14]	10.93	124.9	3.106	0.04764	1.444	64.07	60,001	120,000
OR[3,15]	0.9728	0.1811	0.004307	0.6006	0.9846	1.378	60,001	120,000
OR[3,16]	0.2794	0.3017	0.01329	0.01756	0.1876	1.066	60,001	120,000
OR[3,17]	0.7725	0.5588	0.01624	0.1732	0.6238	2.326	60,001	120,000
OR[3,18]	2.725	3.754	0.119	0.2046	1.568	12.24	60,001	120,000
OR[4,5]	1.04	0.1851	0.004175	0.7257	1.008	1.519	60,001	120,000
OR[4,6]	0.9987	0.2174	0.004848	0.5927	0.9933	1.526	60,001	120,000
OR[4,7]	0.9345	0.1836	0.004833	0.5292	0.964	1.312	60,001	120,000
OR[4,8]	0.4881	0.3765	0.01151	0.08158	0.3935	1.493	60,001	120,000
OR[4,9]	1.254	0.309	0.008943	0.7896	1.209	1.985	60,001	120,000
OR[4,10]	0.5274	0.5936	0.02646	0.03597	0.3396	2.098	60,001	120,000
OR[4,11]	0.6807	0.2425	0.008035	0.3265	0.6393	1.234	60,001	120,000
OR[4,12]	0.5136	0.582	0.02564	0.04066	0.3445	2.115	60,001	120,000
OR[4,13]	16.35	69.19	2.013	0.1728	3.009	132.8	60,001	120,000
OR[4,14]	10.72	118.9	2.998	0.04838	1.447	61.97	60,001	120,000
OR[4,15]	0.9791	0.1807	0.004128	0.637	0.9842	1.408	60,001	120,000
OR[4,16]	0.2818	0.3034	0.01341	0.01743	0.1898	1.093	60,001	120,000
OR[4,17]	0.7761	0.5589	0.0163	0.1644	0.6268	2.395	60,001	120,000
OR[4,18]	2.719	3.716	0.1167	0.2096	1.582	11.92	60,001	120,000
OR[5,6]	0.9767	0.2187	0.004774	0.5448	0.9825	1.484	60,001	120,000
OR[5,7]	0.9141	0.1865	0.004695	0.4873	0.9492	1.26	60,001	120,000
OR[5,8]	0.4677	0.3404	0.01036	0.0822	0.3879	1.358	60,001	120,000
OR[5,9]	1.231	0.3318	0.009517	0.7223	1.177	2.023	60,001	120,000
OR[5,10]	0.5186	0.5976	0.02638	0.03615	0.3292	2.094	60,001	120,000
OR[5,11]	0.6658	0.2411	0.007683	0.3142	0.6253	1.23	60,001	120,000
OR[5,12]	0.5051	0.5922	0.02574	0.04422	0.3302	2.083	60,001	120,000
OR[5,13]	16.03	71.8	1.987	0.1715	2.959	130.4	60,001	120,000
OR[5,14]	10.56	117.2	2.956	0.04809	1.426	61.86	60,001	120,000
OR[5,15]	0.953	0.1584	0.003553	0.6321	0.9693	1.296	60,001	120,000
OR[5,16]	0.2773	0.3066	0.01344	0.01786	0.1819	1.115	60,001	120,000
OR[5,17]	0.7562	0.5426	0.01551	0.1654	0.6113	2.296	60,001	120,000
OR[5,18]	2.693	3.755	0.1195	0.1985	1.542	12.09	60,001	120,000
OR[6,7]	0.9652	0.2306	0.005611	0.4897	0.9798	1.465	60,001	120,000
OR[6,8]	0.5048	0.3955	0.01208	0.08244	0.4028	1.552	60,001	120,000

TABLE 124 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[6,9]	1.308	0.4288	0.01178	0.7103	1.236	2.365	60,001	120,000
OR[6,10]	0.5458	0.6266	0.02732	0.03707	0.3446	2.157	60,001	120,000
OR[6,11]	0.7041	0.2758	0.008852	0.3121	0.6567	1.343	60,001	120,000
OR[6,12]	0.5317	0.6163	0.02655	0.04695	0.3458	2.212	60,001	120,000
OR[6,13]	16.76	73.57	2.06	0.1745	3.127	128.8	60,001	120,000
OR[6,14]	10.93	122.7	3.062	0.05071	1.504	62.55	60,001	120,000
OR[6,15]	1.014	0.2603	0.005967	0.586	0.9945	1.63	60,001	120,000
OR[6,16]	0.2918	0.3188	0.01384	0.01922	0.1913	1.155	60,001	120,000
OR[6,17]	0.8007	0.5925	0.01636	0.1752	0.6381	2.444	60,001	120,000
OR[6,18]	2.841	3.933	0.1263	0.2084	1.595	12.91	60,001	120,000
OR[7,8]	0.5383	0.4246	0.01233	0.0867	0.4241	1.649	60,001	120,000
OR[7,9]	1.395	0.4565	0.0139	0.8077	1.295	2.6	60,001	120,000
OR[7,10]	0.5839	0.67	0.02938	0.0424	0.3661	2.397	60,001	120,000
OR[7,11]	0.7506	0.2931	0.009336	0.3527	0.6948	1.449	60,001	120,000
OR[7,12]	0.5688	0.6636	0.02858	0.0535	0.3705	2.348	60,001	120,000
OR[7,13]	17.57	76.02	2.141	0.1826	3.355	132.3	60,001	120,000
OR[7,14]	11.64	134.1	3.27	0.05443	1.656	65.3	60,001	120,000
OR[7,15]	1.079	0.2661	0.00615	0.7005	1.016	1.797	60,001	120,000
OR[7,16]	0.3115	0.3437	0.01492	0.02298	0.2047	1.219	60,001	120,000
OR[7,17]	0.8511	0.6209	0.01708	0.1888	0.6856	2.547	60,001	120,000
OR[7,18]	3.05	4.215	0.1368	0.2239	1.714	14.33	60,001	120,000
OR[8,9]	4.285	4.116	0.13	0.8094	3.101	15.29	60,001	120,000
OR[8,10]	1.825	2.953	0.1114	0.06651	0.8913	9.311	60,001	120,000
OR[8,11]	2.344	2.488	0.07862	0.3828	1.623	8.663	60,001	120,000
OR[8,12]	1.778	2.949	0.1098	0.06723	0.8737	9.341	60,001	120,000
OR[8,13]	54.1	250	7.15	0.3928	7.709	437.8	60,001	120,000
OR[8,14]	38.58	467.8	10.23	0.1029	3.557	226.3	60,001	120,000
OR[8,15]	3.366	3.382	0.1159	0.6569	2.438	11.92	60,001	120,000
OR[8,16]	0.9715	1.567	0.05868	0.03401	0.4878	4.693	60,001	120,000
OR[8,17]	2.707	3.643	0.1184	0.2615	1.635	12.61	60,001	120,000
OR[8,18]	9.49	19.25	0.6017	0.3936	4.032	53.97	60,001	120,000
OR[9,10]	0.4444	0.5035	0.02233	0.02804	0.2835	1.882	60,001	120,000
OR[9,11]	0.5686	0.2302	0.007678	0.239	0.5306	1.114	60,001	120,000
OR[9,12]	0.4333	0.5018	0.02191	0.03094	0.2805	1.759	60,001	120,000
OR[9,13]	13.6	61.38	1.756	0.1445	2.417	105.6	60,001	120,000
OR[9,14]	8.955	98.02	2.421	0.03736	1.17	54.48	60,001	120,000
OR[9,15]	0.8194	0.2235	0.006122	0.4373	0.795	1.327	60,001	120,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 124 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[9,16]	0.2376	0.2609	0.01146	0.01275	0.1516	0.9647	60,001	120,000
OR[9,17]	0.6426	0.4697	0.01298	0.1333	0.5216	1.873	60,001	120,000
OR[9,18]	2.139	2.853	0.08707	0.1799	1.305	9.181	60,001	120,000
OR[10,11]	3.074	4.322	0.2128	0.3113	1.847	14.04	60,001	120,000
OR[10,12]	1.008	0.276	0.008877	0.5775	0.9644	1.685	60,001	120,000
OR[10,13]	55.97	262	7.207	0.3638	8.582	383.7	60,001	120,000
OR[10,14]	37.52	470.2	11.27	0.09105	4.489	194	60,001	120,000
OR[10,15]	4.669	6.306	0.3041	0.4554	2.871	26.53	60,001	120,000
OR[10,16]	0.5831	0.2309	0.007426	0.2459	0.5486	1.149	60,001	120,000
OR[10,17]	3.557	6.237	0.2474	0.1934	1.878	17.05	60,001	120,000
OR[10,18]	16.09	45.9	2.105	0.3054	4.402	121.9	60,001	120,000
OR[11,12]	0.7888	0.9077	0.03755	0.0783	0.5294	2.995	60,001	120,000
OR[11,13]	26.38	112.3	3.388	0.2515	4.747	189.2	60,001	120,000
OR[11,14]	17.54	206.1	4.953	0.07379	2.26	92.65	60,001	120,000
OR[11,15]	1.599	0.5897	0.01878	0.7501	1.502	3.001	60,001	120,000
OR[11,16]	0.4352	0.478	0.02037	0.03298	0.2954	1.739	60,001	120,000
OR[11,17]	1.259	1.006	0.02827	0.2463	0.969	3.995	60,001	120,000
OR[11,18]	4.393	6.19	0.1776	0.2817	2.437	20.19	60,001	120,000
OR[12,13]	58.61	362.6	8.542	0.3793	9.009	409.6	60,001	120,000
OR[12,14]	40.73	655.4	14.48	0.09474	4.631	193	60,001	120,000
OR[12,15]	4.685	5.933	0.2691	0.4509	2.817	20.32	60,001	120,000
OR[12,16]	0.6139	0.2895	0.009711	0.235	0.5527	1.364	60,001	120,000
OR[12,17]	3.634	6.27	0.2406	0.2045	1.937	16.93	60,001	120,000
OR[12,18]	15.06	36.71	1.509	0.3086	4.474	119.3	60,001	120,000
OR[13,14]	5.53	39.52	0.9571	0.003667	0.4567	44.15	60,001	120,000
OR[13,15]	0.9641	2.463	0.1004	0.007295	0.3162	5.661	60,001	120,000
OR[13,16]	0.2245	0.5699	0.02051	0.001242	0.06062	1.593	60,001	120,000
OR[13,17]	0.7359	2.279	0.08093	0.005101	0.1999	4.611	60,001	120,000
OR[13,18]	2.564	9.984	0.3729	0.01042	0.4719	17.31	60,001	120,000
OR[14,15]	4.573	61.1	1.488	0.01533	0.6399	20.1	60,001	120,000
OR[14,16]	0.8251	3.825	0.1046	0.00282	0.1198	5.837	60,001	120,000
OR[14,17]	3.228	37.11	0.9332	0.01088	0.4266	14.55	60,001	120,000
OR[14,18]	11.66	192.3	3.894	0.01944	1.045	59.85	60,001	120,000
OR[15,16]	0.2941	0.3242	0.01412	0.02061	0.194	1.15	60,001	120,000
OR[15,17]	0.8049	0.5781	0.01617	0.1844	0.6472	2.337	60,001	120,000
OR[15,18]	2.859	3.935	0.1259	0.2136	1.645	13.11	60,001	120,000
OR[16,17]	6.769	12	0.4891	0.3975	3.357	35.34	60,001	120,000
OR[16,18]	29.51	82.34	3.567	0.5747	7.942	243.2	60,001	120,000
OR[17,18]	5.49	10.53	0.3723	0.2458	2.469	32.39	60,001	120,000

Median ranks

TABLE 125 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	7.457	1.605	0.06546	4	8	10	60,001	120,000
rk.class[2]	3.591	2.242	0.08864	1	3	9	60,001	120,000
rk.class[3]	9.338	1.524	0.05377	6	9	12	60,001	120,000
rk.class[4]	4.774	2.818	0.09714	1	5	11	60,001	120,000
rk.class[5]	10.43	1.414	0.05074	7	11	13	60,001	120,000
rk.class[6]	4.989	2.772	0.1259	2	4	12	60,001	120,000
rk.class[7]	6.753	1.942	0.06629	3	7	11	60,001	120,000
rk.class[8]	4.741	2.78	0.1243	1	4	12	60,001	120,000
rk.class[9]	10.93	3.089	0.1193	2	12	13	60,001	120,000
rk.class[10]	8.913	4.313	0.1881	1	11	13	60,001	120,000
rk.class[11]	2.372	1.863	0.07739	1	2	8	60,001	120,000
rk.class[12]	6.763	2.945	0.09328	1	7	12	60,001	120,000
rk.class[13]	9.952	3.188	0.1145	2	11	13	60,001	120,000

TABLE 126 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	7.887	1.915	0.07426	4	8	12	60,001	120,000
rk[2]	3.761	2.776	0.1071	1	3	13	60,001	120,000
rk[3]	12.22	2.477	0.06913	7	12	17	60,001	120,000
rk[4]	12.11	2.432	0.06942	7	12	16	60,001	120,000
rk[5]	12.52	2.476	0.06783	7	13	17	60,001	120,000
rk[6]	11.73	2.851	0.07212	6	12	17	60,001	120,000
rk[7]	10.79	2.817	0.07826	5	11	16	60,001	120,000
rk[8]	5.227	3.785	0.1255	1	5	16	60,001	120,000
rk[9]	14.39	2.566	0.07931	8	15	18	60,001	120,000
rk[10]	5.667	4.145	0.1894	2	4	17	60,001	120,000
rk[11]	7.337	2.8	0.08787	3	7	15	60,001	120,000
rk[12]	5.38	4.108	0.1849	1	4	16	60,001	120,000
rk[13]	14.78	4.979	0.1917	2	17	18	60,001	120,000
rk[14]	11.89	6.55	0.2844	1	16	18	60,001	120,000
rk[15]	11.47	2.615	0.06606	6	11	16	60,001	120,000
rk[16]	2.55	2.49	0.1019	1	2	11	60,001	120,000
rk[17]	7.968	4.593	0.1354	1	7	17	60,001	120,000
rk[18]	13.32	5.238	0.1872	2	16	18	60,001	120,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Adults: acceptability (dropouts) – sensitivity analysis 2 (incomplete outcome data)

See *Table 29* for a summary.

TABLE 127 Raw data used

Study	r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	r[,4]	n[,4]	na[]	t[,1]	t[,2]	t[,3]	t[,4]
Anderson and Rees, 2007[157]	3	17	4	21	NA	NA	NA	NA	2	2	11	NA	NA
Andersson *et al.*, 2012[158]	2	50	0	51	NA	NA	NA	NA	2	11	14	NA	NA
Belotto-Silva *et al.*, 2012[160]	33	88	18	70	NA	NA	NA	NA	2	3	11	NA	NA
Bergeron *et al.*, 2002[161]	22	73	22	77	NA	NA	NA	NA	2	3	6	NA	NA
Bisserbe *et al.*, 1997[162]	23	86	35	82	NA	NA	NA	NA	2	6	9	NA	NA
Chouinard *et al.*, 1990[163]	4	44	6	43	NA	NA	NA	NA	2	1	6	NA	NA
Cordioli *et al.*, 2003[164]	1	24	1	23	NA	NA	NA	NA	2	2	11	NA	NA
Denys *et al.*, 2003[167]	9	75	4	75	NA	NA	NA	NA	2	5	8	NA	NA
Foa *et al.*, 2005[171]	12	32	20	47	16	37	14	33	4	1	9	10	12
Freeman *et al.*, 1994[172]	6	34	13	32	NA	NA	NA	NA	2	4	9	NA	NA
Freeston *et al.*, 1997[173]	0	14	3	15	NA	NA	NA	NA	2	2	11	NA	NA
GlaxoSmithKline, 2005[174]	20	77	28	82	28	82	NA	NA	3	1	5	9	NA
Goodman *et al.*, 1989[176]	6	23	2	23	NA	NA	NA	NA	2	1	4	NA	NA
Goodman *et al.*, 1996[177]	17	80	23	80	NA	NA	NA	NA	2	1	4	NA	NA
Greist *et al.*, 2002[178]	14	69	9	75	NA	NA	NA	NA	2	10	14	NA	NA
Hollander *et al.*, 2003[180]	31	126	43	127	NA	NA	NA	NA	2	1	4	NA	NA
Hollander *et al.*, 2003[181]	15	89	14	88	20	86	19	85	4	1	5	5	5
Jenike *et al.*, 1997[185]	3	21	4	23	NA	NA	NA	NA	2	1	3	NA	NA
Kobak *et al.*, 2005[189]	9	30	8	30	NA	NA	NA	NA	2	1	15	NA	NA
Koran *et al.*, 1996[190]	8	37	15	42	NA	NA	NA	NA	2	4	9	NA	NA
Kronig *et al.*, 1999[191]	25	81	25	86	NA	NA	NA	NA	2	1	6	NA	NA

TABLE 127 Raw data used (*continued*)

Study	r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	r[,4]	n[,4]	na[]	t[,1]	t[,2]	t[,3]	t[,4]
López-Ibor *et al.*, 1996[193]	5	30	3	25	NA	NA	NA	NA	2	3	9	NA	NA
Montgomery *et al.*, 1993[197]	15	57	14	53	13	52	14	55	4	1	3	3	3
Montgomery *et al.*, 2001[198]	17	101	15	100	15	98	16	102	4	1	7	7	7
Mundo *et al.*, 2001[200]	19	115	26	112	NA	NA	NA	NA	2	4	9	NA	NA
Sousa *et al.*, 2006[207]	3	28	3	28	NA	NA	NA	NA	2	6	11	NA	NA
Stein *et al.*, 2007[124]	16	115	29	119	24	116	21	116	4	1	5	13	13
Tollefson *et al.*, 1994[127]	13	89	12	87	22	89	22	90	4	1	3	3	3
Zohar and Judge, 1996[213]	40	100	53	205	36	101	NA	NA	3	1	5	9	NA

NA, not available.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

Key: intervention

1. Placebo (1).
2. Waitlist (2).
3. Fluoxetine (3).
4. Fluvoxamine (3).
5. Paroxetine (3).
6. Sertraline (3).
7. Citalopram (3).
8. Venlafaxine (4).
9. Clomipramine (5).
10. BT (6).
11. CBT (7).
12. BT + clomipramine (8).
13. Escitalopram (3).
14. Psychological placebo (9).
15. Hypericum (10).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 128 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[1,2]	0.5368	0.4823	0.01184	0.08188	0.3911	1.806	60,001	120,000
OR.D[1,3]	1.107	0.1536	0.002988	0.8368	1.098	1.435	60,001	120,000
OR.D[1,4]	0.5482	0.4165	0.007525	0.1029	0.4439	1.609	60,001	120,000
OR.D[1,5]	1.578	0.2737	0.004665	1.105	1.554	2.175	60,001	120,000
OR.D[1,6]	1.349	0.6253	0.01276	0.5019	1.227	2.91	60,001	120,000
OR.D[1,7]	0.8623	0.3524	0.0076	0.3689	0.8054	1.729	60,001	120,000
OR.D[1,8]	1.499	0.7573	0.01471	0.5177	1.335	3.386	60,001	120,000
OR.D[1,9]	0.6353	0.4454	0.009881	0.1439	0.5159	1.824	60,001	120,000
OR.D[1,10]	1.033	0.7204	0.01341	0.2466	0.8391	2.896	60,001	120,000
OR.D[2,3]	3.815	3.673	0.09655	0.6073	2.788	13.19	60,001	120,000
OR.D[2,4]	1.869	2.563	0.0522	0.1416	1.115	8.087	60,001	120,000
OR.D[2,5]	5.456	5.307	0.1369	0.8413	3.947	19.32	60,001	120,000
OR.D[2,6]	4.58	5.203	0.123	0.5442	3.133	17.44	60,001	120,000
OR.D[2,7]	2.586	2.153	0.05721	0.5407	2.029	8.078	60,001	120,000
OR.D[2,8]	5.132	5.82	0.1341	0.5515	3.441	20.35	60,001	120,000
OR.D[2,9]	2.14	2.932	0.07268	0.1828	1.331	8.937	60,001	120,000
OR.D[2,10]	3.588	4.987	0.1072	0.3084	2.14	15.8	60,001	120,000
OR.D[3,4]	0.4992	0.377	0.006642	0.09421	0.4054	1.454	60,001	120,000
OR.D[3,5]	1.439	0.2575	0.003114	1.001	1.419	2.002	60,001	120,000
OR.D[3,6]	1.234	0.5833	0.01131	0.4517	1.122	2.671	60,001	120,000
OR.D[3,7]	0.7845	0.3168	0.006195	0.3418	0.7308	1.563	60,001	120,000
OR.D[3,8]	1.373	0.711	0.01355	0.4659	1.219	3.129	60,001	120,000
OR.D[3,9]	0.582	0.4177	0.009214	0.1306	0.4704	1.69	60,001	120,000
OR.D[3,10]	0.9491	0.6783	0.01254	0.2175	0.7669	2.715	60,001	120,000
OR.D[4,5]	4.676	4.245	0.07812	0.9583	3.507	15.3	60,001	120,000
OR.D[4,6]	4.001	4.251	0.07371	0.5536	2.785	14.51	60,001	120,000
OR.D[4,7]	2.559	2.626	0.04798	0.4166	1.785	9.203	60,001	120,000
OR.D[4,8]	4.444	4.824	0.08092	0.6143	3.099	16.47	60,001	120,000
OR.D[4,9]	1.876	2.358	0.04325	0.1961	1.195	7.612	60,001	120,000
OR.D[4,10]	3.051	4.041	0.06462	0.3062	1.987	12.39	60,001	120,000
OR.D[5,6]	0.8661	0.3962	0.00754	0.3192	0.7938	1.839	60,001	120,000
OR.D[5,7]	0.559	0.2404	0.004717	0.2273	0.5175	1.143	60,001	120,000
OR.D[5,8]	0.9636	0.4861	0.009502	0.3366	0.8614	2.165	60,001	120,000
OR.D[5,9]	0.4083	0.2862	0.006212	0.09316	0.3321	1.166	60,001	120,000
OR.D[5,10]	0.673	0.4854	0.008825	0.1504	0.5407	1.922	60,001	120,000
OR.D[6,7]	0.7694	0.4893	0.009361	0.2154	0.6592	2.02	60,001	120,000
OR.D[6,8]	1.262	0.7268	0.01311	0.3817	1.095	3.066	60,001	120,000

TABLE 128 Class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[6,9]	0.4793	0.2494	0.004438	0.1582	0.425	1.107	60,001	120,000
OR.D[6,10]	0.9297	0.8433	0.01443	0.1532	0.6931	3.107	60,001	120,000
OR.D[7,8]	2.018	1.363	0.02948	0.5075	1.673	5.575	60,001	120,000
OR.D[7,9]	0.8405	0.7029	0.01594	0.1544	0.6413	2.658	60,001	120,000
OR.D[7,10]	1.391	1.216	0.02328	0.2467	1.06	4.459	60,001	120,000
OR.D[8,9]	0.505	0.4269	0.009518	0.09524	0.3845	1.649	60,001	120,000
OR.D[8,10]	0.8652	0.8256	0.01346	0.1305	0.6307	2.967	60,001	120,000
OR.D[9,10]	2.438	2.821	0.04791	0.2808	1.604	9.457	60,001	120,000

TABLE 129 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[1,2]	0.5368	0.4823	0.01184	0.08188	0.3911	1.806	60,001	120,000
OR[1,3]	1.169	0.1838	0.003938	0.8761	1.146	1.592	60,001	120,000
OR[1,4]	1.097	0.1559	0.002968	0.808	1.092	1.434	60,001	120,000
OR[1,5]	1.132	0.1558	0.003222	0.8646	1.121	1.48	60,001	120,000
OR[1,6]	1.071	0.1659	0.003257	0.7602	1.067	1.423	60,001	120,000
OR[1,7]	1.082	0.19	0.003507	0.7187	1.077	1.49	60,001	120,000
OR[1,8]	0.5482	0.4165	0.007525	0.1029	0.4439	1.609	60,001	120,000
OR[1,9]	1.578	0.2737	0.004665	1.105	1.554	2.175	60,001	120,000
OR[1,10]	1.349	0.6253	0.01276	0.5019	1.227	2.91	60,001	120,000
OR[1,11]	0.8623	0.3524	0.0076	0.3689	0.8054	1.729	60,001	120,000
OR[1,12]	1.499	0.7573	0.01471	0.5177	1.335	3.386	60,001	120,000
OR[1,13]	1.11	0.1839	0.003213	0.7808	1.099	1.517	60,001	120,000
OR[1,14]	0.6353	0.4454	0.009881	0.1439	0.5159	1.824	60,001	120,000
OR[1,15]	1.033	0.7204	0.01341	0.2466	0.8391	2.896	60,001	120,000
OR[2,3]	3.991	3.791	0.09895	0.6527	2.937	13.81	60,001	120,000
OR[2,4]	3.794	3.701	0.097	0.5932	2.773	13.15	60,001	120,000
OR[2,5]	3.905	3.762	0.09781	0.6172	2.862	13.56	60,001	120,000
OR[2,6]	3.692	3.59	0.09489	0.5807	2.662	12.9	60,001	120,000
OR[2,7]	3.739	3.647	0.09542	0.5739	2.678	13.1	60,001	120,000
OR[2,8]	1.869	2.563	0.0522	0.1416	1.115	8.087	60,001	120,000
OR[2,9]	5.456	5.307	0.1369	0.8413	3.947	19.32	60,001	120,000
OR[2,10]	4.58	5.203	0.123	0.5442	3.133	17.44	60,001	120,000
OR[2,11]	2.586	2.153	0.05721	0.5407	2.029	8.078	60,001	120,000
OR[2,12]	5.132	5.82	0.1341	0.5515	3.441	20.35	60,001	120,000
OR[2,13]	3.832	3.737	0.09732	0.5977	2.802	13.37	60,001	120,000
OR[2,14]	2.14	2.932	0.07268	0.1828	1.331	8.937	60,001	120,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 129 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[2,15]	3.588	4.987	0.1072	0.3084	2.14	15.8	60,001	120,000
OR[3,4]	0.9513	0.1428	0.001887	0.6309	0.9736	1.231	60,001	120,000
OR[3,5]	0.9816	0.1408	0.001805	0.6889	0.9904	1.287	60,001	120,000
OR[3,6]	0.9279	0.1403	0.002183	0.6145	0.9568	1.183	60,001	120,000
OR[3,7]	0.9381	0.166	0.002505	0.5664	0.969	1.254	60,001	120,000
OR[3,8]	0.475	0.3604	0.006235	0.08722	0.3866	1.368	60,001	120,000
OR[3,9]	1.371	0.2641	0.004059	0.8972	1.355	1.933	60,001	120,000
OR[3,10]	1.175	0.5591	0.01119	0.4245	1.065	2.573	60,001	120,000
OR[3,11]	0.7401	0.2838	0.005498	0.3331	0.6928	1.429	60,001	120,000
OR[3,12]	1.308	0.6796	0.01321	0.4356	1.159	2.983	60,001	120,000
OR[3,13]	0.9621	0.1596	0.002065	0.6226	0.9799	1.296	60,001	120,000
OR[3,14]	0.5536	0.3971	0.008822	0.1239	0.4479	1.616	60,001	120,000
OR[3,15]	0.9016	0.6488	0.01197	0.2064	0.7282	2.592	60,001	120,000
OR[4,5]	1.045	0.1606	0.001942	0.7871	1.012	1.458	60,001	120,000
OR[4,6]	0.9862	0.1509	0.001856	0.6917	0.9905	1.331	60,001	120,000
OR[4,7]	0.9956	0.1725	0.0022	0.6618	0.9961	1.396	60,001	120,000
OR[4,8]	0.5063	0.3878	0.006808	0.09506	0.4095	1.498	60,001	120,000
OR[4,9]	1.454	0.2553	0.003461	1.022	1.431	2.02	60,001	120,000
OR[4,10]	1.247	0.5898	0.01119	0.4577	1.13	2.704	60,001	120,000
OR[4,11]	0.7959	0.3325	0.006539	0.337	0.7346	1.629	60,001	120,000
OR[4,12]	1.387	0.7133	0.01317	0.4674	1.234	3.15	60,001	120,000
OR[4,13]	1.023	0.1789	0.00188	0.7168	1.002	1.463	60,001	120,000
OR[4,14]	0.5875	0.4199	0.008943	0.1324	0.4735	1.7	60,001	120,000
OR[4,15]	0.9589	0.687	0.01226	0.2199	0.7747	2.737	60,001	120,000
OR[5,6]	0.9545	0.143	0.002086	0.6513	0.9749	1.247	60,001	120,000
OR[5,7]	0.9639	0.1642	0.002669	0.5953	0.9834	1.306	60,001	120,000
OR[5,8]	0.4835	0.3548	0.006231	0.09376	0.3971	1.384	60,001	120,000
OR[5,9]	1.406	0.2432	0.00348	0.9812	1.391	1.931	60,001	120,000
OR[5,10]	1.206	0.5681	0.01112	0.4422	1.094	2.618	60,001	120,000
OR[5,11]	0.7681	0.3133	0.006304	0.3297	0.7112	1.549	60,001	120,000
OR[5,12]	1.34	0.6853	0.01281	0.456	1.194	3.065	60,001	120,000
OR[5,13]	0.9871	0.1463	0.00173	0.6905	0.9916	1.323	60,001	120,000
OR[5,14]	0.5689	0.4066	0.008892	0.1267	0.4592	1.653	60,001	120,000
OR[5,15]	0.9261	0.6579	0.01213	0.2148	0.7519	2.654	60,001	120,000
OR[6,7]	1.022	0.1854	0.00209	0.6825	1.003	1.475	60,001	120,000
OR[6,8]	0.5196	0.398	0.006908	0.09647	0.4196	1.524	60,001	120,000
OR[6,9]	1.494	0.2823	0.003616	1.026	1.468	2.14	60,001	120,000
OR[6,10]	1.281	0.6112	0.01176	0.4633	1.166	2.792	60,001	120,000
OR[6,11]	0.8147	0.3334	0.006708	0.3517	0.756	1.641	60,001	120,000
OR[6,12]	1.428	0.7528	0.0149	0.4745	1.261	3.296	60,001	120,000

TABLE 129 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[6,13]	1.051	0.1945	0.002293	0.7376	1.012	1.553	60,001	120,000
OR[6,14]	0.6038	0.4332	0.009467	0.1343	0.4885	1.768	60,001	120,000
OR[6,15]	0.9866	0.7084	0.01321	0.2251	0.7914	2.783	60,001	120,000
OR[7,8]	0.5197	0.4061	0.007301	0.09568	0.4155	1.563	60,001	120,000
OR[7,9]	1.493	0.3328	0.004181	0.968	1.455	2.273	60,001	120,000
OR[7,10]	1.28	0.6299	0.01196	0.4493	1.159	2.853	60,001	120,000
OR[7,11]	0.8157	0.356	0.006692	0.3403	0.7491	1.697	60,001	120,000
OR[7,12]	1.426	0.7698	0.01575	0.4687	1.25	3.443	60,001	120,000
OR[7,13]	1.048	0.22	0.002709	0.7105	1.007	1.594	60,001	120,000
OR[7,14]	0.6042	0.4461	0.009913	0.1318	0.4899	1.769	60,001	120,000
OR[7,15]	0.9865	0.7245	0.01403	0.22	0.7862	2.868	60,001	120,000
OR[8,9]	4.676	4.245	0.07812	0.9583	3.507	15.3	60,001	120,000
OR[8,10]	4.001	4.251	0.07371	0.5536	2.785	14.51	60,001	120,000
OR[8,11]	2.559	2.626	0.04798	0.4166	1.785	9.203	60,001	120,000
OR[8,12]	4.444	4.824	0.08092	0.6143	3.099	16.47	60,001	120,000
OR[8,13]	3.291	2.989	0.05449	0.665	2.462	10.7	60,001	120,000
OR[8,14]	1.876	2.358	0.04325	0.1961	1.195	7.612	60,001	120,000
OR[8,15]	3.051	4.041	0.06462	0.3062	1.987	12.39	60,001	120,000
OR[9,10]	0.8661	0.3962	0.00754	0.3192	0.7938	1.839	60,001	120,000
OR[9,11]	0.559	0.2404	0.004717	0.2273	0.5175	1.143	60,001	120,000
OR[9,12]	0.9636	0.4861	0.009502	0.3366	0.8614	2.165	60,001	120,000
OR[9,13]	0.7191	0.1477	0.001776	0.4735	0.703	1.057	60,001	120,000
OR[9,14]	0.4083	0.2862	0.006212	0.09316	0.3321	1.166	60,001	120,000
OR[9,15]	0.673	0.4854	0.008825	0.1504	0.5407	1.922	60,001	120,000
OR[10,11]	0.7694	0.4893	0.009361	0.2154	0.6592	2.02	60,001	120,000
OR[10,12]	1.262	0.7268	0.01311	0.3817	1.095	3.066	60,001	120,000
OR[10,13]	0.9975	0.4961	0.009793	0.3615	0.8927	2.249	60,001	120,000
OR[10,14]	0.4793	0.2494	0.004438	0.1582	0.425	1.107	60,001	120,000
OR[10,15]	0.9297	0.8433	0.01443	0.1532	0.6931	3.107	60,001	120,000
OR[11,12]	2.018	1.363	0.02948	0.5075	1.673	5.575	60,001	120,000
OR[11,13]	1.483	0.6185	0.01323	0.6176	1.365	3.009	60,001	120,000
OR[11,14]	0.8405	0.7029	0.01594	0.1544	0.6413	2.658	60,001	120,000
OR[11,15]	1.391	1.216	0.02328	0.2467	1.06	4.459	60,001	120,000
OR[12,13]	0.9261	0.4948	0.00824	0.3177	0.8191	2.185	60,001	120,000
OR[12,14]	0.505	0.4269	0.009518	0.09524	0.3845	1.649	60,001	120,000
OR[12,15]	0.8652	0.8256	0.01346	0.1305	0.6307	2.967	60,001	120,000
OR[13,14]	0.586	0.4309	0.009998	0.1292	0.4709	1.713	60,001	120,000
OR[13,15]	0.9556	0.6968	0.0132	0.2162	0.7649	2.795	60,001	120,000
OR[14,15]	2.438	2.821	0.04791	0.2808	1.604	9.457	60,001	120,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Median ranks

TABLE 130 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	5.78	1.344	0.02774	3	6	8	60,001	120,000
rk.class[2]	2.664	2.226	0.05422	1	2	9	60,001	120,000
rk.class[3]	6.692	1.38	0.02303	4	7	9	60,001	120,000
rk.class[4]	2.837	2.135	0.0419	1	2	9	60,001	120,000
rk.class[5]	8.961	1.021	0.01685	7	9	10	60,001	120,000
rk.class[6]	7.226	2.173	0.04225	3	8	10	60,001	120,000
rk.class[7]	4.771	1.969	0.04022	2	4	9	60,001	120,000
rk.class[8]	7.578	2.311	0.04114	3	8	10	60,001	120,000
rk.class[9]	3.207	2.094	0.0453	1	3	9	60,001	120,000
rk.class[10]	5.285	2.857	0.05624	1	5	10	60,001	120,000

TABLE 131 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	7.092	2.338	0.05465	3	7	12	60,001	120,000
rk[2]	3.149	3.453	0.08171	1	2	14	60,001	120,000
rk[3]	10.17	2.411	0.03526	5	10	14	60,001	120,000
rk[4]	8.965	2.477	0.02875	4	9	13	60,001	120,000
rk[5]	9.624	2.378	0.03381	5	10	14	60,001	120,000
rk[6]	8.449	2.552	0.03386	4	8	13	60,001	120,000
rk[7]	8.675	2.786	0.03903	3	9	14	60,001	120,000
rk[8]	3.268	3.238	0.0601	1	2	14	60,001	120,000
rk[9]	13.78	1.326	0.01856	10	14	15	60,001	120,000
rk[10]	10.24	4.218	0.08325	3	12	15	60,001	120,000
rk[11]	5.78	3.485	0.06809	2	5	14	60,001	120,000
rk[12]	10.86	4.307	0.07552	3	13	15	60,001	120,000
rk[13]	9.121	2.662	0.03399	4	9	14	60,001	120,000
rk[14]	3.817	3.428	0.07177	1	3	14	60,001	120,000
rk[15]	7.009	4.923	0.09658	1	5	15	60,001	120,000

Adults/acceptability (dropouts): sensitivity analysis 3 (blinding)

See *Table 30* of the main report for a summary.

TABLE 132 Raw data used

Study	r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	r[,4]	n[,4]	na[]	t[,1]	t[,2]	t[,3]	t[,4]
Albert *et al.*, 2002[155]	1	26	7	47	NA	NA	NA	NA	2	7	8	NA	NA
Andersson *et al.*, 2012[158]	2	50	0	51	NA	NA	NA	NA	2	10	14	NA	NA
Belloch *et al.*, 2008[159]	2	15	2	18	NA	NA	NA	NA	2	9	11	NA	NA
Belotto-Silva *et al.*, 2012[160]	33	88	18	70	NA	NA	NA	NA	2	3	10	NA	NA
Cordioli *et al.*, 2003[164]	1	24	1	23	NA	NA	NA	NA	2	2	10	NA	NA
Cottraux *et al.*, 2001[166]	3	33	2	32	NA	NA	NA	NA	2	9	11	NA	NA
Denys *et al.*, 2003[167]	9	75	4	75	NA	NA	NA	NA	2	5	7	NA	NA
Emmelkamp and Beens, 1991[168]	4	15	5	15	NA	NA	NA	NA	2	9	11	NA	NA
Emmelkamp *et al.*, 1988[169]	1	10	1	10	NA	NA	NA	NA	2	9	11	NA	NA
Foa *et al.*, 2005[171]	12	32	20	47	16	37	14	33	4	1	8	9	12
Goodman *et al.*, 1989[176]	6	23	2	23	NA	NA	NA	NA	2	1	4	NA	NA
Jenike *et al.*, 1990[184]	0	20	2	20	NA	NA	NA	NA	2	1	4	NA	NA
Nakatani *et al.*, 2005[202]	1	11	1	11	1	9	NA	NA	3	4	9	14	NA
O'Connor *et al.*, 1999[203]	0	6	1	7	NA	NA	NA	NA	2	2	10	NA	NA
Perse *et al.*, 1987[205]	2	10	2	10	NA	NA	NA	NA	2	1	4	NA	NA
Sousa *et al.*, 2006[207]	3	28	3	28	NA	NA	NA	NA	2	6	10	NA	NA
Stein *et al.*, 2007[124]	16	115	29	119	24	116	21	116	4	1	5	13	13
Whittal *et al.*, 2005[211]	13	42	11	41	NA	NA	NA	NA	2	9	11	NA	NA

NA, not available.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Key: intervention

1. Placebo (1).
2. Waitlist (2).
3. Fluoxetine (3).
4. Fluvoxamine (3).
5. Paroxetine (3).
6. Sertraline (3).
7. Venlafaxine (4).
8. Clomipramine (5).
9. BT (6).
10. CBT (7).
11. CT (8).
12. BT + clomipramine (9).
13. Escitalopram (3).
14. Psychological placebo (10).

TABLE 133 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[1,2]	152	4922	87.87	0.008968	0.4497	31.84	51,001	100,000
OR.D[1,3]	3979	1.23E+06	3875	0.4603	1.393	8.446	51,001	100,000
OR.D[1,4]	0.6071	0.6553	0.009367	0.1033	0.4765	1.792	51,001	100,000
OR.D[1,5]	1.613	1.243	0.02013	0.4567	1.365	4.242	51,001	100,000
OR.D[1,6]	1.454	0.9819	0.02283	0.389	1.23	3.832	51,001	100,000
OR.D[1,7]	73.75	1239	32.56	0.2699	1.13	32.32	51,001	100,000
OR.D[1,8]	1.401	1.288	0.02571	0.2702	1.102	4.305	51,001	100,000
OR.D[1,9]	1.534	1.585	0.01918	0.3576	1.245	4.265	51,001	100,000
OR.D[1,10]	0.7989	2.118	0.04562	0.01122	0.3155	4.512	51,001	100,000
OR.D[2,3]	32.22	1103	10.24	0.08203	3.185	147.4	51,001	100,000
OR.D[2,4]	11.11	83.76	2.895	0.01178	1.078	63.15	51,001	100,000
OR.D[2,5]	28.7	224	4.765	0.04023	3.027	173.3	51,001	100,000
OR.D[2,6]	23.47	169	3.246	0.0359	2.674	154.7	51,001	100,000
OR.D[2,7]	17.79	105.6	3.952	0.1951	2.643	96.55	51,001	100,000
OR.D[2,8]	22.5	164.5	2.995	0.02847	2.397	154.9	51,001	100,000
OR.D[2,9]	27.55	231.1	4.559	0.03399	2.699	168.1	51,001	100,000
OR.D[2,10]	10	88.01	1.697	0.006203	0.6522	58.37	51,001	100,000
OR.D[3,4]	0.5516	6.26	0.02648	0.03969	0.3283	1.64	51,001	100,000
OR.D[3,5]	1.548	21.95	0.08582	0.1324	0.9603	4.349	51,001	100,000
OR.D[3,6]	1.394	18.9	0.084	0.1135	0.8725	3.93	51,001	100,000
OR.D[3,7]	165.2	17080	104	0.2389	0.8059	10.16	51,001	100,000
OR.D[3,8]	1.339	17.54	0.08425	0.08769	0.7797	4.174	51,001	100,000
OR.D[3,9]	1.51	20.48	0.08574	0.1038	0.879	4.469	51,001	100,000
OR.D[3,10]	0.7554	19.39	0.1018	0.005801	0.2135	3.12	51,001	100,000

TABLE 133 Class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[4,5]	4.067	5.741	0.07591	0.6797	2.888	14.33	51,001	100,000
OR.D[4,6]	3.969	7.597	0.09576	0.5143	2.581	15.37	51,001	100,000
OR.D[4,7]	162.5	5480	72.81	0.3688	2.529	77.18	51,001	100,000
OR.D[4,8]	3.851	10.3	0.1033	0.3951	2.334	15.66	51,001	100,000
OR.D[4,9]	4.291	28.47	0.1184	0.4971	2.638	16.23	51,001	100,000
OR.D[4,10]	2.209	11.24	0.1245	0.01927	0.6745	12.7	51,001	100,000
OR.D[5,6]	1.063	0.8671	0.01063	0.2796	0.9051	2.705	51,001	100,000
OR.D[5,7]	53.63	1217	23.62	0.1463	0.8476	25.91	51,001	100,000
OR.D[5,8]	1.027	1.064	0.01292	0.1933	0.825	3.082	51,001	100,000
OR.D[5,9]	1.174	21.38	0.06714	0.2696	0.9156	3.015	51,001	100,000
OR.D[5,10]	0.6488	2.325	0.03773	0.007115	0.2285	3.77	51,001	100,000
OR.D[6,7]	51.09	980.7	21.95	0.1649	0.9436	28.15	51,001	100,000
OR.D[6,8]	0.9692	0.419	0.006677	0.399	0.8962	1.974	51,001	100,000
OR.D[6,9]	1.261	1.79	0.01434	0.2964	1.01	3.552	51,001	100,000
OR.D[6,10]	0.6732	1.755	0.03503	0.008585	0.2545	3.894	51,001	100,000
OR.D[7,8]	1.511	2.605	0.04271	0.0287	0.9467	6.442	51,001	100,000
OR.D[7,9]	1.693	2.819	0.04429	0.03419	1.07	7.002	51,001	100,000
OR.D[7,10]	0.5852	1.228	0.02428	0.004288	0.2484	3.305	51,001	100,000
OR.D[8,9]	1.557	3.091	0.02495	0.2675	1.11	5.031	51,001	100,000
OR.D[8,10]	0.8188	2.603	0.04028	0.009494	0.2793	4.781	51,001	100,000
OR.D[9,10]	0.7617	3.158	0.04598	0.007292	0.2495	4.548	51,001	100,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 134 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[1,2]	152	4922	87.87	0.008968	0.4497	31.84	51,001	100,000
OR[1,3]	150.8	3586	68.23	0.4545	1.596	47.92	51,001	100,000
OR[1,4]	1.217	0.6273	0.01446	0.3597	1.111	2.71	51,001	100,000
OR[1,5]	1.72	0.8848	0.01686	0.6758	1.553	3.743	51,001	100,000
OR[1,6]	73.78	1696	31.3	0.3077	1.379	31.95	51,001	100,000
OR[1,7]	0.6071	0.6553	0.009367	0.1033	0.4765	1.792	51,001	100,000
OR[1,8]	1.613	1.243	0.02013	0.4567	1.365	4.242	51,001	100,000
OR[1,9]	1.454	0.9819	0.02283	0.389	1.23	3.832	51,001	100,000
OR[1,10]	73.75	1239	32.56	0.2699	1.13	32.32	51,001	100,000
OR[1,11]	1.401	1.288	0.02571	0.2702	1.102	4.305	51,001	100,000
OR[1,12]	1.534	1.585	0.01918	0.3576	1.245	4.265	51,001	100,000
OR[1,13]	1.471	0.689	0.01231	0.6171	1.345	3.052	51,001	100,000
OR[1,14]	0.7989	2.118	0.04562	0.01122	0.3155	4.512	51,001	100,000
OR[2,3]	34.22	264	10.73	0.2374	3.935	156.5	51,001	100,000
OR[2,4]	18.5	134.4	2.619	0.02751	2.502	122.5	51,001	100,000
OR[2,5]	32.51	244.1	9.505	0.05415	3.514	165.2	51,001	100,000
OR[2,6]	23.97	159.1	4.641	0.1471	3.286	138.2	51,001	100,000
OR[2,7]	11.11	83.76	2.895	0.01178	1.078	63.15	51,001	100,000
OR[2,8]	28.7	224	4.765	0.04023	3.027	173.3	51,001	100,000
OR[2,9]	23.47	169	3.246	0.0359	2.674	154.7	51,001	100,000
OR[2,10]	17.79	105.6	3.952	0.1951	2.643	96.55	51,001	100,000
OR[2,11]	22.5	164.5	2.995	0.02847	2.397	154.9	51,001	100,000
OR[2,12]	27.55	231.1	4.559	0.03399	2.699	168.1	51,001	100,000
OR[2,13]	27.22	192.5	7.15	0.04512	3.027	143.9	51,001	100,000
OR[2,14]	10	88.01	1.697	0.006203	0.6522	58.37	51,001	100,000
OR[3,4]	0.7975	0.8508	0.01561	0.01678	0.7818	2.066	51,001	100,000
OR[3,5]	1.117	1.496	0.02527	0.03745	0.9739	3.523	51,001	100,000
OR[3,6]	0.998	1.358	0.01299	0.1535	0.905	2.805	51,001	100,000
OR[3,7]	0.4126	0.6574	0.01098	0.008698	0.2753	1.595	51,001	100,000
OR[3,8]	1.143	1.597	0.02741	0.02543	0.8109	4.296	51,001	100,000
OR[3,9]	1.027	1.388	0.02688	0.02361	0.7378	3.823	51,001	100,000
OR[3,10]	0.7776	0.6861	0.007148	0.2685	0.6659	1.917	51,001	100,000
OR[3,11]	0.9895	1.62	0.02709	0.01931	0.6511	4.049	51,001	100,000
OR[3,12]	1.104	2.034	0.02713	0.02211	0.7441	4.324	51,001	100,000
OR[3,13]	0.9643	1.043	0.02005	0.03015	0.8941	2.856	51,001	100,000
OR[3,14]	0.4151	0.9116	0.01623	0.002788	0.17	2.337	51,001	100,000
OR[4,5]	1.757	1.566	0.03598	0.5864	1.268	5.632	51,001	100,000

TABLE 134 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[4,6]	100.8	3975	44.84	0.3373	1.112	39.76	51,001	100,000
OR[4,7]	0.6237	0.8566	0.01435	0.08239	0.4301	2.36	51,001	100,000
OR[4,8]	1.643	1.742	0.02581	0.324	1.26	5.148	51,001	100,000
OR[4,9]	1.459	1.268	0.02568	0.2825	1.133	4.615	51,001	100,000
OR[4,10]	101.5	2850	47.36	0.2779	0.9784	38.56	51,001	100,000
OR[4,11]	1.41	1.592	0.02855	0.202	1.021	4.845	51,001	100,000
OR[4,12]	1.57	2.265	0.02606	0.2494	1.15	5.256	51,001	100,000
OR[4,13]	1.478	1.2	0.02542	0.5054	1.121	4.393	51,001	100,000
OR[4,14]	0.785	2.859	0.05705	0.01034	0.2822	4.699	51,001	100,000
OR[5,6]	45.35	1173	19.2	0.1867	0.9605	18.74	51,001	100,000
OR[5,7]	0.3742	0.3079	0.004739	0.07501	0.3054	1.066	51,001	100,000
OR[5,8]	1.102	1.129	0.01452	0.2359	0.8748	3.306	51,001	100,000
OR[5,9]	1.003	1.032	0.01642	0.1985	0.7967	3.013	51,001	100,000
OR[5,10]	44.66	887.9	19.56	0.1731	0.7456	17.27	51,001	100,000
OR[5,11]	0.9724	1.31	0.01864	0.1458	0.7106	3.291	51,001	100,000
OR[5,12]	1.07	1.631	0.01582	0.1884	0.7991	3.444	51,001	100,000
OR[5,13]	0.9188	0.4319	0.003572	0.4308	0.8998	1.647	51,001	100,000
OR[5,14]	0.5317	1.788	0.02894	0.0069	0.2026	2.868	51,001	100,000
OR[6,7]	0.5237	1.113	0.01673	0.01317	0.3253	2.155	51,001	100,000
OR[6,8]	1.436	2.266	0.03625	0.04136	0.9614	5.728	51,001	100,000
OR[6,9]	1.29	1.995	0.03352	0.03558	0.8692	5.076	51,001	100,000
OR[6,10]	1.13	1.371	0.02336	0.2315	0.8161	3.98	51,001	100,000
OR[6,11]	1.241	2.215	0.0338	0.03067	0.7737	5.315	51,001	100,000
OR[6,12]	1.398	2.809	0.03729	0.03484	0.8787	5.802	51,001	100,000
OR[6,13]	1.247	1.877	0.03297	0.04378	0.9897	4.4	51,001	100,000
OR[6,14]	0.5442	1.333	0.02444	0.003587	0.2063	3.131	51,001	100,000
OR[7,8]	4.067	5.741	0.07591	0.6797	2.888	14.33	51,001	100,000
OR[7,9]	3.969	7.597	0.09576	0.5143	2.581	15.37	51,001	100,000
OR[7,10]	162.5	5480	72.81	0.3688	2.529	77.18	51,001	100,000
OR[7,11]	3.851	10.3	0.1033	0.3951	2.334	15.66	51,001	100,000
OR[7,12]	4.291	28.47	0.1184	0.4971	2.638	16.23	51,001	100,000
OR[7,13]	3.887	5.254	0.058	0.7515	2.852	12.69	51,001	100,000
OR[7,14]	2.209	11.24	0.1245	0.01927	0.6745	12.7	51,001	100,000
OR[8,9]	1.063	0.8671	0.01063	0.2796	0.9051	2.705	51,001	100,000
OR[8,10]	53.63	1217	23.62	0.1463	0.8476	25.91	51,001	100,000
OR[8,11]	1.027	1.064	0.01292	0.1933	0.825	3.082	51,001	100,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 134 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[8,12]	1.174	21.38	0.06714	0.2696	0.9156	3.015	51,001	100,000
OR[8,13]	1.235	1.519	0.01609	0.2701	0.9917	3.478	51,001	100,000
OR[8,14]	0.6488	2.325	0.03773	0.007115	0.2285	3.77	51,001	100,000
OR[9,10]	51.09	980.7	21.95	0.1649	0.9436	28.15	51,001	100,000
OR[9,11]	0.9692	0.419	0.006677	0.399	0.8962	1.974	51,001	100,000
OR[9,12]	1.261	1.79	0.01434	0.2964	1.01	3.552	51,001	100,000
OR[9,13]	1.413	1.623	0.024	0.2926	1.088	4.286	51,001	100,000
OR[9,14]	0.6732	1.755	0.03503	0.008585	0.2545	3.894	51,001	100,000
OR[10,11]	1.511	2.605	0.04271	0.0287	0.9467	6.442	51,001	100,000
OR[10,12]	1.693	2.819	0.04429	0.03419	1.07	7.002	51,001	100,000
OR[10,13]	1.496	1.557	0.0339	0.04613	1.2	4.728	51,001	100,000
OR[10,14]	0.5852	1.228	0.02428	0.004288	0.2484	3.305	51,001	100,000
OR[11,12]	1.557	3.091	0.02495	0.2675	1.11	5.031	51,001	100,000
OR[11,13]	1.732	3.124	0.03549	0.2743	1.219	5.876	51,001	100,000
OR[11,14]	0.8188	2.603	0.04028	0.009494	0.2793	4.781	51,001	100,000
OR[12,13]	1.45	2.263	0.02083	0.26	1.089	4.543	51,001	100,000
OR[12,14]	0.7617	3.158	0.04598	0.007292	0.2495	4.548	51,001	100,000
OR[13,14]	0.6143	2.41	0.03865	0.007926	0.2316	3.491	51,001	100,000

Median ranks

TABLE 135 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	5.418	1.917	0.05405	2	5	9	51,001	100,000
rk.class[2]	3.984	3.344	0.1012	1	2	10	51,001	100,000
rk.class[3]	7.261	2.131	0.04101	3	8	10	51,001	100,000
rk.class[4]	2.994	1.916	0.04307	1	2	8	51,001	100,000
rk.class[5]	7.046	2.182	0.04165	3	7	10	51,001	100,000
rk.class[6]	6.563	2.13	0.05017	2	7	10	51,001	100,000
rk.class[7]	6.274	2.66	0.07429	2	6	10	51,001	100,000
rk.class[8]	5.941	2.536	0.06181	2	6	10	51,001	100,000
rk.class[9]	6.526	2.477	0.04874	2	7	10	51,001	100,000
rk.class[10]	2.993	2.676	0.07246	1	2	10	51,001	100,000

TABLE 136 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	6.415	2.601	0.07389	2	6	12	51,001	100,000
rk[2]	4.926	4.714	0.1413	1	2	14	51,001	100,000
rk[3]	10.39	3.102	0.07114	4	11	14	51,001	100,000
rk[4]	7.418	3.237	0.07896	2	7	13	51,001	100,000
rk[5]	10.12	2.676	0.05522	4	10	14	51,001	100,000
rk[6]	9.112	3.418	0.07303	2	10	14	51,001	100,000
rk[7]	3.345	2.514	0.0553	1	3	11	51,001	100,000
rk[8]	8.995	3.442	0.06933	3	9	14	51,001	100,000
rk[9]	8.296	3.405	0.08337	3	8	14	51,001	100,000
rk[10]	7.695	3.817	0.1051	2	7	14	51,001	100,000
rk[11]	7.492	3.872	0.09628	2	7	14	51,001	100,000
rk[12]	8.291	3.806	0.07692	2	8	14	51,001	100,000
rk[13]	8.951	2.766	0.05694	3	9	14	51,001	100,000
rk[14]	3.546	3.729	0.09996	1	2	14	51,001	100,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Children and adolescents: clinical effectiveness (Children's Yale–Brown Obsessive–Compulsive Scale) – sensitivity analysis 1 (low overall attrition)

See *Table 38* for a summary.

TABLE 137 Raw data used

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
Barrett *et al.*, 2004[217]	24.04	24	4.14	8.36	22	6.93	NA	NA	NA	NA	NA	NA	2	2	2	9	NA	NA
Bolton *et al.*, 2011[219]	23.3	24	8.3	9.5	36	8	NA	NA	NA	NA	NA	NA	2	2	2	9	NA	NA
de Haan *et al.*, 1998[220]	17.6	10	11.8	9.1	12	9.1	NA	NA	NA	NA	NA	NA	2	2	7	8	NA	NA
DeVeaugh-Geiss *et al.*, 1992[221]	–2.4	29	NA	–10	31	NA	NA	NA	NA	NA	NA	NA	2	1	1	7	NA	NA
Liebowitz *et al.*, 2002[226]	18.55	22	11.44	14.71	21	8.73	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
March *et al.*, 1998[228]	–3.4	95	7.99	–6.8	92	8.34	NA	NA	NA	NA	NA	NA	2	1	1	6	NA	NA
Neziroglu *et al.*, 2000[229]	19.2	5	3.56	16.4	5	5.18	NA	NA	NA	NA	NA	NA	2	2	5	10	NA	NA
Piacentini *et al.*, 2011[230]	17.2	22	10.04	13.3	49	9.31	NA	NA	NA	NA	NA	NA	2	2	3	9	NA	NA
Riddle *et al.*, 1992[231]	14.8	6	7	13.6	7	5.7	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
Storch *et al.*, 2011[233]	18.53	15	8.11	11.13	16	10.53	NA	NA	NA	NA	NA	NA	2	2	2	9	NA	NA
The Pediatric OCD Treatment Study, 2004[236]	21.5	28	5.4	16.5	28	9.1	14	28	9.5	11.2	28	8.6	4	2	1	6	9	11
Williams *et al.*, 2010[235]	19.6	10	6.42	12.09	11	7.46	NA	NA	NA	NA	NA	NA	2	2	2	9	NA	NA

NA, not available.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

Key

1. Placebo (1).
2. Waitlist (2).
3. Psychological placebo (3).
4. Fluoxetine (4).
5. Fluvoxamine (4).
6. Sertraline (4).
7. Clomipramine (5).
8. BT (6).
9. CBT (7).
10. BT + fluvoxamine (8).
11. CBT + sertraline (9).

TABLE 138 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[1,2]	2.471	4.254	0.04991	–6.717	2.678	10.43	60,001	120,000
class.mean.diff[1,3]	–4.879	5.939	0.05252	–16.98	–4.833	6.948	60,001	120,000
class.mean.diff[1,4]	–3.651	4.109	0.02343	–12.37	–3.65	5.012	60,001	120,000
class.mean.diff[1,5]	–5.281	4.024	0.02711	–12.97	–5.438	3.279	60,001	120,000
class.mean.diff[1,6]	–8.746	5.186	0.05006	–19.24	–8.693	1.434	60,001	120,000
class.mean.diff[1,7]	–8.815	3.767	0.04254	–16.67	–8.731	–1.379	60,001	120,000
class.mean.diff[1,8]	0.2639	99.73	0.2666	–195.2	0.2606	196.1	60,001	120,000
class.mean.diff[1,9]	–10.37	3.942	0.0225	–18.48	–10.34	–2.396	60,001	120,000
class.mean.diff[2,3]	–7.35	5.144	0.0299	–17.29	–7.525	3.555	60,001	120,000
class.mean.diff[2,4]	–6.122	5.605	0.04701	–17.24	–6.272	5.586	60,001	120,000
class.mean.diff[2,5]	–7.752	5.155	0.04911	–17.15	–8.051	3.338	60,001	120,000
class.mean.diff[2,6]	–11.22	4.622	0.03467	–20.2	–11.3	–1.699	60,001	120,000
class.mean.diff[2,7]	–11.29	2.292	0.01522	–15.49	–11.43	–6.302	60,001	120,000
class.mean.diff[2,8]	–2.207	99.82	0.2719	–197.7	–2.057	193.8	60,001	120,000
class.mean.diff[2,9]	–12.84	4.905	0.03839	–22.23	–13.05	–2.42	60,001	120,000
class.mean.diff[3,4]	1.229	6.964	0.05114	–12.77	1.218	15.34	60,001	120,000
class.mean.diff[3,5]	–0.4019	6.707	0.05144	–13.43	–0.5988	13.56	60,001	120,000
class.mean.diff[3,6]	–3.867	6.664	0.04516	–17.32	–3.806	9.334	60,001	120,000
class.mean.diff[3,7]	–3.936	4.597	0.02564	–13.3	–3.925	5.317	60,001	120,000
class.mean.diff[3,8]	5.143	99.92	0.2723	–190.4	5.036	201.1	60,001	120,000
class.mean.diff[3,9]	–5.492	6.376	0.04277	–18.37	–5.508	7.428	60,001	120,000
class.mean.diff[4,5]	–1.63	5.688	0.03357	–12.95	–1.782	10.29	60,001	120,000
class.mean.diff[4,6]	–5.095	6.439	0.04859	–18.23	–5.069	7.824	60,001	120,000
class.mean.diff[4,7]	–5.165	5.235	0.04034	–15.99	–5.112	5.531	60,001	120,000
class.mean.diff[4,8]	3.915	99.81	0.2666	–191.6	3.966	199.8	60,001	120,000
class.mean.diff[4,9]	–6.72	5.336	0.02461	–17.73	–6.691	4.15	60,001	120,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 138 Class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[5,6]	–3.465	4.932	0.04626	–13.73	–3.342	5.82	60,001	120,000
class.mean.diff[5,7]	–3.534	4.916	0.04128	–13.94	–3.353	5.827	60,001	120,000
class.mean.diff[5,8]	5.545	99.8	0.2687	–190.2	5.557	201.4	60,001	120,000
class.mean.diff[5,9]	–5.09	5.429	0.03003	–16.57	–4.93	5.561	60,001	120,000
class.mean.diff[6,7]	–0.06935	4.832	0.03434	–9.674	–0.08316	9.604	60,001	120,000
class.mean.diff[6,8]	9.01	99.88	0.2713	–186.5	9.135	205.2	60,001	120,000
class.mean.diff[6,9]	–1.625	6.011	0.04339	–13.52	–1.671	10.61	60,001	120,000
class.mean.diff[7,8]	9.079	99.81	0.2712	–186.3	9.163	204.8	60,001	120,000
class.mean.diff[7,9]	–1.556	4.423	0.03107	–10.42	–1.609	7.512	60,001	120,000
class.mean.diff[8,9]	–10.64	99.8	0.2678	–206.6	–10.73	185	60,001	120,000

TABLE 139 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[1,2]	2.471	4.254	0.04991	–6.717	2.678	10.43	60,001	120,000
treat.mean.diff[1,3]	–4.879	5.939	0.05252	–16.98	–4.833	6.948	60,001	120,000
treat.mean.diff[1,4]	–3.182	2.968	0.02477	–9.123	–3.215	2.866	60,001	120,000
treat.mean.diff[1,5]	–3.642	6.385	0.02701	–17.44	–3.651	10.31	60,001	120,000
treat.mean.diff[1,6]	–4.095	2.574	0.01928	–9.473	–4.04	1.102	60,001	120,000
treat.mean.diff[1,7]	–5.281	4.024	0.02711	–12.97	–5.438	3.279	60,001	120,000
treat.mean.diff[1,8]	–8.746	5.186	0.05006	–19.24	–8.693	1.434	60,001	120,000
treat.mean.diff[1,9]	–8.815	3.767	0.04254	–16.67	–8.731	–1.379	60,001	120,000
treat.mean.diff[1,10]	0.2639	99.73	0.2666	–195.2	0.2606	196.1	60,001	120,000
treat.mean.diff[1,11]	–10.37	3.942	0.0225	–18.48	–10.34	–2.396	60,001	120,000
treat.mean.diff[2,3]	–7.35	5.144	0.0299	–17.29	–7.525	3.555	60,001	120,000
treat.mean.diff[2,4]	–5.653	5.001	0.05007	–15.18	–5.845	4.865	60,001	120,000
treat.mean.diff[2,5]	–6.113	7.448	0.04875	–21.47	–6.269	9.754	60,001	120,000
treat.mean.diff[2,6]	–6.566	4.444	0.04359	–14.99	–6.748	2.867	60,001	120,000
treat.mean.diff[2,7]	–7.752	5.155	0.04911	–17.15	–8.051	3.338	60,001	120,000
treat.mean.diff[2,8]	–11.22	4.622	0.03467	–20.2	–11.3	–1.699	60,001	120,000
treat.mean.diff[2,9]	–11.29	2.292	0.01522	–15.49	–11.43	–6.302	60,001	120,000
treat.mean.diff[2,10]	–2.207	99.82	0.2719	–197.7	–2.057	193.8	60,001	120,000
treat.mean.diff[2,11]	–12.84	4.905	0.03839	–22.23	–13.05	–2.42	60,001	120,000
treat.mean.diff[3,4]	1.697	6.507	0.05416	–11.24	1.662	14.9	60,001	120,000
treat.mean.diff[3,5]	1.237	8.525	0.05203	–16.21	1.204	18.89	60,001	120,000
treat.mean.diff[3,6]	0.784	6.073	0.04761	–11.36	0.7809	13.12	60,001	120,000
treat.mean.diff[3,7]	–0.4019	6.707	0.05144	–13.43	–0.5988	13.56	60,001	120,000

TABLE 139 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[3,8]	–3.867	6.664	0.04516	–17.32	–3.806	9.334	60,001	120,000
treat.mean.diff[3,9]	–3.936	4.597	0.02564	–13.3	–3.925	5.317	60,001	120,000
treat.mean.diff[3,10]	5.143	99.92	0.2723	–190.4	5.036	201.1	60,001	120,000
treat.mean.diff[3,11]	–5.492	6.376	0.04277	–18.37	–5.508	7.428	60,001	120,000
treat.mean.diff[4,5]	–0.4598	6.181	0.01977	–14.4	–0.1438	13.03	60,001	120,000
treat.mean.diff[4,6]	–0.913	3.208	0.02058	–7.98	–0.5303	5.333	60,001	120,000
treat.mean.diff[4,7]	–2.099	4.957	0.03573	–11.63	–2.261	8.27	60,001	120,000
treat.mean.diff[4,8]	–5.564	5.862	0.05201	–17.46	–5.511	5.995	60,001	120,000
treat.mean.diff[4,9]	–5.633	4.583	0.0439	–15.09	–5.557	3.418	60,001	120,000
treat.mean.diff[4,10]	3.446	99.76	0.2674	–192.1	3.492	199	60,001	120,000
treat.mean.diff[4,11]	–7.189	4.714	0.02868	–16.81	–7.143	2.24	60,001	120,000
treat.mean.diff[5,6]	–0.4533	6.174	0.01938	–14.45	–0.1494	13.01	60,001	120,000
treat.mean.diff[5,7]	–1.639	7.493	0.03619	–17.22	–1.765	14.15	60,001	120,000
treat.mean.diff[5,8]	–5.104	8.093	0.05014	–21.92	–5.037	11.51	60,001	120,000
treat.mean.diff[5,9]	–5.173	7.174	0.04209	–20.44	–5.091	9.874	60,001	120,000
treat.mean.diff[5,10]	3.906	99.94	0.2665	–191.8	3.929	199.6	60,001	120,000
treat.mean.diff[5,11]	–6.729	7.247	0.02775	–22.07	–6.672	8.425	60,001	120,000
treat.mean.diff[6,7]	–1.186	4.666	0.0301	–10.21	–1.375	8.722	60,001	120,000
treat.mean.diff[6,8]	–4.651	5.503	0.04559	–15.79	–4.608	6.166	60,001	120,000
treat.mean.diff[6,9]	–4.72	3.962	0.03644	–12.9	–4.687	3.202	60,001	120,000
treat.mean.diff[6,10]	4.359	99.76	0.266	–191	4.419	200.1	60,001	120,000
treat.mean.diff[6,11]	–6.276	4.071	0.01856	–14.61	–6.278	2.007	60,001	120,000
treat.mean.diff[7,8]	–3.465	4.932	0.04626	–13.73	–3.342	5.82	60,001	120,000
treat.mean.diff[7,9]	–3.534	4.916	0.04128	–13.94	–3.353	5.827	60,001	120,000
treat.mean.diff[7,10]	5.545	99.8	0.2687	–190.2	5.557	201.4	60,001	120,000
treat.mean.diff[7,11]	–5.09	5.429	0.03003	–16.57	–4.93	5.561	60,001	120,000
treat.mean.diff[8,9]	–0.06935	4.832	0.03434	–9.674	–0.08316	9.604	60,001	120,000
treat.mean.diff[8,10]	9.01	99.88	0.2713	–186.5	9.135	205.2	60,001	120,000
treat.mean.diff[8,11]	–1.625	6.011	0.04339	–13.52	–1.671	10.61	60,001	120,000
treat.mean.diff[9,10]	9.079	99.81	0.2712	–186.3	9.163	204.8	60,001	120,000
treat.mean.diff[9,11]	–1.556	4.423	0.03107	–10.42	–1.609	7.512	60,001	120,000
treat.mean.diff[10,11]	–10.64	99.8	0.2678	–206.6	–10.73	185	60,001	120,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Median ranks

TABLE 140 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	7.268	1.042	0.00809	5	7	9	60,001	120,000
rk.class[2]	7.974	1.049	0.008874	5	8	9	60,001	120,000
rk.class[3]	5.095	1.939	0.01367	1	5	9	60,001	120,000
rk.class[4]	5.551	1.746	0.01018	2	6	9	60,001	120,000
rk.class[5]	4.854	1.675	0.01267	2	5	8	60,001	120,000
rk.class[6]	3.335	1.728	0.01424	1	3	7	60,001	120,000
rk.class[7]	3.156	1.264	0.009132	1	3	6	60,001	120,000
rk.class[8]	5.168	3.9	0.01086	1	7	9	60,001	120,000
rk.class[9]	2.598	1.455	0.009453	1	2	6	60,001	120,000

TABLE 141 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	9.028	1.221	0.00986	6	9	11	60,001	120,000
rk[2]	9.741	1.4	0.01252	6	10	11	60,001	120,000
rk[3]	5.932	2.619	0.02003	1	6	10	60,001	120,000
rk[4]	6.881	1.901	0.01429	3	7	10	60,001	120,000
rk[5]	6.491	2.716	0.01087	1	7	11	60,001	120,000
rk[6]	6.311	1.659	0.009755	3	6	9	60,001	120,000
rk[7]	5.552	2.245	0.01702	2	5	10	60,001	120,000
rk[8]	3.706	2.199	0.0186	1	3	9	60,001	120,000
rk[9]	3.397	1.542	0.01208	1	3	7	60,001	120,000
rk[10]	6.2	4.881	0.01359	1	9	11	60,001	120,000
rk[11]	2.76	1.678	0.01035	1	2	7	60,001	120,000

Children and adolescents: clinical effectiveness (Children's Yale–Brown Obsessive–Compulsive Scale) – sensitivity analysis 2 (incomplete outcome data)

See *Table 39* for a summary.

TABLE 142 Raw data used

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
Bolton and Perrin, 2008[218]	21.1	10	5.9	13.9	10	10.74	NA	NA	NA	NA	NA	NA	2	2	2	8	NA	NA
Bolton *et al.*, 2011[219]	23.3	24	8.3	9.5	36	8	NA	NA	NA	NA	NA	NA	2	2	2	9	NA	NA
de Haan *et al.*, 1998[220]	17.6	10	11.8	9.1	12	9.1	NA	NA	NA	NA	NA	NA	2	2	7	8	NA	NA
DeVeaugh-Geiss *et al.*, 1992[221]	–2.4	29	NA	–10	31	NA	NA	NA	NA	NA	NA	NA	2	1	1	7	NA	NA
Freeman *et al.*, 2008[223]	17.1	20	7.57	14.45	22	8.16	NA	NA	NA	NA	NA	NA	2	2	3	9	NA	NA
Geller *et al.*, 2001[224]	–5.2	32	7.4	–9.5	71	9.2	NA	NA	NA	NA	NA	NA	2	1	1	4	NA	NA
Liebowitz *et al.*, 2002[226]	18.55	22	11.44	14.71	21	8.73	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
March *et al.*, 1998[228]	–3.4	95	7.99	–6.8	92	8.34	NA	NA	NA	NA	NA	NA	2	1	1	6	NA	NA
Piacentini *et al.*, 2011[230]	17.2	22	10.04	13.3	49	9.31	NA	NA	NA	NA	NA	NA	2	2	3	9	NA	NA
Riddle *et al.*, 1992[231]	14.8	6	7	13.6	7	5.7	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
Riddle *et al.*, 2001[232]	20.9	63	8.5	18.2	57	8.6	NA	NA	NA	NA	NA	NA	2	2	1	5	NA	NA
Storch *et al.*, 2011[233]	18.53	15	8.11	11.13	16	10.53	NA	NA	NA	NA	NA	NA	2	2	2	9	NA	NA
Storch *et al.*, 2013[234]	15.43	14	9.72	15.56	16	6.62	NA	NA	NA	NA	NA	NA	2	2	11	12	NA	NA
The Pediatric OCD Treatment Study, 2004[236]	21.5	28	5.4	16.5	28	9.1	14	28	9.5	11.2	28	8.6	4	2	1	6	9	11
Williams *et al.*, 2010[235]	19.6	10	6.42	12.09	11	7.46	NA	NA	NA	NA	NA	NA	2	2	2	9	NA	NA

NA, not available.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Key: intervention (class)

1. Placebo (1).
2. Waitlist (2).
3. Psychological placebo (3).
4. Fluoxetine (4).
5. Fluvoxamine (4).
6. Sertraline (4).
7. Clomipramine (5).
8. BT (6).
9. CBT (7).
10. BT + fluvoxamine (8).
11. CBT + sertraline (9).
12. CBT + placebo (10).

TABLE 143 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[1,2]	1.363	3.049	0.05907	–5.013	1.444	7.121	60,001	120,000
class.mean.diff[1,3]	–5.085	3.408	0.06288	–11.91	–5.098	1.569	60,001	120,000
class.mean.diff[1,4]	–3.548	2.208	0.01677	–8.156	–3.565	1.161	60,001	120,000
class.mean.diff[1,5]	–6.145	2.705	0.03675	–11.25	–6.214	–0.5892	60,001	120,000
class.mean.diff[1,6]	–9.581	4.048	0.07981	–17.62	–9.588	–1.608	60,001	120,000
class.mean.diff[1,7]	–8.365	2.526	0.0484	–13.52	–8.269	–3.482	60,001	120,000
class.mean.diff[1,8]	0.4373	100.3	0.2885	–195.9	0.2245	197.4	60,001	120,000
class.mean.diff[1,9]	–10.23	2.556	0.03305	–15.4	–10.18	–5.203	60,001	120,000
class.mean.diff[1,10]	–10.06	4.455	0.06724	–18.84	–10.04	–1.324	60,001	120,000
class.mean.diff[2,3]	–6.448	2.971	0.04237	–12.22	–6.502	–0.4866	60,001	120,000
class.mean.diff[2,4]	–4.911	3.642	0.05624	–11.91	–5.009	2.769	60,001	120,000
class.mean.diff[2,5]	–7.508	3.7	0.06175	–14.38	–7.615	0.277	60,001	120,000
class.mean.diff[2,6]	–10.94	3.667	0.06444	–18.06	–10.93	–3.692	60,001	120,000
class.mean.diff[2,7]	–9.727	1.92	0.02752	–13.36	–9.745	–5.811	60,001	120,000
class.mean.diff[2,8]	–0.9256	100.3	0.294	–197.3	–1.027	195.9	60,001	120,000
class.mean.diff[2,9]	–11.59	3.526	0.05615	–18.31	–11.63	–4.384	60,001	120,000
class.mean.diff[2,10]	–11.42	5.085	0.07934	–21.21	–11.46	–1.213	60,001	120,000
class.mean.diff[3,4]	1.537	3.955	0.062	–6.206	1.52	9.541	60,001	120,000
class.mean.diff[3,5]	–1.06	4.09	0.06442	–8.793	–1.139	7.256	60,001	120,000
class.mean.diff[3,6]	–4.496	4.464	0.07391	–13.16	–4.444	4.25	60,001	120,000
class.mean.diff[3,7]	–3.279	2.249	0.03004	–7.671	–3.273	1.118	60,001	120,000
class.mean.diff[3,8]	5.523	100.3	0.2939	–190.7	5.457	202.6	60,001	120,000
class.mean.diff[3,9]	–5.142	3.815	0.05885	–12.49	–5.151	2.435	60,001	120,000
class.mean.diff[3,10]	–4.97	5.277	0.07936	–15.19	–4.989	5.491	60,001	120,000
class.mean.diff[4,5]	–2.597	3.469	0.0402	–9.328	–2.655	4.54	60,001	120,000

TABLE 143 Class effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[4,6]	–6.033	4.535	0.07846	–15.04	–6.033	2.981	60,001	120,000
class.mean.diff[4,7]	–4.816	3.221	0.04684	–11.51	–4.736	1.559	60,001	120,000
class.mean.diff[4,8]	3.986	100.3	0.2891	–192.4	3.761	201.1	60,001	120,000
class.mean.diff[4,9]	–6.68	3.239	0.03296	–13.41	–6.659	–0.1466	60,001	120,000
class.mean.diff[4,10]	–6.507	4.878	0.06746	–16.16	–6.535	3.121	60,001	120,000
class.mean.diff[5,6]	–3.436	3.95	0.07453	–11.41	–3.362	4.149	60,001	120,000
class.mean.diff[5,7]	–2.219	3.42	0.05284	–9.22	–2.15	4.204	60,001	120,000
class.mean.diff[5,8]	6.583	100.3	0.2923	–189.9	6.298	203.6	60,001	120,000
class.mean.diff[5,9]	–4.083	3.628	0.0451	–11.48	–4.054	2.863	60,001	120,000
class.mean.diff[5,10]	–3.91	5.151	0.07278	–14.44	–3.836	5.87	60,001	120,000
class.mean.diff[6,7]	1.216	3.842	0.06653	–6.371	1.209	8.742	60,001	120,000
class.mean.diff[6,8]	10.02	100.4	0.2999	–186.6	9.879	207	60,001	120,000
class.mean.diff[6,9]	–0.6469	4.525	0.07643	–9.481	–0.5944	8.237	60,001	120,000
class.mean.diff[6,10]	–0.474	5.83	0.09455	–11.89	–0.4557	11.04	60,001	120,000
class.mean.diff[7,8]	8.802	100.3	0.2931	–187.7	8.671	205.9	60,001	120,000
class.mean.diff[7,9]	–1.863	3.047	0.04461	–7.749	–1.912	4.25	60,001	120,000
class.mean.diff[7,10]	–1.691	4.754	0.07025	–11.01	–1.702	7.813	60,001	120,000
class.mean.diff[8,9]	–10.67	100.3	0.2919	–207.5	–10.56	185.8	60,001	120,000
class.mean.diff[8,10]	–10.49	100.4	0.2988	–207.9	–10.35	185.9	60,001	120,000
class.mean.diff[9,10]	0.1729	3.673	0.05314	–7.111	0.1936	7.347	60,001	120,000

TABLE 144 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[1,2]	1.363	3.049	0.05907	–5.013	1.444	7.121	60,001	120,000
treat.mean.diff[1,3]	–5.085	3.408	0.06288	–11.91	–5.098	1.569	60,001	120,000
treat.mean.diff[1,4]	–3.59	1.493	0.02012	–6.527	–3.608	–0.5575	60,001	120,000
treat.mean.diff[1,5]	–3.21	1.824	0.01881	–6.796	–3.282	0.5665	60,001	120,000
treat.mean.diff[1,6]	–3.849	1.457	0.01748	–6.925	–3.797	–1.009	60,001	120,000
treat.mean.diff[1,7]	–6.145	2.705	0.03675	–11.25	–6.214	–0.5892	60,001	120,000
treat.mean.diff[1,8]	–9.581	4.048	0.07981	–17.62	–9.588	–1.608	60,001	120,000
treat.mean.diff[1,9]	–8.365	2.526	0.0484	–13.52	–8.269	–3.482	60,001	120,000
treat.mean.diff[1,10]	0.4373	100.3	0.2885	–195.9	0.2245	197.4	60,001	120,000
treat.mean.diff[1,11]	–10.23	2.556	0.03305	–15.4	–10.18	–5.203	60,001	120,000
treat.mean.diff[1,12]	–10.06	4.455	0.06724	–18.84	–10.04	–1.324	60,001	120,000
treat.mean.diff[2,3]	–6.448	2.971	0.04237	–12.22	–6.502	–0.4866	60,001	120,000

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 144 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[2,4]	–4.952	3.313	0.0598	–11.14	–5.064	1.913	60,001	120,000
treat.mean.diff[2,5]	–4.573	3.463	0.05694	–11.05	–4.669	2.673	60,001	120,000
treat.mean.diff[2,6]	–5.212	3.132	0.05392	–11.14	–5.286	1.235	60,001	120,000
treat.mean.diff[2,7]	–7.508	3.7	0.06175	–14.38	–7.615	0.277	60,001	120,000
treat.mean.diff[2,8]	–10.94	3.667	0.06444	–18.06	–10.93	–3.692	60,001	120,000
treat.mean.diff[2,9]	–9.727	1.92	0.02752	–13.36	–9.745	–5.811	60,001	120,000
treat.mean.diff[2,10]	–0.9256	100.3	0.294	–197.3	–1.027	195.9	60,001	120,000
treat.mean.diff[2,11]	–11.59	3.526	0.05615	–18.31	–11.63	–4.384	60,001	120,000
treat.mean.diff[2,12]	–11.42	5.085	0.07934	–21.21	–11.46	–1.213	60,001	120,000
treat.mean.diff[3,4]	1.496	3.655	0.06534	–5.54	1.487	8.809	60,001	120,000
treat.mean.diff[3,5]	1.875	3.798	0.0631	–5.363	1.842	9.512	60,001	120,000
treat.mean.diff[3,6]	1.236	3.49	0.05974	–5.649	1.255	8.097	60,001	120,000
treat.mean.diff[3,7]	–1.06	4.09	0.06442	–8.793	–1.139	7.256	60,001	120,000
treat.mean.diff[3,8]	–4.496	4.464	0.07391	–13.16	–4.444	4.25	60,001	120,000
treat.mean.diff[3,9]	–3.279	2.249	0.03004	–7.671	–3.273	1.118	60,001	120,000
treat.mean.diff[3,10]	5.523	100.3	0.2939	–190.7	5.457	202.6	60,001	120,000
treat.mean.diff[3,11]	–5.142	3.815	0.05885	–12.49	–5.151	2.435	60,001	120,000
treat.mean.diff[3,12]	–4.97	5.277	0.07936	–15.19	–4.989	5.491	60,001	120,000
treat.mean.diff[4,5]	0.3796	2.009	0.02054	–3.652	0.1615	4.763	60,001	120,000
treat.mean.diff[4,6]	–0.2596	1.749	0.01835	–4.184	–0.093	3.129	60,001	120,000
treat.mean.diff[4,7]	–2.556	3.06	0.04071	–8.389	–2.637	3.633	60,001	120,000
treat.mean.diff[4,8]	–5.991	4.271	0.0814	–14.44	–5.982	2.48	60,001	120,000
treat.mean.diff[4,9]	–4.775	2.846	0.05069	–10.58	–4.674	0.6795	60,001	120,000
treat.mean.diff[4,10]	4.027	100.3	0.2895	–192.2	3.917	200.9	60,001	120,000
treat.mean.diff[4,11]	–6.638	2.862	0.03593	–12.41	–6.611	–1.025	60,001	120,000
treat.mean.diff[4,12]	–6.465	4.648	0.07035	–15.64	–6.48	2.628	60,001	120,000
treat.mean.diff[5,6]	–0.6391	1.982	0.01744	–5.16	–0.3132	3.009	60,001	120,000
treat.mean.diff[5,7]	–2.935	3.26	0.04117	–9.154	–2.966	3.687	60,001	120,000
treat.mean.diff[5,8]	–6.371	4.394	0.07759	–15.11	–6.364	2.291	60,001	120,000
treat.mean.diff[5,9]	–5.154	3.018	0.04755	–11.34	–5.07	0.6257	60,001	120,000
treat.mean.diff[5,10]	3.647	100.3	0.2892	–192.8	3.437	200.6	60,001	120,000
treat.mean.diff[5,11]	–7.018	3.045	0.03503	–13.23	–6.992	–1.057	60,001	120,000
treat.mean.diff[5,12]	–6.845	4.756	0.06888	–16.18	–6.841	2.535	60,001	120,000
treat.mean.diff[6,7]	–2.296	3.041	0.04011	–7.992	–2.375	4.008	60,001	120,000
treat.mean.diff[6,8]	–5.732	4.171	0.07775	–13.95	–5.759	2.71	60,001	120,000
treat.mean.diff[6,9]	–4.515	2.629	0.04471	–9.766	–4.472	0.6213	60,001	120,000
treat.mean.diff[6,10]	4.286	100.3	0.2887	–192	4.05	201.2	60,001	120,000

TABLE 144 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[6,11]	–6.379	2.655	0.0324	–11.66	–6.391	–1.043	60,001	120,000
treat.mean.diff[6,12]	–6.206	4.519	0.0671	–15.09	–6.259	2.72	60,001	120,000
treat.mean.diff[7,8]	–3.436	3.95	0.07453	–11.41	–3.362	4.149	60,001	120,000
treat.mean.diff[7,9]	–2.219	3.42	0.05284	–9.22	–2.15	4.204	60,001	120,000
treat.mean.diff[7,10]	6.583	100.3	0.2923	–189.9	6.298	203.6	60,001	120,000
treat.mean.diff[7,11]	–4.083	3.628	0.0451	–11.48	–4.054	2.863	60,001	120,000
treat.mean.diff[7,12]	–3.91	5.151	0.07278	–14.44	–3.836	5.87	60,001	120,000
treat.mean.diff[8,9]	1.216	3.842	0.06653	–6.371	1.209	8.742	60,001	120,000
treat.mean.diff[8,10]	10.02	100.4	0.2999	–186.6	9.879	207	60,001	120,000
treat.mean.diff[8,11]	–0.6469	4.525	0.07643	–9.481	–0.5944	8.237	60,001	120,000
treat.mean.diff[8,12]	–0.474	5.83	0.09455	–11.89	–0.4557	11.04	60,001	120,000
treat.mean.diff[9,10]	8.802	100.3	0.2931	–187.7	8.671	205.9	60,001	120,000
treat.mean.diff[9,11]	–1.863	3.047	0.04461	–7.749	–1.912	4.25	60,001	120,000
treat.mean.diff[9,12]	–1.691	4.754	0.07025	–11.01	–1.702	7.813	60,001	120,000
treat.mean.diff[10,11]	–10.67	100.3	0.2919	–207.5	–10.56	185.8	60,001	120,000
treat.mean.diff[10,12]	–10.49	100.4	0.2988	–207.9	–10.35	185.9	60,001	120,000
treat.mean.diff[11,12]	0.1729	3.673	0.05314	–7.111	0.1936	7.347	60,001	120,000

Median ranks

TABLE 145 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	8.648	0.8166	0.01045	7	9	10	60,001	120,000
rk.class[2]	9.054	0.9307	0.01243	7	9	10	60,001	120,000
rk.class[3]	6.049	1.573	0.02325	3	6	9	60,001	120,000
rk.class[4]	6.821	1.339	0.01517	4	7	9	60,001	120,000
rk.class[5]	5.334	1.626	0.02244	2	5	8	60,001	120,000
rk.class[6]	3.359	1.859	0.03424	1	3	7	60,001	120,000
rk.class[7]	3.873	1.331	0.01948	1	4	6	60,001	120,000
rk.class[8]	5.719	4.398	0.01267	1	9	10	60,001	120,000
rk.class[9]	2.856	1.325	0.01815	1	3	6	60,001	120,000
rk.class[10]	3.287	1.987	0.02956	1	3	8	60,001	120,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 146 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	10.63	0.8384	0.01047	9	11	12	60,001	120,000
rk[2]	10.93	1.222	0.01717	7	11	12	60,001	120,000
rk[3]	6.699	2.218	0.0375	3	6	11	60,001	120,000
rk[4]	7.809	1.556	0.02128	4	8	10	60,001	120,000
rk[5]	8.164	1.645	0.01718	5	8	11	60,001	120,000
rk[6]	7.589	1.473	0.01721	4	8	10	60,001	120,000
rk[7]	5.689	2.069	0.02781	2	6	10	60,001	120,000
rk[8]	3.501	2.162	0.04068	1	3	9	60,001	120,000
rk[9]	3.935	1.45	0.02115	1	4	7	60,001	120,000
rk[10]	6.75	5.384	0.01547	1	11	12	60,001	120,000
rk[11]	2.872	1.381	0.0184	1	3	6	60,001	120,000
rk[12]	3.426	2.298	0.03362	1	3	10	60,001	120,000

Children and adolescents: clinical effectiveness (Children's Yale–Brown Obsessive–Compulsive Scale) – sensitivity analysis 3 (blinding)

See *Table 40* for a summary.

TABLE 147 Raw data used

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
Bolton *et al.*, 2011[219]	23.3	24	8.3	9.5	36	8	NA	NA	NA	NA	NA	NA	2	2	2	7	NA	NA
Freeman *et al.*, 2008[223]	17.1	20	7.57	14.45	22	8.16	NA	NA	NA	NA	NA	NA	2	2	3	7	NA	NA
Liebowitz *et al.*, 2002[226]	18.55	22	11.44	14.71	21	8.73	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
Piacentini *et al.*, 2011[230]	17.2	22	10.04	13.3	49	9.31	NA	NA	NA	NA	NA	NA	2	2	3	7	NA	NA
Riddle *et al.*, 2001[232]	20.9	63	8.5	18.2	57	8.6	NA	NA	NA	NA	NA	NA	2	2	1	5	NA	NA
Storch *et al.*, 2011[233]	18.53	15	8.11	11.13	16	10.53	NA	NA	NA	NA	NA	NA	2	2	2	7	NA	NA
Storch *et al.*, 2013[234]	15.43	14	9.72	15.56	16	6.62	NA	NA	NA	NA	NA	NA	2	2	8	9	NA	NA
The Pediatric OCD Treatment Study, 2004[236]	21.5	28	5.4	16.5	28	9.1	14	28	9.5	11.2	28	8.6	4	2	1	6	7	8
Williams *et al.*, 2010[235]	19.6	10	6.42	12.09	11	7.46	NA	NA	NA	NA	NA	NA	2	2	2	7	NA	NA

NA, not available.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Key: intervention (class)

1. Placebo (1).
2. Waitlist (2).
3. Psychological placebo (3).
4. Fluoxetine (4).
5. Fluvoxamine (4).
6. Sertraline (4).
7. CBT (5).
8. CBT + sertraline (6).
9. CBT + placebo (7).

TABLE 148 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
class.mean.diff[1,2]	3.103	4.279	0.05724	–5.736	3.191	11.54	61,001	129,600
class.mean.diff[1,3]	–3.943	4.497	0.05359	–13.04	–3.963	5.258	61,001	129,600
class.mean.diff[1,4]	–3.795	3.219	0.02787	–10.55	–3.782	2.974	61,001	129,600
class.mean.diff[1,5]	–7.18	3.555	0.04741	–14.33	–7.206	0.08779	61,001	129,600
class.mean.diff[1,6]	–9.972	3.442	0.03088	–16.91	–10	–2.862	61,001	129,600
class.mean.diff[1,7]	–9.758	5.575	0.05763	–20.78	–9.741	1.458	61,001	129,600
class.mean.diff[2,3]	–7.046	3.673	0.02754	–14.15	–7.139	0.6016	61,001	129,600
class.mean.diff[2,4]	–6.898	4.989	0.05415	–16.72	–6.996	3.421	61,001	129,600
class.mean.diff[2,5]	–10.28	2.417	0.02076	–14.83	–10.37	–5.221	61,001	129,600
class.mean.diff[2,6]	–13.07	4.567	0.04721	–21.98	–13.16	–3.638	61,001	129,600
class.mean.diff[2,7]	–12.86	6.334	0.06788	–25.26	–12.89	0.008206	61,001	129,600
class.mean.diff[3,4]	0.1485	5.165	0.05022	–10.34	0.1485	10.63	61,001	129,600
class.mean.diff[3,5]	–3.237	2.788	0.02048	–8.806	–3.246	2.374	61,001	129,600
class.mean.diff[3,6]	–6.029	4.778	0.04467	–15.67	–6.047	3.646	61,001	129,600
class.mean.diff[3,7]	–5.815	6.489	0.0665	–18.68	–5.803	7.188	61,001	129,600
class.mean.diff[4,5]	–3.385	4.379	0.04524	–12.36	–3.378	5.519	61,001	129,600
class.mean.diff[4,6]	–6.177	4.328	0.03163	–15.06	–6.185	2.796	61,001	129,600
class.mean.diff[4,7]	–5.964	6.165	0.0578	–18.28	–5.939	6.432	61,001	129,600
class.mean.diff[5,6]	–2.792	3.9	0.03758	–10.6	–2.81	5.091	61,001	129,600
class.mean.diff[5,7]	–2.578	5.867	0.0621	–14.14	–2.525	9.12	61,001	129,600
class.mean.diff[6,7]	0.2136	4.395	0.04491	–8.512	0.2153	8.938	61,001	129,600

TABLE 149 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
treat.mean.diff[1,2]	3.103	4.279	0.05724	–5.736	3.191	11.54	61,001	129,600
treat.mean.diff[1,3]	–3.943	4.497	0.05359	–13.04	–3.963	5.258	61,001	129,600
treat.mean.diff[1,4]	–3.846	3.071	0.0307	–10.08	–3.821	2.399	61,001	129,600
treat.mean.diff[1,5]	–3.268	2.696	0.02486	–8.812	–3.27	2.223	61,001	129,600
treat.mean.diff[1,6]	–4.268	2.802	0.03029	–9.965	–4.217	1.422	61,001	129,600
treat.mean.diff[1,7]	–7.18	3.555	0.04741	–14.33	–7.206	0.08779	61,001	129,600
treat.mean.diff[1,8]	–9.972	3.442	0.03088	–16.91	–10	–2.862	61,001	129,600
treat.mean.diff[1,9]	–9.758	5.575	0.05763	–20.78	–9.741	1.458	61,001	129,600
treat.mean.diff[2,3]	–7.046	3.673	0.02754	–14.15	–7.139	0.6016	61,001	129,600
treat.mean.diff[2,4]	–6.948	5.017	0.05902	–16.83	–7.039	3.328	61,001	129,600
treat.mean.diff[2,5]	–6.371	4.811	0.05586	–15.88	–6.456	3.49	61,001	129,600
treat.mean.diff[2,6]	–7.371	4.452	0.05062	–15.96	–7.468	1.824	61,001	129,600
treat.mean.diff[2,7]	–10.28	2.417	0.02076	–14.83	–10.37	–5.221	61,001	129,600
treat.mean.diff[2,8]	–13.07	4.567	0.04721	–21.98	–13.16	–3.638	61,001	129,600
treat.mean.diff[2,9]	–12.86	6.334	0.06788	–25.26	–12.89	0.008206	61,001	129,600
treat.mean.diff[3,4]	0.09769	5.192	0.05513	–10.48	0.09801	10.5	61,001	129,600
treat.mean.diff[3,5]	0.6747	5.009	0.05222	–9.585	0.6688	10.71	61,001	129,600
treat.mean.diff[3,6]	–0.3247	4.648	0.0465	–9.636	–0.3322	9.015	61,001	129,600
treat.mean.diff[3,7]	–3.237	2.788	0.02048	–8.806	–3.246	2.374	61,001	129,600
treat.mean.diff[3,8]	–6.029	4.778	0.04467	–15.67	–6.047	3.646	61,001	129,600
treat.mean.diff[3,9]	–5.815	6.489	0.0665	–18.68	–5.803	7.188	61,001	129,600
treat.mean.diff[4,5]	0.5771	3.215	0.02133	–5.973	0.279	7.537	61,001	129,600
treat.mean.diff[4,6]	–0.4224	3.286	0.02684	–7.602	–0.1731	6.282	61,001	129,600
treat.mean.diff[4,7]	–3.335	4.417	0.05087	–12.21	–3.336	5.573	61,001	129,600
treat.mean.diff[4,8]	–6.126	4.357	0.03743	–15	–6.131	2.769	61,001	129,600
treat.mean.diff[4,9]	–5.913	6.179	0.06194	–18.22	–5.884	6.419	61,001	129,600
treat.mean.diff[5,6]	–0.9994	3.068	0.02282	–7.796	–0.5784	4.947	61,001	129,600
treat.mean.diff[5,7]	–3.912	4.194	0.04733	–12.31	–3.896	4.609	61,001	129,600
treat.mean.diff[5,8]	–6.704	4.128	0.033	–14.98	–6.721	1.816	61,001	129,600
treat.mean.diff[5,9]	–6.49	6.022	0.05815	–18.43	–6.527	5.726	61,001	129,600
treat.mean.diff[6,7]	–2.912	3.743	0.04114	–10.37	–2.903	4.544	61,001	129,600
treat.mean.diff[6,8]	–5.704	3.671	0.02713	–13.02	–5.727	1.755	61,001	129,600
treat.mean.diff[6,9]	–5.49	5.729	0.05522	–16.8	–5.502	6.003	61,001	129,600
treat.mean.diff[7,8]	–2.792	3.9	0.03758	–10.6	–2.81	5.091	61,001	129,600
treat.mean.diff[7,9]	–2.578	5.867	0.0621	–14.14	–2.525	9.12	61,001	129,600
treat.mean.diff[8,9]	0.2136	4.395	0.04491	–8.512	0.2153	8.938	61,001	129,600

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Median ranks

TABLE 150 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	5.879	0.8012	0.008782	4	6	7	61,001	129,600
rk.class[2]	6.662	0.714	0.007736	5	7	7	61,001	129,600
rk.class[3]	4.332	1.189	0.01151	1	4	6	61,001	129,600
rk.class[4]	4.285	1.223	0.01049	1	4	7	61,001	129,600
rk.class[5]	2.799	0.9752	0.009909	1	3	5	61,001	129,600
rk.class[6]	1.85	0.905	0.008695	1	2	4	61,001	129,600
rk.class[7]	2.193	1.424	0.01474	1	2	6	61,001	129,600

TABLE 151 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	7.744	0.9853	0.01082	5	8	9	61,001	129,600
rk[2]	8.541	1.04	0.01128	5	9	9	61,001	129,600
rk[3]	5.303	1.899	0.02138	1	5	8	61,001	129,600
rk[4]	5.239	1.737	0.01652	2	5	8	61,001	129,600
rk[5]	5.641	1.567	0.01309	2	6	8	61,001	129,600
rk[6]	4.989	1.469	0.01242	2	5	8	61,001	129,600
rk[7]	3.137	1.399	0.01545	1	3	6	61,001	129,600
rk[8]	1.951	1.119	0.01031	1	2	5	61,001	129,600
rk[9]	2.456	1.907	0.01931	1	2	8	61,001	129,600

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Children and adolescents: clinical effectiveness (Children's Yale–Brown Obsessive–Compulsive Scale) – sensitivity analysis 4 (post hoc), excluding studies that have used a waitlist as control

This is a post hoc analysis.

TABLE 152 Raw data used

Study	y[,1]	n[,1]	sd[,1]	y[,2]	n[,2]	sd[,2]	y[,3]	n[,3]	sd[,3]	y[,4]	n[,4]	sd[,4]	na[]	out[]	t[,1]	t[,2]	t[,3]	t[,4]
de Haan *et al.*, 1998[220]	17.6	10	11.8	9.1	12	9.1	NA	NA	NA	NA	NA	NA	2	2	6	7	NA	NA
DeVeaugh-Geiss *et al.*, 1992[221]	–2.4	29	NA	–10	31	NA	NA	NA	NA	NA	NA	NA	2	1	1	6	NA	NA
Freeman *et al.*, 2008[223]	17.1	20	7.57	14.45	22	8.16	NA	NA	NA	NA	NA	NA	2	2	2	8	NA	NA
Geller *et al.*, 2001[224]	–5.2	32	7.4	–9.5	71	9.2	NA	NA	NA	NA	NA	NA	2	1	1	3	NA	NA
Liebowitz *et al.*, 2002[226]	18.55	22	11.44	14.71	21	8.73	NA	NA	NA	NA	NA	NA	2	2	1	3	NA	NA
March *et al.*, 1998[228]	–3.4	95	7.99	–6.8	92	8.34	NA	NA	NA	NA	NA	NA	2	1	1	5	NA	NA
Neziroglu *et al.*, 2000[229]	19.2	5	3.56	16.4	5	5.18	NA	NA	NA	NA	NA	NA	2	2	4	9	NA	NA
Piacentini *et al.*, 2011[230]	17.2	22	10.04	13.3	49	9.31	NA	NA	NA	NA	NA	NA	2	2	2	8	NA	NA
Riddle *et al.*, 1992[231]	14.8	6	7	13.6	7	5.7	NA	NA	NA	NA	NA	NA	2	2	1	3	NA	NA
Riddle *et al.*, 2001[232]	20.9	63	8.5	18.2	57	8.6	NA	NA	NA	NA	NA	NA	2	2	1	4	NA	NA
Storch *et al.*, 2013[234]	15.43	14	9.72	15.56	16	6.62	NA	NA	NA	NA	NA	NA	2	2	10	11	NA	NA
The Pediatric OCD Treatment Study, 2004[236]	21.5	28	5.4	16.5	28	9.1	14	28	9.5	11.2	28	8.6	4	2	1	5	8	10

Notes
t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

Key

1. Placebo (1).
2. Psychological placebo (2).
3. Fluoxetine (3).
4. Fluvoxamine (3).
5. Sertraline (3).
6. Clomipramine (4).
7. BT (5).
8. CBT (6).
9. BT + fluvoxamine (7).
10. Sertraline + CBT (8).
11. Placebo + CBT (9).

TABLE 153 Class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
D[2]	–3.815	3.248	0.04646	–10.08	–3.845	2.654	101,001	186,000
D[3]	–3.475	2.094	0.01409	–7.803	–3.513	1.013	101,001	186,000
D[4]	–7.621	2.641	0.03338	–12.82	–7.61	–2.436	101,001	186,000
D[5]	–16.08	5.547	0.1055	–26.99	–16.05	–5.252	101,001	186,000
D[6]	–7.066	2.5	0.03558	–11.88	–7.105	–2.151	101,001	186,000
D[7]	–5.892	3.626	0.0444	–13.01	–5.914	1.201	101,001	186,000
D[8]	–9.898	2.383	0.02919	–14.5	–9.936	–5.157	101,001	186,000
D[9]	–9.725	4.246	0.0648	–17.96	–9.716	–1.401	101,001	186,000

TABLE 154 Individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
d[2]	–3.815	3.248	0.04646	–10.08	–3.845	2.654	101,001	186,000
d[3]	–3.561	1.385	0.01635	–6.31	–3.564	–0.7715	101,001	186,000
d[4]	–3.17	1.635	0.0186	–6.288	–3.24	0.2024	101,001	186,000
d[5]	–3.725	1.299	0.01303	–6.36	–3.714	–1.192	101,001	186,000
d[6]	–7.621	2.641	0.03338	–12.82	–7.61	–2.436	101,001	186,000
d[7]	–16.08	5.547	0.1055	–26.99	–16.05	–5.252	101,001	186,000
d[8]	–7.066	2.5	0.03558	–11.88	–7.105	–2.151	101,001	186,000
d[9]	–5.892	3.626	0.0444	–13.01	–5.914	1.201	101,001	186,000
d[10]	–9.898	2.383	0.02919	–14.5	–9.936	–5.157	101,001	186,000
d[11]	–9.725	4.246	0.0648	–17.96	–9.716	–1.401	101,001	186,000

Please note that these figures can be directly compared with *Table 37* using the correct key for the treatment. For example, the posterior MD for CBT (treatment #8 in this table) is –7.06 (95% CrI –11.88 to –2.15) and this compares with a MD of –8.66 (95% CrI –14.38 to –3.14) from *Table 37* of the main text of the report.

Median ranks

TABLE 155 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	8.771	0.5095	0.004998	7	9	9	101,001	186,000
rk.class[2]	6.852	1.472	0.01982	3	7	9	101,001	186,000
rk.class[3]	7.017	1.181	0.01059	4	7	9	101,001	186,000
rk.class[4]	4.436	1.615	0.0214	2	4	8	101,001	186,000
rk.class[5]	1.524	1.233	0.01822	1	1	5	101,001	186,000
rk.class[6]	4.633	1.35	0.01805	2	5	7	101,001	186,000
rk.class[7]	5.448	1.985	0.02561	2	6	9	101,001	186,000
rk.class[8]	2.945	1.156	0.01379	1	3	6	101,001	186,000
rk.class[9]	3.375	1.905	0.02738	1	3	8	101,001	186,000

TABLE 156 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	10.77	0.5484	0.005578	9	11	11	101,001	186,000
rk[2]	7.767	2.226	0.03217	3	8	11	101,001	186,000
rk[3]	7.969	1.473	0.0173	5	8	10	101,001	186,000
rk[4]	8.389	1.435	0.01459	5	9	10	101,001	186,000
rk[5]	7.819	1.391	0.01456	5	8	10	101,001	186,000
rk[6]	4.564	1.873	0.02389	2	4	9	101,001	186,000
rk[7]	1.55	1.372	0.01955	1	1	6	101,001	186,000
rk[8]	4.79	1.629	0.02138	2	5	9	101,001	186,000
rk[9]	5.913	2.565	0.03303	2	6	11	101,001	186,000
rk[10]	2.959	1.215	0.01403	1	3	6	101,001	186,000
rk[11]	3.512	2.227	0.0313	1	3	10	101,001	186,000

Please note that these figures can be directly compared with *Table 37* of the main report using the correct key for the treatment. For example, the posterior median rank for CBT (treatment #8 in this table) is 5 (95% CrI 2 to 9) and this compares with a median rank of 3 (95% CrI 1 to 7) in *Table 37*.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Children and adolescents: acceptability (dropouts) – sensitivity analysis 1 (low overall attrition)

See *Table 45* for a summary.

TABLE 157 Raw data used

Study	r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	r[,4]	n[,4]	na[]	t[,1]	t[,2]	t[,3]	t[,4]
Asbahr *et al.*, 2005[216]	1.5	21	0.5	21	NA	NA	NA	NA	2	5	8	NA	NA
Bolton and Perrin, 2008[218]	0.5	11	2.5	11	NA	NA	NA	NA	2	2	7	NA	NA
Bolton *et al.*, 2011[219]	3	24	2	36	NA	NA	NA	NA	2	2	8	NA	NA
de Haan *et al.*, 1998[220]	0.5	11	1.5	14	NA	NA	NA	NA	2	6	7	NA	NA
DeVeaugh-Geiss *et al.*, 1992[221]	2	29	4	31	NA	NA	NA	NA	2	1	6	NA	NA
Liebowitz *et al.*, 2002[226]	4	22	1	21	NA	NA	NA	NA	2	1	4	NA	NA
March *et al.*, 1990[227]	0.5	9	2.5	9	NA	NA	NA	NA	2	1	6	NA	NA
March *et al.*, 1998[228]	13	95	18	92	NA	NA	NA	NA	2	1	5	NA	NA
Piacentini *et al.*, 2011[230]	5	22	8	49	NA	NA	NA	NA	2	3	8	NA	NA
Riddle *et al.*, 1992[231]	1	6	1	7	NA	NA	NA	NA	2	1	4	NA	NA
Storch *et al.*, 2011[233]	0.5	16	2.5	17	NA	NA	NA	NA	2	2	8	NA	NA
The Pediatric OCD Treatment Study, 2004[236]	7	28	2	28	3	28	3	28	4	1	5	8	9
Williams *et al.*, 2010[235]	1	10	1	11	NA	NA	NA	NA	2	2	8	NA	NA

NA, not available.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

Key: intervention (class)

1. Placebo (1).
2. Waitlist (2).
3. Psychological placebo (3).
4. Fluoxetine (4).
5. Sertraline (4).
6. Clomipramine (5).
7. BT (6).
8. CBT (7).
9. CBT + sertraline (8).

TABLE 158 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[1,2]	2.004	47.63	0.1619	0.0234	0.4655	7.378	100,001	200,000
OR.D[1,3]	88.6	16,920	37.98	0.01715	0.6795	23.59	100,001	200,000
OR.D[1,4]	684,500	2.78×10^{8}	620,500	5.23×10^{-4}	0.5795	448.1	100,001	200,000
OR.D[1,5]	8.66	154.5	0.4221	0.3588	3.12	36.01	100,001	200,000
OR.D[1,6]	549.4	82,090	215.8	0.2338	8.088	695.2	100,001	200,000
OR.D[1,7]	1.066	8.235	0.03168	0.04269	0.4677	4.388	100,001	200,000
OR.D[1,8]	3.44	437.9	0.9819	0.03391	0.5395	7.327	100,001	200,000
OR.D[2,3]	51,760	2.31×10^{7}	51,600	0.05413	1.464	46.74	100,001	200,000
OR.D[2,4]	4.72E+06	1.89×10^{9}	4.23×10^{6}	8.12×10^{-4}	1.253	1366	100,001	200,000
OR.D[2,5]	144.4	12,320	31.54	0.2732	6.881	254.4	100,001	200,000
OR.D[2,6]	3556	442,300	2258	0.6616	17.25	1572	100,001	200,000
OR.D[2,7]	2.059	65.74	0.1484	0.1543	1	7.432	100,001	200,000
OR.D[2,8]	112.1	25,660	58.84	0.04329	1.134	36.74	100,001	200,000
OR.D[3,4]	3.44×10^{6}	1.21×10^{9}	2.70×10^{6}	4.15×10^{-4}	0.8422	1197	100,001	200,000
OR.D[3,5]	10,220	3.81×10^{6}	8978	0.08597	4.645	328.6	100,001	200,000
OR.D[3,6]	19,690	3.17×10^{6}	7701	0.1442	12.25	2389	100,001	200,000
OR.D[3,7]	10.39	1595	3.596	0.04189	0.6821	10.91	100,001	200,000
OR.D[3,8]	903.2	224100	500.6	0.01527	0.7741	43.04	100,001	200,000
OR.D[4,5]	3.91×10^{6}	8.33×10^{8}	1.85×10^{6}	0.005661	5.669	8118	100,001	200,000
OR.D[4,6]	3.32×10^{7}	6.47×10^{9}	1.52×10^{7}	0.01022	15.05	43550	100,001	200,000
OR.D[4,7]	2.91×10^{6}	1.12×10^{9}	2.50×10^{6}	8.74×10^{-4}	0.8002	1087	100,001	200,000
OR.D[4,8]	999,300	2.49×10^{8}	555,300	9.15×10^{-4}	0.923	1347	100,001	200,000
OR.D[5,6]	83.25	4380	29.29	0.0845	2.501	180.1	100,001	200,000
OR.D[5,7]	0.8665	32.12	0.07764	0.005902	0.1475	2.731	100,001	200,000
OR.D[5,8]	26.11	10530	23.55	0.004559	0.1674	4.631	100,001	200,000
OR.D[6,7]	1.037	169.8	0.3847	6.35×10^{-4}	0.05713	1.861	100,001	200,000
OR.D[6,8]	20.67	5441	12.17	4.50×10^{-4}	0.0643	4.102	100,001	200,000
OR.D[7,8]	7.098	382.1	0.8866	0.06605	1.146	20.08	100,001	200,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 159 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[1,2]	2.004	47.63	0.1619	0.0234	0.4655	7.378	100,001	200,000
OR[1,3]	88.6	16,920	37.98	0.01715	0.6795	23.59	100,001	200,000
OR[1,4]	0.8653	5.695	0.01689	0.02994	0.4078	3.622	100,001	200,000
OR[1,5]	1.241	15.18	0.03805	0.1239	0.7938	4.08	100,001	200,000
OR[1,6]	8.66	154.5	0.4221	0.3588	3.12	36.01	100,001	200,000
OR[1,7]	549.4	82,090	215.8	0.2338	8.088	695.2	100,001	200,000
OR[1,8]	1.066	8.235	0.03168	0.04269	0.4677	4.388	100,001	200,000
OR[1,9]	3.44	437.9	0.9819	0.03391	0.5395	7.327	100,001	200,000
OR[2,3]	51,760	2.31×10^{7}	51,600	0.05413	1.464	46.74	100,001	200,000
OR[2,4]	35.04	5064	11.88	0.02154	0.851	32.7	100,001	200,000
OR[2,5]	9.823	567.3	1.408	0.1006	1.676	30.07	100,001	200,000
OR[2,6]	144.4	12,320	31.54	0.2732	6.881	254.4	100,001	200,000
OR[2,7]	3556	442,300	2258	0.6616	17.25	1572	100,001	200,000
OR[2,8]	2.059	65.74	0.1484	0.1543	1	7.432	100,001	200,000
OR[2,9]	112.1	25,660	58.84	0.04329	1.134	36.74	100,001	200,000
OR[3,4]	1408	510,700	1142	0.008377	0.5765	38.53	100,001	200,000
OR[3,5]	1087	261,300	582.5	0.03144	1.155	38.62	100,001	200,000
OR[3,6]	10,220	3.81×10^{6}	8978	0.08597	4.645	328.6	100,001	200,000
OR[3,7]	19,690	3.17×10^{6}	7701	0.1442	12.25	2389	100,001	200,000
OR[3,8]	10.39	1595	3.596	0.04189	0.6821	10.91	100,001	200,000
OR[3,9]	903.2	224,100	500.6	0.01527	0.7741	43.04	100,001	200,000
OR[4,5]	10.07	389.9	0.9028	0.1496	1.74	36.51	100,001	200,000
OR[4,6]	257	44,410	101.2	0.364	8.065	255	100,001	200,000
OR[4,7]	6226	402,100	3626	0.3259	21.21	3037	100,001	200,000
OR[4,8]	12.04	957.4	2.632	0.05211	1.163	32.01	100,001	200,000
OR[4,9]	36.51	5828	13.04	0.04467	1.339	48.11	100,001	200,000
OR[5,6]	31.28	1904	4.73	0.2996	4.02	82.71	100,001	200,000
OR[5,7]	1133	117,700	330.8	0.2693	10.45	1099	100,001	200,000
OR[5,8]	1.351	13	0.04127	0.06476	0.601	5.613	100,001	200,000
OR[5,9]	5.107	431.8	0.964	0.04742	0.6859	10.67	100,001	200,000
OR[6,7]	83.25	4380	29.29	0.0845	2.501	180.1	100,001	200,000
OR[6,8]	0.8665	32.12	0.07764	0.005902	0.1475	2.731	100,001	200,000
OR[6,9]	26.11	10,530	23.55	0.004559	0.1674	4.631	100,001	200,000
OR[7,8]	1.037	169.8	0.3847	6.35×10^{-4}	0.05713	1.861	100,001	200,000
OR[7,9]	20.67	5441	12.17	4.50×10^{-4}	0.0643	4.102	100,001	200,000
OR[8,9]	7.098	382.1	0.8866	0.06605	1.146	20.08	100,001	200,000

Median ranks

TABLE 160 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	4.718	1.504	0.01493	2	5	7	100,001	200,000
rk.class[2]	3.238	1.793	0.0165	1	3	7	100,001	200,000
rk.class[3]	4.044	2.134	0.01497	1	4	8	100,001	200,000
rk.class[4]	3.814	2.477	0.01057	1	4	8	100,001	200,000
rk.class[5]	6.438	1.479	0.01284	2	7	8	100,001	200,000
rk.class[6]	7.125	1.44	0.01217	3	8	8	100,001	200,000
rk.class[7]	3.128	1.385	0.009781	1	3	6	100,001	200,000
rk.class[8]	3.495	1.948	0.01222	1	3	7	100,001	200,000

TABLE 161 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	5.523	1.667	0.01742	2	6	8	100,001	200,000
rk[2]	3.66	2.179	0.02084	1	3	8	100,001	200,000
rk[3]	4.599	2.555	0.01836	1	4	9	100,001	200,000
rk[4]	3.355	2.229	0.01983	1	3	8	100,001	200,000
rk[5]	4.82	1.842	0.01277	1	5	8	100,001	200,000
rk[6]	7.444	1.66	0.01503	2	8	9	100,001	200,000
rk[7]	8.128	1.631	0.01371	3	9	9	100,001	200,000
rk[8]	3.518	1.677	0.01318	1	3	7	100,001	200,000
rk[9]	3.953	2.31	0.01463	1	4	9	100,001	200,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Children and adolescents: acceptability (dropouts) – sensitivity analysis 2 (incomplete outcome data)

See *Table 46* for a summary.

TABLE 162 Raw data used

Study	r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	r[,4]	n[,4]	na[]	t[,1]	t[,2]	t[,3]	t[,4]
Asbahr *et al.*, 2005[216]	1.5	21	0.5	21	NA	NA	NA	NA	2	6	9	NA	NA
Bolton and Perrin, 2008[218]	0.5	11	2.5	11	NA	NA	NA	NA	2	2	8	NA	NA
Bolton *et al.*, 2011[219]	3	24	2	36	NA	NA	NA	NA	2	2	9	NA	NA
de Haan *et al.*, 1998[220]	0.5	11	1.5	14	NA	NA	NA	NA	2	7	8	NA	NA
DeVeaugh-Geiss *et al.*, 1992[221]	2	29	4	31	NA	NA	NA	NA	2	1	7	NA	NA
Freeman *et al.*, 2008[223]	5	20	6	22	NA	NA	NA	NA	2	3	9	NA	NA
Geller *et al.*, 2001[224]	12	32	22	71	NA	NA	NA	NA	2	1	4	NA	NA
Liebowitz *et al.*, 2002[226]	4	22	1	21	NA	NA	NA	NA	2	1	4	NA	NA
March *et al.*, 1998[228]	13	95	18	92	NA	NA	NA	NA	2	1	6	NA	NA
Piacentini *et al.*, 2011[230]	5	22	8	49	NA	NA	NA	NA	2	3	9	NA	NA
Riddle *et al.*, 1992[231]	1	6	1	7	NA	NA	NA	NA	2	1	4	NA	NA
Riddle *et al.*, 2001[232]	27	63	19	57	NA	NA	NA	NA	2	1	5	NA	NA
Storch *et al.*, 2011[233]	0.5	16	2.5	17	NA	NA	NA	NA	2	2	9	NA	NA
Storch *et al.*, 2013[234]	6	14	3	16	NA	NA	NA	NA	2	10	11	NA	NA
The Pediatric OCD Treatment Study, 2004[236]	7	28	2	28	3	28	3	28	4	1	6	9	10
Williams *et al.*, 2010[235]	1	10	1	11	NA	NA	NA	NA	2	2	9	NA	NA

NA, not available.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

Key: intervention (class)

1. Placebo (1).
2. Waitlist (2).
3. Psychological placebo (3).
4. Fluoxetine (4).
5. Fluvoxamine (4).
6. Sertraline (4).
7. Clomipramine (5).
8. BT (6).
9. CBT (7).
10. CBT + sertraline (8).
11. CBT + placebo (9).

TABLE 163 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[1,2]	0.9409	8.238	0.0271	0.04177	0.4769	4.166	100,001	200,000
OR.D[1,3]	1.162	20.74	0.05403	0.05146	0.5519	4.709	100,001	200,000
OR.D[1,4]	323.1	74,690	167.2	0.05674	0.7056	7.78	100,001	200,000
OR.D[1,5]	4.559	31.82	0.1309	0.2264	2.013	20.91	100,001	200,000
OR.D[1,6]	130.6	11,210	55.65	0.2705	5.953	307.3	100,001	200,000
OR.D[1,7]	0.6984	2.111	0.01182	0.07205	0.4809	2.387	100,001	200,000
OR.D[1,8]	0.8992	4.497	0.01937	0.06399	0.519	3.502	100,001	200,000
OR.D[1,9]	0.9197	47.47	0.1255	0.006346	0.1373	2.595	100,001	200,000
OR.D[2,3]	2.362	16.71	0.04775	0.1402	1.159	10.14	100,001	200,000
OR.D[2,4]	693.5	140,500	313.1	0.06187	1.48	38.89	100,001	200,000
OR.D[2,5]	19.6	260.4	0.9916	0.258	4.276	99	100,001	200,000
OR.D[2,6]	546.2	100,600	378.3	0.7216	12.23	775.6	100,001	200,000
OR.D[2,7]	1.451	3.293	0.01678	0.2085	0.9965	5.226	100,001	200,000
OR.D[2,8]	4.23	172.5	0.4978	0.07702	1.073	17.45	100,001	200,000
OR.D[2,9]	7.159	916	2.08	0.008978	0.2873	10.88	100,001	200,000
OR.D[3,4]	1253	324,800	724.4	0.05251	1.285	32.02	100,001	200,000
OR.D[3,5]	44.45	6459	14.47	0.2018	3.748	92.32	100,001	200,000
OR.D[3,6]	525	70,130	275.8	0.3997	10.81	842	100,001	200,000
OR.D[3,7]	1.161	2.123	0.008579	0.208	0.8647	3.616	100,001	200,000
OR.D[3,8]	4.912	612.9	1.385	0.06947	0.9334	13.59	100,001	200,000
OR.D[3,9]	9.693	1846	4.138	0.008141	0.2491	8.657	100,001	200,000
OR.D[4,5]	2292	4.33×10^5	965.6	0.1206	2.9	83.47	100,001	200,000
OR.D[4,6]	1.10×10^4	1.64×10^6	3716	0.1866	8.626	893.3	100,001	200,000
OR.D[4,7]	891.5	222,800	501.7	0.03788	0.6786	11.68	100,001	200,000
OR.D[4,8]	1501	500,300	1136	0.03585	0.7311	15.94	100,001	200,000
OR.D[4,9]	512.7	151,200	340.3	0.004535	0.1964	9.29	100,001	200,000
OR.D[5,6]	30.75	618.7	5.422	0.1535	2.88	138.2	100,001	200,000
OR.D[5,7]	1.345	281.2	0.6446	0.01375	0.2306	3.039	100,001	200,000
OR.D[5,8]	1.186	57.18	0.1337	0.01204	0.2456	4.467	100,001	200,000
OR.D[5,9]	2.598	552.8	1.244	0.001577	0.06598	2.639	100,001	200,000
OR.D[6,7]	0.344	17.33	0.04053	0.001409	0.08033	1.582	100,001	200,000
OR.D[6,8]	0.5686	11.68	0.03208	0.001141	0.08434	2.951	100,001	200,000
OR.D[6,9]	1.336	220.7	0.5204	1.77×10^{-4}	0.02216	1.646	100,001	200,000
OR.D[7,8]	2.403	28.68	0.08785	0.1208	1.076	10.36	100,001	200,000
OR.D[7,9]	3.044	271.4	0.6238	0.01256	0.2917	7.321	100,001	200,000
OR.D[8,9]	0.6063	7.055	0.01773	0.0269	0.2772	2.556	100,001	200,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 164 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[1,2]	0.9409	8.238	0.0271	0.04177	0.4769	4.166	100,001	200,000
OR[1,3]	1.162	20.74	0.05403	0.05146	0.5519	4.709	100,001	200,000
OR[1,4]	0.7185	0.5733	0.003248	0.1921	0.6427	1.702	100,001	200,000
OR[1,5]	0.8515	2.364	0.00837	0.18	0.6874	2.306	100,001	200,000
OR[1,6]	0.9138	0.9901	0.005231	0.2467	0.7994	2.183	100,001	200,000
OR[1,7]	4.559	31.82	0.1309	0.2264	2.013	20.91	100,001	200,000
OR[1,8]	130.6	11,210	55.65	0.2705	5.953	307.3	100,001	200,000
OR[1,9]	0.6984	2.111	0.01182	0.07205	0.4809	2.387	100,001	200,000
OR[1,10]	0.8992	4.497	0.01937	0.06399	0.519	3.502	100,001	200,000
OR[1,11]	0.9197	47.47	0.1255	0.006346	0.1373	2.595	100,001	200,000
OR[2,3]	2.362	16.71	0.04775	0.1402	1.159	10.14	100,001	200,000
OR[2,4]	4.048	85	0.293	0.1189	1.332	16.43	100,001	200,000
OR[2,5]	5.451	303.6	0.7032	0.1237	1.429	19.91	100,001	200,000
OR[2,6]	3.901	29.03	0.135	0.1811	1.673	18.02	100,001	200,000
OR[2,7]	19.6	260.4	0.9916	0.258	4.276	99	100,001	200,000
OR[2,8]	546.2	100,600	378.3	0.7216	12.23	775.6	100,001	200,000
OR[2,9]	1.451	3.293	0.01678	0.2085	0.9965	5.226	100,001	200,000
OR[2,10]	4.23	172.5	0.4978	0.07702	1.073	17.45	100,001	200,000
OR[2,11]	7.159	916	2.08	0.008978	0.2873	10.88	100,001	200,000
OR[3,4]	3.342	67.2	0.1859	0.1036	1.16	13.52	100,001	200,000
OR[3,5]	4.468	155.6	0.4065	0.1076	1.245	16.12	100,001	200,000
OR[3,6]	3.579	146	0.3305	0.161	1.453	14.04	100,001	200,000
OR[3,7]	44.45	6459	14.47	0.2018	3.748	92.32	100,001	200,000
OR[3,8]	525	70,130	275.8	0.3997	10.81	842	100,001	200,000
OR[3,9]	1.161	2.123	0.008579	0.208	0.8647	3.616	100,001	200,000
OR[3,10]	4.912	612.9	1.385	0.06947	0.9334	13.59	100,001	200,000
OR[3,11]	9.693	1846	4.138	0.008141	0.2491	8.657	100,001	200,000
OR[4,5]	1.589	7.636	0.02302	0.2631	1.031	5.289	100,001	200,000
OR[4,6]	1.713	8.746	0.02764	0.351	1.155	5.412	100,001	200,000
OR[4,7]	10.99	613.5	1.773	0.3015	3.197	44.76	100,001	200,000
OR[4,8]	281.9	29,060	112	0.3747	9.569	575	100,001	200,000
OR[4,9]	1.335	7.801	0.03151	0.1006	0.7536	5.269	100,001	200,000
OR[4,10]	1.919	35.42	0.09533	0.08909	0.8093	7.612	100,001	200,000
OR[4,11]	3.761	465.6	1.106	0.009238	0.2194	5.183	100,001	200,000
OR[5,6]	1.689	10.48	0.02893	0.2646	1.09	5.342	100,001	200,000
OR[5,7]	10.61	303.4	0.7695	0.2478	2.978	43.33	100,001	200,000

TABLE 164 Individual effects (*continued*)

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[5,8]	232	14,570	74.32	0.3297	8.827	556.1	100,001	200,000
OR[5,9]	1.332	9.608	0.03469	0.08188	0.7004	5.164	100,001	200,000
OR[5,10]	2.526	133.9	0.32	0.07279	0.7585	7.397	100,001	200,000
OR[5,11]	5.982	1149	2.583	0.008041	0.2022	4.912	100,001	200,000
OR[6,7]	7.599	152.4	0.4333	0.249	2.535	33.89	100,001	200,000
OR[6,8]	188.7	13,640	73.49	0.3203	7.444	430.4	100,001	200,000
OR[6,9]	0.8856	1.744	0.01158	0.1004	0.6035	3.192	100,001	200,000
OR[6,10]	1.227	16.02	0.04059	0.08275	0.6481	4.863	100,001	200,000
OR[6,11]	1.85	310.7	0.7309	0.008378	0.1736	3.568	100,001	200,000
OR[7,8]	30.75	618.7	5.422	0.1535	2.88	138.2	100,001	200,000
OR[7,9]	1.345	281.2	0.6446	0.01375	0.2306	3.039	100,001	200,000
OR[7,10]	1.186	57.18	0.1337	0.01204	0.2456	4.467	100,001	200,000
OR[7,11]	2.598	552.8	1.244	0.001577	0.06598	2.639	100,001	200,000
OR[8,9]	0.344	17.33	0.04053	0.001409	0.08033	1.582	100,001	200,000
OR[8,10]	0.5686	11.68	0.03208	0.001141	0.08434	2.951	100,001	200,000
OR[8,11]	1.336	220.7	0.5204	1.77×10^{-4}	0.02216	1.646	100,001	200,000
OR[9,10]	2.403	28.68	0.08785	0.1208	1.076	10.36	100,001	200,000
OR[9,11]	3.044	271.4	0.6238	0.01256	0.2917	7.321	100,001	200,000
OR[10,11]	0.6063	7.055	0.01773	0.0269	0.2772	2.556	100,001	200,000

Median ranks

TABLE 165 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	6.095	1.553	0.02176	3	6	9	100,001	200,000
rk.class[2]	4.004	2.131	0.02932	1	4	8	100,001	200,000
rk.class[3]	4.418	2.155	0.02419	1	4	9	100,001	200,000
rk.class[4]	4.886	2.138	0.01902	1	5	9	100,001	200,000
rk.class[5]	7.119	1.902	0.02102	2	8	9	100,001	200,000
rk.class[6]	8.213	1.55	0.02074	3	9	9	100,001	200,000
rk.class[7]	3.877	1.582	0.01946	1	4	7	100,001	200,000
rk.class[8]	4.272	2.058	0.02425	1	4	8	100,001	200,000
rk.class[9]	2.117	1.903	0.01846	1	1	8	100,001	200,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 166 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	7.678	1.802	0.02494	4	8	11	100,001	200,000
rk[2]	4.73	2.867	0.04154	1	4	10	100,001	200,000
rk[3]	5.226	2.898	0.03468	1	5	10	100,001	200,000
rk[4]	5.403	2.308	0.02558	1	5	10	100,001	200,000
rk[5]	5.733	2.417	0.02381	1	6	10	100,001	200,000
rk[6]	6.491	2.104	0.02158	2	7	10	100,001	200,000
rk[7]	8.794	2.463	0.02683	2	10	11	100,001	200,000
rk[8]	10.04	2.015	0.02746	3	11	11	100,001	200,000
rk[9]	4.523	2.189	0.02989	1	4	9	100,001	200,000
rk[10]	5.013	2.748	0.03233	1	5	10	100,001	200,000
rk[11]	2.369	2.431	0.02302	1	1	10	100,001	200,000

Children and adolescents: acceptability (dropouts) – sensitivity analysis 3 (blinding)

See *Table 47* for a summary.

TABLE 167 Raw data used

Study	r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	r[,4]	n[,4]	na[]	t[,1]	t[,2]	t[,3]	t[,4]
Asbahr *et al.*, 2005[216]	1.5	21	0.5	21	NA	NA	NA	NA	2	6	7	NA	NA
Bolton *et al.*, 2011[219]	3	24	2	36	NA	NA	NA	NA	2	2	7	NA	NA
Freeman *et al.*, 2008[223]	5	20	6	22	NA	NA	NA	NA	2	3	7	NA	NA
Liebowitz *et al.*, 2002[226]	4	22	1	21	NA	NA	NA	NA	2	1	4	NA	NA
Piacentini *et al.*, 2011[230]	5	22	8	49	NA	NA	NA	NA	2	3	7	NA	NA
Riddle *et al.*, 2001[232]	27	63	19	57	NA	NA	NA	NA	2	1	5	NA	NA
Storch *et al.*, 2011[233]	0.5	16	2.5	17	NA	NA	NA	NA	2	2	7	NA	NA
Storch *et al.*, 2013[234]	6	14	3	16	NA	NA	NA	NA	2	8	9	NA	NA
The Pediatric OCD Treatment Study, 2004[236]	7	28	2	28	3	28	3	28	4	1	6	7	8
Williams *et al.*, 2010[235]	1	10	1	11	NA	NA	NA	NA	2	2	7	NA	NA

NA, not available.

Notes

t[i,1], type of treatment [i] per arm [1] – [i] takes the values 1 = placebo, 2 = waitlist, 3 = fluoxetine, 4 = fluvoxamine, 5 = paroxetine, 6 = sertraline, 7 = citalopram, 8 = venlafaxine, 9 = clomipramine, 10 = BT, 11 = CBT, 12 = CT, 13 = hypericum, 14 = fluvoxamine and CBT, 15 = clomipramine and BT, 16 = escitalopram, 17 = psychological placebo; t[i,2], type of treatment [i] per arm [2]; t[i,3], type of treatment [i] per arm [3]; t[i,4], type of treatment [i] per arm [4]; y[i,1], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [1]; y[i,2], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [2]; y[i,3], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [3]; y[i,4], total mean YBOCS scores at end of study (positive) or mean change from baseline (negative) for arm [4]; n[i,1], total number of patients for arm [1]; n[i,2], total number of patients for arm [2]; n[i,3], total number of patients for arm [3]; n[i,4], total number of patients for arm [4]; sd[i,1], SD of mean total score or change from baseline for arm [1]; sd[i,2], SD of mean total score or change from baseline for arm [2]; sd[i,3], SD of mean total score or change from baseline for arm [3]; sd[i,4], SD of mean total score or change from baseline for arm [4].

Key: intervention (class)

1. Placebo (1).
2. Waitlist (2).
3. Psychological placebo (3).
4. Fluoxetine (4).
5. Fluvoxamine (4).
6. Sertraline (4).
7. CBT (5).
8. CBT + sertraline (6).
9. CBT + placebo (7).

TABLE 168 Class effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR.D[1,2]	3.763	305.6	0.9887	0.008369	0.2633	4.365	91,001	200,000
OR.D[1,3]	82.62	19,310	44.19	0.01173	0.3215	5.323	91,001	200,000
OR.D[1,4]	372.9	54,740	121.5	0.006197	0.3773	15.56	91,001	200,000
OR.D[1,5]	1.043	40.1	0.1593	0.01888	0.2756	2.5	91,001	200,000
OR.D[1,6]	4.388	634.1	2.031	0.02267	0.3584	4.282	91,001	200,000
OR.D[1,7]	2549	906,900	2023	0.001884	0.09901	4.014	91,001	200,000
OR.D[2,3]	37.09	4857	10.85	0.09322	1.202	20.43	91,001	200,000
OR.D[2,4]	7017	1.49E+06	3328	0.01486	1.384	168.8	91,001	200,000
OR.D[2,5]	2.246	36.64	0.08773	0.1656	1.041	8.465	91,001	200,000
OR.D[2,6]	350.7	56,730	127.7	0.05515	1.332	47.05	91,001	200,000
OR.D[2,7]	40,130	1.12E+07	25,170	0.005716	0.3793	35.75	91,001	200,000
OR.D[3,4]	6359	1.40E+06	3131	0.01157	1.136	130.7	91,001	200,000
OR.D[3,5]	2.005	53.18	0.125	0.1408	0.8544	5.568	91,001	200,000
OR.D[3,6]	773.2	221,200	495.5	0.04658	1.104	32.98	91,001	200,000
OR.D[3,7]	49,850	2.04E+07	45,660	0.004622	0.3091	24.7	91,001	200,000
OR.D[4,5]	1407	168,400	372.8	0.01008	0.7556	50.93	91,001	200,000
OR.D[4,6]	1829	232,900	522.6	0.01211	0.974	87.08	91,001	200,000
OR.D[4,7]	5410	1.32E+06	2957	0.001433	0.2713	56.51	91,001	200,000
OR.D[5,6]	30.1	4063	9.31	0.08929	1.287	21.18	91,001	200,000
OR.D[5,7]	1781	433,200	979.3	0.007595	0.3615	18.66	91,001	200,000
OR.D[6,7]	449.2	191,700	427.9	0.01618	0.285	4.439	91,001	200,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 169 Individual effects

Interventions compared	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
OR[1,2]	3.763	305.6	0.9887	0.008369	0.2633	4.365	91,001	200,000
OR[1,3]	82.62	19,310	44.19	0.01173	0.3215	5.323	91,001	200,000
OR[1,4]	0.7078	9.981	0.02973	0.01278	0.2972	2.497	91,001	200,000
OR[1,5]	1.361	39.79	0.09724	0.0647	0.542	3.524	91,001	200,000
OR[1,6]	2.148	550.9	1.256	0.03273	0.3309	2.428	91,001	200,000
OR[1,7]	1.043	40.1	0.1593	0.01888	0.2756	2.5	91,001	200,000
OR[1,8]	4.388	634.1	2.031	0.02267	0.3584	4.282	91,001	200,000
OR[1,9]	2549	906,900	2023	0.001884	0.09901	4.014	91,001	200,000
OR[2,3]	37.09	4857	10.85	0.09322	1.202	20.43	91,001	200,000
OR[2,4]	909.1	322,300	726.3	0.0211	1.063	49.41	91,001	200,000
OR[2,5]	759.3	114,200	268.3	0.07927	2.04	83.19	91,001	200,000
OR[2,6]	56.27	9489	22.25	0.07649	1.23	31.66	91,001	200,000
OR[2,7]	2.246	36.64	0.08773	0.1656	1.041	8.465	91,001	200,000
OR[2,8]	350.7	56,730	127.7	0.05515	1.332	47.05	91,001	200,000
OR[2,9]	40,130	1.12E+07	25170	0.005716	0.3793	35.75	91,001	200,000
OR[3,4]	326.9	50,620	116.6	0.01739	0.8772	36.11	91,001	200,000
OR[3,5]	472.8	64,440	151.3	0.0607	1.665	61.34	91,001	200,000
OR[3,6]	75.49	11,180	25.07	0.06565	1.011	21.89	91,001	200,000
OR[3,7]	2.005	53.18	0.125	0.1408	0.8544	5.568	91,001	200,000
OR[3,8]	773.2	221,200	495.5	0.04658	1.104	32.98	91,001	200,000
OR[3,9]	49,850	2.04E+07	45,660	0.004622	0.3091	24.7	91,001	200,000
OR[4,5]	94.89	12,400	29.51	0.1718	1.59	59.8	91,001	200,000
OR[4,6]	135.6	24,550	54.73	0.07889	1.074	32.55	91,001	200,000
OR[4,7]	55.09	9875	22.29	0.04075	0.9672	34.13	91,001	200,000
OR[4,8]	164.9	25,630	57.6	0.04778	1.253	54.58	91,001	200,000
OR[4,9]	2876	4.79E+05	1121	0.004735	0.3589	37.53	91,001	200,000
OR[5,6]	10.24	1850	4.172	0.04129	0.6941	6.434	91,001	200,000
OR[5,7]	20.95	5141	11.65	0.02488	0.5203	8.125	91,001	200,000
OR[5,8]	96.62	19,130	46.34	0.029	0.6658	14.55	91,001	200,000
OR[5,9]	1.35E+06	6.03E+08	1.35E+06	0.002772	0.1847	12.21	91,001	200,000
OR[6,7]	1.954	31.68	0.1074	0.07761	0.8458	7.118	91,001	200,000
OR[6,8]	7.992	449.5	1.027	0.07516	1.106	14.78	91,001	200,000
OR[6,9]	893.2	206,200	460.9	0.006087	0.3081	13.37	91,001	200,000
OR[7,8]	30.1	4063	9.31	0.08929	1.287	21.18	91,001	200,000
OR[7,9]	1781	433,200	979.3	0.007595	0.3615	18.66	91,001	200,000
OR[8,9]	449.2	191,700	427.9	0.01618	0.285	4.439	91,001	200,000

Median ranks

TABLE 170 Median ranks: class effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk.class[1]	6.162	1.207	0.01402	3	7	7	91,001	200,000
rk.class[2]	3.612	1.885	0.02214	1	3	7	91,001	200,000
rk.class[3]	4.006	1.792	0.01616	1	4	7	91,001	200,000
rk.class[4]	4.123	1.991	0.01434	1	4	7	91,001	200,000
rk.class[5]	3.587	1.341	0.01295	1	4	6	91,001	200,000
rk.class[6]	4.209	1.688	0.01611	1	4	7	91,001	200,000
rk.class[7]	2.3	1.794	0.01636	1	1	7	91,001	200,000

TABLE 171 Median ranks: individual effects

Intervention code	Mean	SD	MC_error	val2.5pc	Median	val97.5pc	Start	Sample
rk[1]	7.961	1.434	0.01674	4	8	9	91,001	200,000
rk[2]	4.425	2.559	0.03144	1	4	9	91,001	200,000
rk[3]	4.918	2.445	0.02401	1	5	9	91,001	200,000
rk[4]	4.472	2.465	0.02435	1	4	9	91,001	200,000
rk[5]	6.116	2.142	0.01966	2	7	9	91,001	200,000
rk[6]	4.821	2.033	0.01934	1	5	9	91,001	200,000
rk[7]	4.374	1.862	0.02014	1	4	8	91,001	200,000
rk[8]	5.18	2.29	0.02194	2	5	9	91,001	200,000
rk[9]	2.733	2.384	0.02166	1	1	9	91,001	200,000

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 10 Economic evaluation

Office for National Statistics life tables stratified by age and gender

TABLE 172 Mortality rates between age x and $(x + 1)$

Age (years)	Males	Females
12 (mean age of children and adolescents)	0.0001	0.0001
13	0.0001	0.0001
14	0.0001	0.0001
15	0.0002	0.0001
16	0.0002	0.0001
17	0.0004	0.0002
18	0.0005	0.0002
36 (mean age of adults)	0.0011	0.0006
37	0.0012	0.0007
38	0.0013	0.0008
39	0.0014	0.0008
40	0.0016	0.0009
41	0.0016	0.0010
42	0.0018	0.0011

PubMed search strategy for longitudinal studies of the course of obsessive–compulsive disorder symptom severity conducted October 2014

Search	Search term	Hits
#1	Case control studies [MeSH Terms]	667,981
#2	Cohort studies [MeSH Terms]	1,355,328
#3	Case control [Text Word]	210,456
#4	Cohort analy*[Text Word]	4462
#5	Longitudinal [Text Word]	186,703
#6	#1 Or #2 Or #3 Or #4 Or #5	1,605,453
#7	#6 AND (obsessive*AND compulsi*)	1995
#8	#7 AND (yale Or brown or scale)	561

MeSH, Medical Subject Heading.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Search strategy for studies of utility scores in patients with obsessive–compulsive disorder conducted August 2014

Date	Database	Number of hits	Total hits this database	Total hits overall
5 August 2013	MEDLINE 1950 to present on Ovid	403	403	
6 August 2013	MEDLINE In-Process & Other Non-Indexed Citations – current week	44	44	447

Database: MEDLINE 1950 to present

Date of search: 5 August 2014.

Search strategy

1. exp quality of life/ (119,318)
2. quality of life.tw. (137,047)
3. life quality.tw. (3389)
4. hql.tw. (81)
5. (sf 36 or sf36 or sf thirtysix or sf thirty six or short form 36 or short form thirty six or short form thirty-six or short form 36).tw. (15,158)
6. qol.tw. (17,845)
7. (euroqol or eq5d or eq 5d).tw. (3723)
8. qaly$.tw. (4832)
9. quality adjusted life year$.tw. (5700)
10. hye$.tw. (630)
11. health$ year$ equivalent$.tw. (38)
12. health utilit$.tw. (1062)
13. hui.tw. (643)
14. quality of wellbeing$.tw. (6)
15. quality of well being.tw. (323)
16. qwb.tw. (166)
17. (qald$ or qale$ or qtime$).tw. (110)
18. standard gamble$.tw. (650)
19. time trade off.tw. (728)
20. time tradeoff.tw. (199)
21. tto.tw. (576)
22. visual analog$ scale$.tw. (26,566)
23. discrete choice experiment$.tw. (414)
24. (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or short form six or short form six).tw. (984)
25. health state$ utilit$.tw. (281)
26. health state$ value$.tw. (128)
27. health state$ preference$.tw. (83)
28. or/1-27 (213341)
29. obsessive compulsive disorder/ (11,322)
30. (obsess$ and (personalit$ or compuls$)).tw. (11,266)
31. or/29-30 (15,018)
32. 28 and 31 (403)

Database: MEDLINE In-Process & Other Non-Indexed Citations – current week

Date of search: 6 August 2014.

Search strategy

1. exp quality of life/ (0)
2. quality of life.tw. (15,810)
3. life quality.tw. (385)
4. hql.tw. (5)
5. (sf 36 or sf36 or sf thirtysix or sf thirty six or short form 36 or short form thirty six or short form thirty-six or short form 36).tw. (1455)
6. qol.tw. (2086)
7. (euroqol or eq5d or eq 5d).tw. (601)
8. qaly$.tw. (563)
9. quality adjusted life year$.tw. (649)
10. hye$.tw. (69)
11. health$ year$ equivalent$.tw. (1)
12. health utilit$.tw. (113)
13. hui.tw. (81)
14. quality of wellbeing$.tw. (2)
15. quality of well being.tw. (11)
16. qwb.tw. (6)
17. (qald$ or qale$ or qtime$).tw. (16)
18. standard gamble$.tw. (39)
19. time trade off.tw. (56)
20. time tradeoff.tw. (7)
21. tto.tw. (62)
22. visual analog$ scale$.tw. (3247)
23. discrete choice experiment$.tw. (80)
24. (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or short form six or short form six).tw. (398)
25. health state$ utilit$.tw. (35)
26. health state$ value$.tw. (11)
27. health state$ preference$.tw. (10)
28. or/1-27 (20097)
29. obsessive compulsive disorder/ (0)
30. (obsess$ and (personalit$ or compuls$)).tw. (1072)
31. or/29-30 (1072)
32. 28 and 31 (44)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Results of other sensitivity analyses: adults

TABLE 173 Low overall attrition

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
FLV + CBT	7273	3.221	57,144	89,352
CBT	7477	3.234	57,212	89,557
SSRIs	5845	3.195	58,045	89,990
VEN	5801	3.202	58,229	90,244
CLO	5719	3.223	58,744	90,975
CT	6579	3.335	60,131	93,486
BT	6713	3.343	60,139	93,566
CLO + BT				

CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

TABLE 174 Low risk of bias in 'incomplete outcome assessment'

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
CBT	7451	3.221	56,972	89,183
CLO	5894	3.180	57,711	89,514
SSRIs	5866	3.189	57,909	89,796
BT	6963	3.244	57,909	90,345
VEN	5846	3.191	57,965	89,870
CLO + BT	6892	3.260	58,318	90,923
CT				
FLV + CBT				

CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

TABLE 175 Low risk of bias in 'blinding of outcome assessor'

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
CBT	7533	3.180	56,063	87,861
SSRIs	5937	3.172	57,495	89,210
VEN	5902	3.177	57,639	89,409
CLO	5894	3.181	57,721	89,528
BT	6915	3.271	58,514	91,228
CLO + BT	6929	3.272	58,516	91,238
CT	6744	3.277	58,803	91,576
FLV + CBT				

CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

TABLE 176 Definition of full response

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
CBT	7567	3.207	56,565	88,631
FLV + CBT	7306	3.196	56,619	88,582
SSRIs	5901	3.182	57,745	89,568
CLO	5869	3.188	57,897	89,779
VEN	5852	3.191	57,970	89,881
CLO + BT	6891	3.274	58,579	91,314
CT	6707	3.286	59,021	91,885
BT	6820	3.297	59,111	92,076

CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

TABLE 177 Cost of initial therapy (minimum)

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
FLV + CBT	6412	3.219	57,968	90,158
CBT	6498	3.238	58,267	90,649
SSRIs	5770	3.208	58,390	90,471
CLO	5737	3.215	58,563	90,713
VEN	5724	3.220	58,668	90,863
CLO + BT	6186	3.299	59,799	92,792
CT	5986	3.313	60,272	93,401
BT	6119	3.320	60,291	93,495

CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

TABLE 178 Transition from full to partial response

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
FLV + CBT	7047	3.255	58,051	90,601
CBT	7233	3.283	58,418	91,243
SSRIs	5585	3.254	59,494	92,033
CLO	5558	3.259	59,614	92,200
VEN	5521	3.266	59,801	92,462
CLO + BT	6665	3.325	59,830	93,078
BT	6620	3.342	60,218	93,637
CT	6483	3.337	60,259	93,629

CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 179 Change cost of long-term care

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
FLV + CBT	6615	3.219	57,765	89,955
CBT	6774	3.238	57,991	90,373
SSRIs	5237	3.208	58,924	91,004
CLO	5176	3.215	59,124	91,274
VEN	5137	3.220	59,254	91,450
CLO + BT	5912	3.299	60,074	93,067
CT	5678	3.313	60,580	93,709
BT	5777	3.320	60,633	93,838

CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

TABLE 180 Low cost of SSRI

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
FLV + CBT	7206	3.219	57,174	89,364
CBT	7428	3.238	57,337	89,719
SSRIs	5764	3.208	58,396	90,477
CLO	5751	3.215	58,549	90,699
VEN	5727	3.220	58,664	90,860
CLO + BT	6778	3.299	59,208	92,201
CT	6590	3.313	59,668	92,797
BT	6715	3.320	59,695	92,899

CLO, clomipramine; FLV, fluvoxamine; VEN, venlafaxine.

Results of other sensitivity analyses: children and adolescents

TABLE 181 Low overall attrition

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
BT	6905	3.257	58,242	90,816
CLO	5578	3.266	59,735	92,392
SSRIs	5538	3.277	59,993	92,758
CBT	6615	3.339	60,166	93,556
SER + CBT	6562	3.350	60,437	93,936

CLO, clomipramine; SER, sertraline.

TABLE 182 Low risk of bias in 'incomplete outcome assessment'

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
BT	6780	3.268	58,580	91,259
CLO	5457	3.294	60,431	93,375
CBT	6469	3.365	60,829	94,478
SSRIs	5390	3.312	60,848	93,967
SER + CBT	6422	3.374	61,052	94,789

CLO, clomipramine; SER, sertraline.

TABLE 183 Low risk of bias in 'blinding of outcome assessor'

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
CBT	6732	3.298	£59,223	£92,201
SSRIs	5610	3.259	£59,574	£92,166
SER + CBT	6618	3.319	£59,754	£92,940

CLO, clomipramine; SER, sertraline.

TABLE 184 Definition of full response

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
BT	6807	3.244	58,080	90,523
CLO	5590	3.263	59,677	92,311
SSRIs	5506	3.286	60,216	93,077
CBT	6572	3.343	60,289	93,719
SER + CBT	6518	3.354	60,561	94,101

CLO, clomipramine; SER, sertraline.

TABLE 185 Cost of initial therapy (minimum)

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
BT	6376	3.254	58,710	91,254
CLO	5508	3.280	60,094	92,895
SSRIs	5381	3.311	60,840	93,951
CBT	6017	3.368	61,347	95,028
SER + CBT	5976	3.376	61,549	95,311

CLO, clomipramine; SER, sertraline.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Skapinakis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 186 Transition from full to partial response

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
BT	6619	3.286	59,102	91,963
CLO	5360	3.315	60,931	94,077
CBT	6328	3.397	61,616	95,588
SER + CBT	6302	3.402	61,739	95,760
SSRIs	5220	3.350	61,776	95,274

CLO, clomipramine; SER, sertraline.

TABLE 187 Change cost of long-term care

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
BT	6073	3.254	59,014	91,557
CLO	4740	3.280	60,862	93,663
SSRIs	4515	3.311	61,707	94,818
CBT	5383	3.368	61,980	95,662
SER + CBT	5314	3.376	62,210	95,972

CLO, clomipramine; SER, sertraline.

TABLE 188 Low cost of SSRIs

Intervention	Total costs, £	Total QALYs	NMB (£20,000), £	NMB (£30,000), £
BT	6762	3.254	58,325	90,868
CLO	5515	3.280	60,087	92,888
SSRIs	5378	3.311	60,844	93,954
CBT	6459	3.368	60,905	94,586
SER + CBT	6418	3.376	61,107	94,869

CLO, clomipramine; SER, sertraline.

EME
HS&DR
HTA
PGfAR
PHR

Part of the NIHR Journals Library
www.journalslibrary.nihr.ac.uk

This report presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health

Published by the NIHR Journals Library