Web-Based Rumination-Focused Cognitive Behavioural Therapy (i-RFCBT) for High-Ruminating University Students: an examination of feasibility and efficacy

Submitted by Lorna Zoe Cook to the University of Exeter as a thesis for the degree of

Doctor of Philosophy in Psychology, January 2020

I certify that all material in this thesis which is not my own work has been identified and that no material has previously been submitted and approved for the award of a degree by this or any other University.

Signature: ……..

Acknowledgements

To my PhD supervisors, Ed Watkins and Paul Farrand, I wish to express my sincere gratitude. I am also very grateful to the University of Exeter for the financial support that enabled me to undertake this PhD. I would also like to thank Mohammod Mostazir for his input on the statistical analyses. I am also very thankful for the help received from the following people: Jenny Cadman, Rosario Melero, Luke O'Shea, Yusuke Umegaki, Josie Bannon, Sarah Lane and Mark Sawyer. I also want to thank my family for their support and Richard, for being there throughout. Finally, special thanks to everyone who participated in my research studies.

Abstract

Depression is both highly prevalent and highly impactful in the student population. The aim of the PhD was to assess internet-based rumination-focused cognitive-behavioural therapy (i-RFCBT) as an intervention to reduce the impact of depression in university students.

The intervention was first implemented as a treatment within a university Wellbeing service. An audit of treatment usage and clinical outcomes (*N* = 82) found the intervention significantly reduced acute depressive and anxious symptoms. Within a case series subsample (*N* = 26) there were improvements in clinical outcomes as well as significant reductions in rumination, consistent with the hypothesised mechanism of change.

Acute treatment has a limited impact on the disease burden of depression within a population. A greater focus on prevention is identified as a priority. A qualitative study was conducted to investigate the acceptability of i-RFCBT as a preventive intervention.

Having established that the intervention was acceptable, the RESPOND randomised-controlled trial (*N* = 235) tested whether guided i-RFCBT was an efficacious at preventing the incidence of depression in UK undergraduates with elevated rumination and worry. The trial found that guided i-RFCBT reduced the incidence of a major depressive episode (MDE) over the course of the 12-month follow-up period by 34% relative to usual care, although this difference was not significant. Baseline stress was a significant moderator of the intervention effect, such that participants with higher stress levels experienced a significant benefit of i-RFCBT in reducing the incidence of MDE relative to usual

care. Short- to- medium- term improvements in worry, rumination and depressive symptoms were also found.

As guided interventions are limited in terms of scalability, an additional, quasi phase-II pilot feasibility arm was incorporated within the RESPOND trial to test the acceptability and estimate the effect sizes of unguided i-RFCBT. The pattern of effects for unguided i-RFCBT was similar to that of guided i-RFCBT. The clinical implications of the thesis findings are discussed.

Table of Contents

List of Tables

Table of Figures

List of abbreviations

ABC: antecedent-behaviour-consequence

AMHS: Adult Mental Health Services

ATS: Attitudes Towards Self scale

BA: Behavioural Activation

BCT: Behaviour Change Technique

BDI: Beck Depression Inventory

CACE: Complier average causal effect

CAMHS: Child and Adolescent Mental Health Services

(c/i) CBT: (computerised/internet-based) Cognitive-behavioural therapy

CES-D: Center for Epidemiologic Studies Depression Scale

CI: confidence interval

CMD: Common mental health disorder

CMS: Content Management System

CONSORT: Consolidated standards of reporting trials

CUDOS: Context, Usefulness, Development, OptionS

DALY: Disability adjusted life year

DSM-IV/-V: Diagnostic and Statistical Manual of Mental Disorders (version 4/ version 5)

EMA: Ecological momentary assessment

EPQ-R: Eysenck Personality Questionnaire-Revised Neuroticism sub-scale

ES: effect size

EU: European Union

GAD: Generalised anxiety disorder

GAD-7: Generalised anxiety disorder 7-item scale

GDP: Gross Domestic Product

GP: General practitioner

HE: Higher Education

HEI: Higher Education Institution

HINT: Habit Index of Negative Thinking

HR: Hazard ratio

HRSD: Hamilton Rating Scale for Depression

IAPT: Improving Access to Psychological Therapies

IOM: Institute of Medicine

IPT: Interpersonal therapy

IRR: Incidence rate ratio

ITT: Intention-To-Treat

MBCT: Mindfulness-based Cognitive Therapy

MDD: Major depressive disorder

MDE: Major depressive episode

MI: multiple imputation

MRC: Medical Research Council

NHS: National Health Service

NICE: National Institute for Health and Care Excellence

NNT: numbers needed to treat

NUS: Nation Union of Students

OECD: Organisation for Economic Co-operation and Development

OR: odds ratio

PHQ-8/PHQ-9: Patient health questionnaire-8 item or 9 item

PSQ: Psychosis Screening Questionnaire

PSWQ: Penn State Worry Questionnaire

PWP: Psychological Wellbeing Practitioner

RCT: Randomised controlled trial

RD: risk difference

(i-)RFCBT: (Web-based) Rumination-focused cognitive-behavioural therapy

RH: Ruminative Habit scale

RNT: repetitive negative thought

RR: relative risk

RRS: Ruminative Response Scale of the Response Styles Questionnaire

RST: Response Styles Theory

RT: repetitive thought

SAD: Social Anxiety Disorder

SCID-I: Structured Clinical Interview for DSM-IV

SMD: standardised mean difference

SRHI: Self-Report Habit Index

TAU: treatment as usual

TIDieR checklist: Template for Intervention Description and Replication

UCLA: University of California, Los Angeles

UK: United Kingdom

WHO: World Health Organisation

WMH-ICS: World Mental Health International College Student Initiative

Notes on thesis structure

This thesis reports on three studies: an open audit and multiple baseline case series; a qualitative study and a randomised-controlled trial (RCT) evaluating internet-based rumination-focused cognitive-behavioural therapy (i-RFCBT). The protocol (Chapter 5) and the outcomes (Chapter 6) of the RCT have been published. The open audit and multiple baseline case series (Chapter 3) are currently under review. The chapters reporting these studies that have been submitted for publication take a paper-based approach, with the articles reported exactly as submitted or published, with the only amendments made to formatting and numbering of tables and figures. As these papers were written as individual manuscripts, there is some repetition across these chapters. Appendix 1 details the individual contribution made by the candidate to these co-authored manuscripts.

These three chapters contain a preface that details how the study contributes to the overall body of work reported in the thesis. The overall aim of the thesis is to evaluate the effectiveness of i-RFCBT for reducing depression (both as a treatment and a preventive intervention) in university students. Both rumination and depression are highly prevalent and highly impactful in the student population and novel interventions are needed to improve student wellbeing.

The thesis begins with a review of the key literature (Chapter 1) concerning the burden of depression with a particular focus on young people and students. It outlines the case for prevention and the reasons why prevention in students may be particularly valuable in terms of reducing disease burden. The review then outlines the key definitions and concepts in prevention

research and the main findings from meta-analyses of preventive interventions in young people. Key adaptations to improve the effectiveness of preventive interventions are then discussed. First, the need for internet-based interventions to improve accessibility is outlined and the effectiveness of existing internet-based interventions discussed. Second, the case is made for targeting preventive interventions at underlying risk factors, such as rumination. The evidence for rumination as a risk factor and the development and previous evaluations of face-to-face rumination-focused cognitive-behavioural therapy (RFCBT) and internet-based RFCBT (i-RFCBT) are then presented.

The intervention under evaluation (i-RFCBT) in this thesis is then presented in greater detail in Chapter 2, following the Template for Intervention Description and Replication (TIDieR) checklist (Hoffmann et al., 2014) to improve the reporting of interventions. The aim of this chapter is therefore to provide the reader with the key features as recommended by Hoffman et al. (2014) of both the guided and unguided variants of i-RFCBT in more detail than is included in subsequent chapters.

Chapter 3 reports an open audit and multiple baseline case series of guided i-RFCBT, delivered in the Wellbeing Centre at the University of Exeter. While there is evidence of the effectiveness of i-RFCBT for the prevention of depression in young adults (Topper, Emmelkamp, Watkins, & Ehring, 2017), the effectiveness of the intervention as a treatment for students with clinical levels of depression or anxiety has not yet been tested. The aim of this study was to test the hypothesis that guided i-RFCBT would be effective for the treatment of acute symptoms of depression and anxiety, when delivered in a clinical setting.

The remaining studies presented in the thesis sought to evaluate i-RFCBT as a preventive intervention for students presenting with elevated rumination, but not currently meeting diagnostic criteria for depression. As the Topper et al. (2017) study was conducted in younger adolescents and outside the UK, it was unclear whether i-RFCBT would be acceptable and effective as a preventive intervention in UK undergraduates and the remaining studies therefore sought to test this.

Chapter 4 reports on a qualitative analysis of an online focus group conducted with high-ruminating students to assess the acceptability of internet-based interventions (as opposed to face-to-face sessions) for prevention, and the acceptability of i-RFCBT in particular, with reference to the design and content.

Chapters 5 and 6 report on the RESPOND trial. The primary aim is to replicate and extend the Topper et al. (2017) findings in a phase III randomised controlled trial, comparing guided i-RFCBT to care as usual. In addition, given the need for widespread dissemination in prevention, the feasibility and estimated effect sizes for the comparison of unguided i-RFCBT to care as usual are tested in a pilot feasibility study. Chapter 5 presents the published protocol for the RESPOND trial and Chapter 6 reports the outcomes of the trial.

The thesis concludes with a General Discussion (Chapter 7), which summarises the key findings from the individual studies, theoretical and clinical implications, strengths and limitations of the programme of work and makes suggestions for future research.

CHAPTER 1: Introduction

1.1 Overview of Chapter structure

This thesis is focused on examining the potential of internet-delivered RFCBT (i-RFCBT) for the treatment and prevention of depression in undergraduates. To provide the background for these studies, this introduction will review the prevalence and impact of depression, particularly in young people and students, and review the need for more scalable and accessible prevention interventions for undergraduates. It will then consider the evidence base for interventions in students and summarise the literature on internet interventions in this population. It will then introduce the rationale for focusing on rumination as an important mechanism in this population and the evidence that targeting rumination may be beneficial for both the treatment of acute depression and the prevention of future episodes.

1.2 The Global Burden of Depression

Depression is highly prevalent worldwide. The World Health Organisation (WHO) estimated 322 million people (4.4% of the global population) suffered from depression in 2015 (WHO, 2017). The number of people who experience depression during their lifetime has been estimated at 16.6%-19% (Kessler et al., 2005). However, the use of retrospective reports may mean this figure is an underestimate (Patten, 2003). One prospective study following a cohort from birth estimated the lifetime prevalence of depression to be as high as 41.4% (Moffitt et al., 2010).

Clinical depression is diagnosed when a constellation of symptoms meets the agreed criteria for a major depressive episode (MDE), such as those

outlined in the American Psychological Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-V; American Psychiatric Association, 2013). The two core symptoms for diagnosis are a sustained depressed mood and a loss of interest or pleasure in daily activities. Additional symptoms include: a change in appetite, difficulties sleeping, psychomotor agitation or retardation, lack of energy, feelings of worthlessness or inappropriate guilt, impaired concentration or decision-making, and recurrent thoughts about death or suicidal ideation. A diagnosis of MDE requires the presence of at least five of these symptoms, including at least one core symptom, most of the day, nearly every day for a minimum of two weeks. In addition, these symptoms must be severe enough to cause significant distress or functional impairment (e.g. to occupational or social roles).

Depression has a significant impact on the individual affected, as well as those close to them. It impacts on a wide range of domains, including physical health, education, employment, interpersonal relationships and, at its most severe, is a major factor in self-harm and suicide (WHO, 2008). Worldwide there are around 800, 000 deaths due to suicide each year and for every completed suicide there may be as many as twenty attempted suicides (WHO, 2019).

The high prevalence rates and wide-ranging negative consequences combine to make depression the single leading cause of disability worldwide, accounting for 7.5% of years lived with disability in 2015 (WHO, 2017). The World Health Organisation (2004) introduced the DALY (disability adjusted life year) as a standardised measure of burden of disease, incorporating premature death and years of 'healthy' life lost due to illness or disability. Overall,

depression was the third largest burden of disease worldwide in 2004 (WHO, 2008), and in first place among middle- and high-income countries. It is expected to be the leading cause of disease burden worldwide by 2030 (WHO, 2008).

There is also a clear gender bias in depression. Globally, 5.1% of women and 3.6% of men suffered from depression in 2015 (WHO, 2017). Additionally, for females it is the leading cause of disease burden in both high income and low to middle income countries (WHO, 2008).

With this disease burden comes a considerable economic impact. Across the European Union (EU), mental ill-health accounted for approximately 4% GDP in 2015 (600bn Euros) (OECD/EU, 2018). While the majority of this cost is direct, in terms of payment for healthcare (190bn Euros; 1.3% GDP) and social security (170bn Euros; 1.2% GDP), a considerable proportion is due to indirect costs, such as lower employment rates and reduced productivity (240bn Euros; 1.6%).

1.3 Depression in Young People and Students

The age of onset of common mental disorders (CMDs) typically occurs during adolescence or young adulthood. In a review of epidemiological age-of-onset studies, Kessler et al. (2007) identified the median age of onset (inter-quartile range) as 25-45 (IQR: 17-65) for mood disorders and 25-53 (IQR: 15-75) for certain anxiety disorders (panic disorder, generalised anxiety disorder, post-traumatic stress disorder). The incidence of depression rises steeply from the age of fourteen through to young adulthood (Hankin et al., 2015). Significant biological and social changes that may increase the risk for depression are taking place during adolescence and into young adulthood (Thapar, Collishaw,

Pine, & Thapar, 2012). For example, the sex differences in depression rates that emerge during adolescence have been linked to hormonal changes during female puberty rather than age alone. Oestrogen acts as a mediator of the stress response in the prefrontal cortex in animal studies (Shansky et al., 2004), suggesting pubertal changes in females may increase stress reactivity (Thapar et al., 2012).

Thapar et al. (2012) identify a range of factors, which are often correlated or interact with one another to increase the risk of depression. For example, distal risk factors such as genetics and adverse childhood events, in combination with hormonal changes and brain maturation, can influence sensitivity to stressors as well as directly impacting biological systems such as the brain structure and neuroendocrine system (Thapar et al., 2012). Two brain circuits, linked to threat and reward, show altered activation (an increase in the threat circuit and a dampening in the reward circuit) in depressed individuals. These circuits mature during adolescence and there is evidence that genetic risk factors, stressors and hormones influence the development of these circuits, increasing the risk of depression (Gotlib et al., 2010; Pine, 2003).

Depression is 3 to 4 times more prevalent in individuals with a depressed parent, due to both inherited and environmental risks (Rice, Harold, & Thapar, 2002). Twin and family studies have found that adolescents (especially girls) with genetic risk factors show increased sensitivity to environmental factors (Gene-Environment interaction) but also a greater likelihood of experiencing stressors (Gene-Environment correlation). While both acute and chronic stress increase risk, ongoing interpersonal stress appears to be particularly detrimental during adolescence (Thapar et al., 2012). Peer and romantic

relationships become increasingly important during adolescence and ongoing interpersonal stress within these relationships increases risk for depression (Hankin et al., 2015).

In the UK, the most recent Adult Psychiatric Morbidity Survey (McManus, Bebbington, Jenkins, & Brugha, 2016) reported an increase in the prevalence of depression and anxiety disorders (together referred to as common mental disorders, or CMD) in 16 to 24-year-olds, rising from 15% in 1993 to 19% in 2014. This increase has been driven by the steep incline in CMD rates among young women, rising from 19.2% in 1993 to 26.0% in 2014, while rates in young men have remained fairly constant (8.4% in 1993 to 9.1% in 2014). Young women are now almost three times more likely than young men to report clinically significant symptoms of depression and/or anxiety.

Around half of all disease burden among young adults in high-income countries is attributable to mental disorders (WHO, 2008) and individuals with early onset are also at greater risk of developing chronic depression (Pine, Cohen, Gurley, Brook, & Ma, 1998), suggesting targeting adolescents and young adults could significantly reduce the overall disease burden of depression.

Within this age range, there is evidence that Higher Education (HE) students experience a heightened risk of poor mental health. In a survey of 1135 UK undergraduates, McIntyre, Worsley, Corcoran, Harrison Woods, and Bentall (2018) report 42.2% of respondents scoring in the clinical range for anxiety and 25% for depression (22.2% co-morbid for both anxiety and depression). Across a survey of 13,984 first-year students in 8 countries (Australia, Belgium, Germany, Mexico, Northern Ireland, South Africa, Spain,

and United States), 35.3% reported a lifetime prevalence of at least one mental disorder (WHO World Mental Health International College Student (WMH-ICS) Initiative; Auerbach et al., 2018). Major Depressive Disorder (MDD) was the most common, with participants reporting 21.2% lifetime prevalence; 18.5% 12-month prevalence, followed by Generalised Anxiety Disorder (GAD): 18.6% lifetime prevalence, 16.7% 12-month prevalence. Suicidal thoughts and behaviours within the WMH-ICS sample ranged from 1.1% - 8.4% in the past year (Bruffaerts et al., 2019).

While the WMH-ICS survey found the majority of clinical cases had an onset prior to university (Auerbach et al., 2018), only first-year students were surveyed and a recent large-scale survey of 37,654 students from 140 universities across England, Scotland and Wales (conducted between August-October 2018) suggests that mental health may deteriorate during university attendance (Pereira et al., 2019). Overall, Pereira et al. (2019) found 33.9% of respondents had experienced a serious personal, emotional, behavioural or mental health problem requiring professional help, with 21.5% receiving a formal diagnosis. Of these formal diagnoses, depression was the most prevalent (10.2%), followed by anxiety disorders (8.4%). Across the entire sample, 42.8% reported being ‘often’ or ‘always’ worried, with rates peaking in the 2nd year and remaining high in the 3rd year. One in three students reported ‘often’ or ‘always’ feeling isolated. Difficulties with substance misuse and thoughts of self-harm were also more frequently reported by 2nd and 3rd years than 1st years, suggesting overall that mental wellbeing decreases during the course of university attendance and that this is a high-risk period for the first onset or recurrence of a mental disorder in young adults.

There may be factors specific to the university environment that negatively affect wellbeing. The university setting involves a number of potential stressors such as moving away from home for the first time, academic pressure, loss of contact with existing social support, the need for budgeting, exposure to drug use, and a lack of sleep (Lee, Kang, & Yum, 2005; Voelker, 2004). In terms of developmental stage, students are often of an age at which they are developing their identity and exploring options for the future, a developmental transition which is linked to greater self-doubt and depression (Lewinsohn, Rohde, & Seeley, 1998; Michael, Hueisman, Gerard, Gilligan, & Gustafson, 2006).

Wörfel, Gusy, Lohmann, Töpritz, and Kleiber (2015) examined the impact of the university environment on mental health with a survey of 1707 students at two German universities. Within this sample, 14.2% screened positive for depressive disorder and 16.3% for an anxiety disorder (with 8.4% comorbid for both depression and anxiety). Significant predictors of anxiety were study demands, the subjective amount of time available to complete academic tasks, and lack of social support provided by fellow students. These three factors were also significant predictors of depression, together with additional predictors of qualification potential (perceived learning and career opportunities) and subjective ability to influence one's studies e.g. "I can choose courses and study focuses according to my interests". These findings suggest that both the academic and social demands of the university environment, as well as uncertainties about the future, may have an impact on students' mental wellbeing.

The experience of a mental disorder while at university is associated with considerable functional impairments. In the WMH-ICS sample (Alonso et al.,

2019), 20.4% (10% of students with no mental health disorder, compared to 42.9% of students with a mental health disorder) reported a severe role impairment in at least one domain (home management/chores; college/work; close personal relationships; social life). Those with more disorders reported more severe role impairment, indicating co-morbidity is particularly detrimental to functioning. Overall, students with depression or GAD were most likely to report severe role impairment, with the highest levels of impairment in the two social domains (close personal relationships, social life). Logistic regression indicated those with MDE were four times more likely than those without MDE to report any significant role impairment (OR = 4.0, 95% CI 3.3-4.8), with the highest odds in the two social categories (close relationships: OR = 4.4, 95% CI 3.4-5.5; social life: OR = 4.3 95% CI 3.4-5.4). Assuming this is a causal relationship, almost half of this severe role impairment could be prevented if mental disorders were eradicated (Alonso et al., 2019), thereby considerably reducing the disease burden of depression among students.

1.4 The need for prevention

Although there is robust evidence for the efficacy of pharmacological and psychological treatments for acute depression (Nathan & Gorman, 2015), such an approach alone is insufficient to tackle the global burden of depression. The treatment of depression has risen considerably since the 1970s, but the prevalence of depression at a societal level has not decreased (Ormel, Kessler, & Schoevers, 2019). There are several reasons why acute treatment alone does not reduce overall prevalence: lack of available treatments; unwillingness to seek help; insufficient dosage and/or quality of treatment; high relapse and

recurrence rates; and high influx, such that, even with successful treatment of existing cases, new cases are continually adding to the prevalence.

One important factor is that the majority of individuals with depression cannot or do not access treatment. Globally, fewer than 50% of people receive treatment, while in some areas this figure is under 10% (Marcus, Yasamy, van Ommeren, Chisholm, & Saxena, 2012), in many cases due to lack of availability. The number of individuals requiring treatment far outweighs the number of therapists available, so the burden of depression cannot be reduced solely using the traditional face-to-face model of psychotherapy, whereby treatment is delivered one-to-one or in small groups (Kazdin & Blase, 2011).

Even when treatments are available, individuals may be unwilling to seek treatment due to a range of barriers such as: a lack of perceived need; lack of awareness about available treatment options; scepticism about treatment effectiveness; worry about stigmatisation; gender and cultural barriers i.e. a perceived need to project a particular social identity (Doblyte & Jimenez-Mejias, 2017; Nubel, Mullender, Hapke, & Jacobi, 2019). In addition, the nature of depressive symptoms (e.g. extreme fatigue, feeling hopeless or worthless) can also be a barrier to people seeking treatment, as people may feel too tired or overwhelmed to begin tackling their problems (WHO, 2012).

Many people who are in need of treatment do not receive the standard of treatment recommended in clinical guidelines (Ormel et al., 2019). When individuals do access treatments, there is a wide variation in both the amount and quality received. In a survey of 51,547 adults across 21 countries conducted by the WHO (Thornicroft et al., 2017), of those participants who both met criteria for major depression and also recognised their own need for

treatment (approximately 2.6% of total sample), the majority (71.1%) had sought and received at least one treatment session. However, minimally adequate treatment, as defined by Wang et al. (2007), includes: a) ≥ 1-month medication with ≥ 4 visits to a medical doctor or b) psychotherapy, consisting of ≥ 8 sessions with a professional, such as a counsellor, social worker, religious leader. Using this definition, only 41.0% of those treated met the criteria for receiving a minimally adequate treatment. Once the individuals who received no treatment are taken into account, this equates to only 16.5% of individuals with a 12-month diagnosis of MDD receiving minimally adequate treatment. Even among high-income countries, where perceived need for treatment was higher and such treatments more widely available, only 22% received these minimally adequate treatments. In addition, treatment guidelines are underpinned by evidence of efficacy in RCTs which may overestimate effects that can be achieved in less controlled clinical settings, in particular with respect to longer-term outcomes (Ormel et al., 2019). This is partly due to patients not completing a full treatment course, which reduces its effectiveness (Kazdin, 1996).

One reason for ineffective treatments is that, while several treatment approaches are equally effective at the population level, individual responses are highly heterogeneous, so it is difficult to know in advance which treatment is suitable for a specific patient, which leads to a trial-and-error approach by clinicians (Cuijpers & Christensen, 2017) and patients often require several different treatments before responding (Malhi & Mann, 2018).

Kessler et al. (2017) identified a range of baseline predictors of poorer overall treatment response, or differential responses between treatment approaches, including: socio-demographic factors (e.g. older age, non-white

ethnicity), depressive history and symptoms (e.g. earlier onset, recurrent episodes, higher symptom severity), presence of co-morbid symptoms (e.g. anxiety, sleep disturbances), presence of stressors (e.g. childhood abuse, high levels of current stress) and personality traits (e.g. neuroticism). However, testing the differential effects of large numbers of moderators requires large samples and considerable timeframes, so it remains unclear which (combinations of) characteristics best predict treatment response.

While there remains insufficient evidence for matching a particular therapy to a particular individual, patient preferences are an important consideration. Ramanuj, Ferenchick, & Pincus (2019) recommend providing patients with a range of treatment options, and using shared decision making between the clinician and the patient to select a particular treatment, weighing up personal preferences, circumstances, co-morbidity, and the potential benefits and harms of each approach. This leads to a more personalised treatment approach and may improve clinical outcomes.

In a recent trial of Morita Therapy (a Japanese psychotherapy), using a mixed methods approach, Sugg et al. (2020) found that a combination of attitudes towards the underlying principles of Morita therapy and towards the practicalities of completing treatment were linked to treatment adherence and outcomes. A preference for a more analytical, cognitive-based approach made it difficult for some participants to identify with the underlying principles of Morita therapy (e.g. inattention to symptoms) and participants who did not like the treatment approach had poorer treatment outcomes, regardless of how many sessions they attended. This highlights the importance of taking patient preference into account when selecting a treatment.

Even with successful acute treatment, depression is highly recurrent, with current treatments having a limited impact on long-term outcomes: 60% of cases treated in specialist settings relapse within five years and 85% relapse within 15 years (Hardeveld, Spijker, De Graaf, Nolen, & Beekman, 2010). Even among less severe cases treated only in primary care, approximately half experienced a recurrence within five years (Steinert, Hofmann, Kruse, & Leichsenring, 2014). More effective interventions with longer-lasting effects are therefore required to reduce the disease burden of depression.

With specific reference to closing the treatment gap, Ormel et al. (2019) recommend a greater emphasis on early intervention, to reduce the risk of recurrence; the elimination of waiting lists; stepped care; better monitoring of antidepressant adherence with more regular check-ins with one's GP; and more use of psychological rather than pharmacological treatments. These approaches require addressing several barriers, including early recognition of need for treatment, timely access to good quality treatment and improved compliance by both patient and clinician, and a greater monitoring of the severity of symptoms so that treatment can be stepped up if symptoms are not improving.

However, even if the treatment gap could be fully closed, focusing only on improving access to and efficacy of acute treatments will not be sufficient to significantly reduce the disease burden of depression. Andrews, Issakidis, Sanderson, Corry, and Lapsley (2004) estimated that even if optimal acute treatment could achieve full coverage, only 34% of the disease burden would be eliminated. One reason why treatment does not reduce the overall prevalence is because depression is a high influx disorder, such that a large proportion of

cases are of relatively recent onset (Beekman, Smit, Stek, Reynolds, & Cuijpers, 2010). Given that treatments are only available to those who already have a diagnosis of depression, improving only these acute treatments will still have no impact on the number of new cases, or incidence (Muñoz, Cuijpers, Smit, Barrera, & Leykin, 2010). While acute treatment offered to individuals with a diagnosis may shorten the duration of a depressive episode, a focus on prevention of new cases (i.e. reducing incidence) is necessary to have a significant impact on the overall disease burden of depression (Jorm & Yap, 2019).

In contrast to chronic physical disorders, which typically have an onset later in life, chronic mental disorders typically have an early onset, during the important transition from childhood to adulthood, during which time young people are undertaking education, developing habitual health behaviours, becoming more independent, and entering employment (Jorm & Yap, 2019). Mental ill health during this period can negatively impact these key developmental milestones, with potential life-long negative consequences. Prevention early in life is therefore posited to be the most effective means of reducing the disease burden of depression (Jorm & Yap, 2019). A further advantage of preventing the first onset of depression is that this also reduces the likelihood of any future episodes, thereby reducing the overall need for long-term treatment of recurrent episodes (Muñoz et al., 2010). There is therefore a convincing argument that prevention, in addition to acute treatment, is vital to reduce the global disease burden of depression (Ormel et al., 2019; Topper, Emmelkamp, & Ehring, 2010).

1.5 The need for prevention in university students

Student demand for mental health treatments has increased in recent years. Almost all (94%) UK Higher Education Institutions (HEIs) reported an increase in demand for in-house counselling services between 2012-17, with 61% reporting an increase of over 25% (Thorley, 2017).

Despite this increased demand, there remains a high level of unmet need. In the WMH-ICS sample, only 25.3% of students with any 12-month mental disorder and 29.5% of those with 12-month suicidal thoughts or behaviours had accessed treatment services within the same 12-month period (Bruffaerts et al., 2019). Similarly, in the UK, the National Union of Students (NUS, 2015) surveyed 1093 students about mental health services and found 54% of those in need of treatment did not access university services and 33% did not know where to access support if needed. A more recent survey (Pereira et al., 2019) demonstrated increased awareness of services available at university, with 80.1% aware of services available, but of the 33% of students reporting a current need for support, only 1 in 3 had accessed these university services. In addition, 75.6% of those reporting a diagnosed condition had concealed symptoms from friends and family due to fear of being stigmatised.

When support is accessed, there are mixed findings relating to how helpful this treatment is. For example, one survey found that students accessing in-house services (N = 615) were generally satisfied, with 81% rating the quality of support as better than or similar to expected (Unite Students, 2019). The most notable criticisms were that 1 in 5 rated the continuity of care and the speed of getting support as worse than expected, indicating that there is an issue with providing timely and ongoing support.

In contrast, another survey of 376 UK students found less positive views on the quality of support available (Batchelor, Pitman, Sharpington, Stock, & Cage, 2019). In this survey, 55.9% had accessed support since starting university (40.4% GP, 31.6% university counselling services, 20.5% university mental health advisors). Almost half reported that there was insufficient time in a GP consultation to discuss both their condition and treatment options in sufficient detail. Of those who had attended a talking therapy, 41% rated it unhelpful. Of the 125 students in this sample who had accessed NHS services, 73 suggested improvements, including reducing waiting times; more accessible treatments (more variety, longer/more regular appointments and a lower threshold for referral, so treatment is received before symptoms reach a crisis point); patient-centred care that ensures the student feels listened to and supported; more effective treatments; better communication between in-house university services and NHS services; and more follow-up care to check progress is maintained longer term.

The transition to university presents some unique challenges to accessing treatment (Universities UK, 2018). During this period, students often move to a new geographical area and can face difficulties accessing GP services in both their university and home location. In addition, students typically fall within the age range for the transition of care between Child and Adolescent Mental Health Services (CAMHS) to Adult Mental Health services (AMHS), which generally occurs at age 18, although some CAMHS services discharge at 16 or after 18 (NHS, 2019). This is often a high-risk period, as the young person faces new challenges and loses contact with trusted support staff (Healthcare Safety Investigation Branch, 2018). A considerable proportion (25-50%) of under-25s disengage from ongoing treatment during this phase, which may lead to a crisis

(Healthcare Safety Investigation Branch, 2018). The Royal College of Psychiatrists (RCPsych, 2019) have welcomed the NHS long-term plan for a 0-25 years old service model to cover this challenging transition period.

University support staff have echoed these difficulties, highlighting insufficient co-operation between in-house and NHS services (Student Minds, 2014). Support staff view the current NHS services as inadequate, with the university services having to replace rather than complement the NHS provision. Referral procedures to NHS services take considerable time, during which the student may be falling behind academically. In addition, the lack of shared information between home and university locations can leave students without adequate support for lengthy periods (Student Minds, 2014).

While these structural barriers are significant once a student has expressed a need for help, there is also a range of barriers that may prevent a student from seeking help at all. The Student Minds (2014) survey identifies several attitudinal barriers, including fear of judgment (particularly by peers), normalising stress, finding it difficult to admit you are struggling, stigma (seeing mental illness as a weakness) and social isolation.

In a survey of 2573 UK first-year students (Unite Students, 2019), 17% reported a mental health condition. Of these (*N* = 452), 52% reported that their condition is ‘something I need to deal with myself’, with qualitative research finding that students felt a need to solve their problems independently, or with the support of peers, as part of the transition to adulthood. While 38% felt able to discuss their difficulties with friends, only 27% felt comfortable reaching out for help when needed and 23% trusted that their university could provide the right support, demonstrating a reluctance to access university services.

Reasons for not accessing the university services included not being confident that treatment would help, not wanting to talk, and not wanting the university to know about one's issues (Unite Students, 2019).

Ebert et al. (2019) also highlighted attitudinal barriers. The WMH-ICS sample were asked about their intentions to use support as well as specific reasons why they would not access this support. Only 24.6% reported that they would definitely seek help for a future emotional problem. Of the remaining 75.4% participants who were uncertain about seeking help in the future, 28.6% met criteria for at least one disorder, with 8.8% reporting suicidal ideation and 7.8% reporting a suicidal plan in the past 12 months, indicating a reluctance to seek help even among students who have experienced acute and severe symptoms. In terms of barriers, the most frequently endorsed reasons for not choosing to seek help were: 'preference to handle problem alone' (56.4%), 'wanting to talk to friends/relatives instead' (48%) and 'being too embarrassed' (32.2%). Major depression and GAD significantly increased the likelihood of reporting 'embarrassment' as a barrier to help-seeking.

Cage, Stock, Sharpington, Pitman, and Batchelor (2018) surveyed the help-seeking intentions of 376 UK students (the same sample as Batchelor et al., 2019). Students were asked to rate their likelihood of seeking help from informal sources (parents, other family members, friends, intimate partner) and formal sources (GP, mental health professionals, helplines) as well as the option 'I would not seek help from anyone'. Self-stigma, whereby stigmatising attitudes are internalised and targeted towards one's own mental health (Corrigan, Watson, & Barr, 2006) and the act of help-seeking (Tucker et al., 2013) predicted a lower intention to seek formal help and a higher intention not

to seek help from anyone. Depressive symptoms also predicted a reduced intention to seek informal support as well as a likelihood not to seek any support at all, suggesting students with depression are at risk of keeping their symptoms hidden from those around them.

A qualitative study of students' views of mental illness stigma identified a close link between academic demands and a lack of disclosure or help-seeking (Wada et al., 2019). In terms of sources of stigma, students felt the competitive nature of university fostered a reluctance to disclose symptoms due to a fear of being seen as less capable than one's peers. This could lead to an individual withdrawing from social and academic activities and not having a sense of belonging to social circles within the university. In addition, students felt that difficulties distinguishing normal responses to stressful periods (e.g. increased anxiety during exam periods) from more maladaptive responses indicative of a mental disorder led to self-blame, such as viewing clinical symptoms as being a result of laziness or lack of self-discipline. This self-blame was offered as an explanation for delaying help-seeking. The students in this qualitative study identified a need for increased awareness of symptoms and greater promotion and availability of resources as means to overcome these barriers to help-seeking. In particular, students recommended easier access to services through one-stop facilities, increasing the number of counselling staff and offering online services.

These barriers to help-seeking may be particularly acute among international students. At the University of Plymouth, international students make up approximately 10% of the student population but only 2.8% of the users of the in-house counselling service (Bentley, 2017). In a survey

completed by 103 international students, wellbeing scores were lower among those who had never lived abroad prior to moving to Plymouth. In this survey, students with higher levels of wellbeing reported more active coping mechanisms, such as talking to others and engaging in activities, whereas those with poorer wellbeing engaged in more avoidant behaviours, such as not sharing their difficulties and not completing assignments. Students with lower wellbeing reported a preference for managing their problems alone.

In focus group discussions (Bentley, 2017) participants described the transition to university in terms of loss (moving away from their previous culture and social circle), rather than in terms of gaining new experiences. The adjustment to a new culture and language increased feelings of homesickness and made it more difficult to form new friendships. Despite these additional challenges compared to home students, international students reported a range of barriers to help-seeking, including: seeing treatment as a form of failure or only for those who were really unwell, a preference for self-reliance, and not seeing talking as beneficial. In addition, cultural and language barriers made it harder to attend in-person sessions, as students felt the staff may not understand their background and not offer culturally appropriate support.

Taken together, these findings indicate that current in-person treatments are not meeting the needs of students. There is a reluctance among students to seek formal support, with individuals minimising or concealing their symptoms until the point where these symptoms are having a major detrimental impact on their academic achievement. There is a need for students to have access to interventions before their symptoms are having such a significant impact. In particular, given the findings that (self-)stigma acts as a barrier to seeking help,

this suggests that anonymous, confidential, private, self-help interventions may encourage students to engage with an intervention before their symptoms are having a detrimental impact on their studies, thereby improving overall resilience and reducing the risk of experiencing clinical depression.

Student resilience, as defined by McIntosh and Shaw (2017), incorporates the internal factors of self-management (e.g. ability to set goals and persist towards these goals) and emotional control (e.g. not dwelling on or overreacting to negative events) as well as the external factors of social integration in the university setting, support networks (ability to seek help from both formal and informal sources), and social relationships (satisfaction with current relationships). Scores from a survey of 6504 UK students demonstrated a strong positive correlation between resilience and overall life satisfaction. Students with a self-declared mental health condition scored significantly lower on all domains of resilience, but particularly emotional control, reporting dwelling and losing self-confidence when faced with setbacks. Although emotional control was particularly poor for those with a self-declared mental health condition, two thirds of the sample reported problems with emotional control in response to stressors. Females were found to score 8 percentage points lower on the emotional control subscale than males. Both life satisfaction and resilience were negatively correlated with a desire to drop out of university. Interventions aimed at preventing mental health conditions and improving life satisfaction and resilience among students may therefore have wide-ranging positive impacts on individual students, as well as the university as a whole, with improved retention rates.

The shift in priorities towards prevention, early intervention and building resilience among students has been driven by an increase in the number of student suicides in recent years (79% increase in student suicides from 2007 to 2015; Thorley, 2017) as well as the increased demand for and cost of treatment services, with universities having a duty of care to support students in crisis (Universities UK, 2017). Universities UK (2017) has made a strong case for a change in the approach to improving student wellbeing, focusing on promoting wellbeing, improving resilience and prevention/early intervention. Specific recommendations for improving student mental health and reducing demand for overstretched clinical services include: a greater emphasis on prevention rather than reacting to crises; supporting students through risky transition periods (e.g. school to university); training staff to identify early signs of disorder in their students, as well as themselves to promote earlier intervention; and rigorous data collection to evidence both the need for and efficacy of any interventions, thereby justifying further investment in services (Universities UK, 2017).

1.6 Preventing Depression

The review of depression, and particularly its impact in university students, has indicated the need for preventive interventions. In this section, key concepts and evidence from depression prevention trials are reviewed.

1.6.1 Defining prevention and key concepts in prevention trials

The original framework for categorising preventive interventions for mental health disorders was derived from the different stages of prevention for physical disorders: primary, secondary and tertiary (WHO, 2004). Within this framework, the aim of primary prevention is to reduce the risk of ever developing a disorder in healthy individuals. Secondary prevention targets

individuals with a diagnosis, but in the early stages to prevent advancement of the disorder. Finally, tertiary prevention focuses on relapse prevention to improve long-term outcomes.

An alternative framework from the Institute of Medicine (IOM; National Research Council & Institute of Medicine, 2009) uses a stricter definition of prevention that focuses only on interventions delivered prior to any clinical diagnosis. Any intervention aimed at preventing the worsening of symptoms in clinical cases or relapse prevention, even in individuals who are well at the time of the intervention, would be classed as treatment under this framework. The IOM (2009) distinguishes between three forms of prevention, depending on the target population: universal, selective, and indicated. Universal interventions are delivered to an entire population. Selective interventions are targeted at a subgroup of the population deemed to be at higher risk due to shared social, cognitive, behavioural or emotional vulnerability factors such as parental history of depression, poverty, trauma, or bereavement. Indicated interventions are delivered to individuals presenting with early (but subclinical) symptoms, with the aim of preventing these symptoms reaching the threshold for clinical diagnosis. In order for a study to be classed as a preventive intervention for depression under this framework, the intervention must therefore take place before the first onset of clinical depression (Mrazek & Haggerty, 1994).

There are a number of methodological issues to consider in trials of preventive interventions. Demonstrating true prevention effects using symptom severity alone is difficult. In contrast to treatment, which aims to reduce symptom severity, the goal of prevention is to prevent the worsening of symptoms or the occurrence of the disorder. Horowitz and Garber (2006)

argued that demonstrating a true preventive effect in terms of change in depressive symptoms would require an increase in symptom severity in the control group and no increase, or a significantly reduced increase, in the intervention group. Using this definition, only 4 of the 30 trials reviewed by Horowitz and Garber (2006) met these criteria for prevention. Stice, Shaw, Bohon, Marti, and Rohde (2009) found a significant reduction in symptoms relative to controls in 13 out of 46 reviewed trials, but in 12 of these studies symptoms reduced not only in the intervention group but also in the control group. Clearly a greater reduction in symptoms relative to controls is a favourable clinical outcome of an intervention, but such outcomes are more accurately classed as treatment effects rather than preventive effects (Topper et al., 2010).

Several authors (e.g. Cuijpers, van Straten, Smit, Mihalopoulos, & Beekman, 2008) argue that true prevention effects are only demonstrated if there is a lower incidence rate for the occurrence of depression in the intervention condition compared to controls. Where incidence is used as an outcome measure, effect sizes such as the incidence rate ratio (IRR) represent a measure of the impact of a preventive intervention. IRR measures relative risk i.e. the incidence rate in an intervention group compared to the incidence rate in the control group (Muñoz et al., 2010), where an IRR of 1 indicates no difference and IRR < 1 indicates a reduced incidence rate in the intervention arm relative to the control arm. For ease of interpretation, this is often reported as a percentage reduction in risk (1-IRR = % change). Incidence rates can also be used to calculate the numbers needed to treat (NNT; how many individuals need to receive the intervention in order to prevent one new case), which indicates the effort needed to produce population-level health gains (Smit,

Beekman, Cuijpers, de Graaf, & Vollebergh, 2004). A low NNT is therefore desirable in terms of maximising the efficiency of a preventive intervention (Cuijpers, 2009).

In order to calculate an accurate IRR, a formal diagnosis of depression requires the administration of a diagnostic interview, such as the Structured Clinical Interview for DSM disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 2002), by a specially trained clinician. However, given the time required to complete a full interview, most studies use self-report questionnaires e.g. PHQ-9 (Kroenke, Spitzer, & Williams, 2001) or CES-D (Radloff, 1977) to examine change in symptom severity, with some including a designated cut-off signifying likely clinical diagnosis ("clinical caseness") as a proxy for measuring formal incidence rates, which may result in a greater number of false positives than more conservative diagnostic interviews (Topper et al., 2017).

As well as the additional time needed to accurately measure incidence, another challenge in designing prevention trials with diagnostic outcomes is ensuring that they are sufficiently powered to detect genuine effects. The power to detect a prevention effect depends on the base rate of incidence for depression in the respective sample: when the base rate is low, such as in a general population, it is harder to detect a change in rates of depression, and larger effect sizes are needed to detect an intervention effect. As such, for the same effect size, there is likely to be less power to detect a reduction in incidence in a trial of a universal intervention than in a trial of a selective/indicated prevention, where the base rate of incidence is necessarily higher. For example, Muñoz et al. (2010) calculated that 17,253 participants are needed to detect a 22% reduction in incidence if the base rate is 1.7%, the

reported incidence in the general population (De Graaf, Bijl, Ravelli, Smit, & Vollebergh, 2002). One way of increasing statistical power would be to improve the effectiveness of the intervention (i.e. increase the effect size), but in universal samples where the base-rate is low, detecting larger effect sizes would still require large samples e.g. doubling the effect size to 44% on the same base-rate would still require 7866 participants (Muñoz et al., 2010). Statistical power is also increased if the base rate is higher, for example if the incidence rate in controls is 30% then a 22% reduction in this incidence would require a sample size of 735 per arm (Muñoz et al., 2010). This is the reason why many prevention studies choose to focus on high-risk populations to ensure that sufficient statistical power can be yielded with a more practical sample size.

Another important aspect of detecting a significant preventive effect is to ensure there is a sufficient follow-up period. Given that enough time is needed for new cases of depression to develop, a short follow-up may underestimate the effectiveness of an intervention as its benefits may not be observed within this short timeframe. This is another reason for focusing on higher risk samples, who are more likely than universal samples to develop depression within a measurable timeframe.

It is important to note that, in trials that rely solely on symptom measures, the lack of follow-up may conversely lead to an overestimate of intervention effects. Several authors (e.g. Van Voorhees et al., 2011) have pointed out that an intervention may have an impact on symptom severity in the short term, but without a sufficient follow up, it remains unclear whether such effects are maintained over time. It may, therefore, be that reporting only symptoms

measures post-test but either failing to track these over a longer follow-up period or failing to include diagnostic measures to calculate incidence rates, leads to an overestimation of preventive effects. Trials assessing the prevention of depression should therefore select participants at high short-term risk to ensure the base rate of new cases is high enough to detect a significant effect within a realistic follow-up period and include diagnostic measures to ensure any positive short-term effects on symptom severity translate into a reduction in incidence.

1.6.2 How effective are preventive interventions in young people?

There is evidence that preventive interventions can be beneficial for improving symptoms of depression and anxiety in young people. Several earlier meta-analyses (Horowitz & Garber, 2006; Merry et al., 2011; Stice et al., 2009) have assessed the effectiveness of universal and selective/indicated prevention in children and adolescents, with the majority of interventions using a cognitive-behavioural therapy (CBT) approach. Topper et al. (2017) converted the different effect sizes from these three meta-analyses (Horowitz & Garber, 2006; Merry et al., 2011; Stice et al., 2009) into Cohen's *d* for ease of comparison, with *d* = 0.2 representing a small effect size, *d* = 0.5 a medium effect and *d* = 0.8 a large effect. Across the three meta-analyses the mean effect of universal interventions was *d* = 0.04 - 0.12 post-intervention and *d* = 0.02 – 0.12 at follow-up, representing only small-to-insignificant effect sizes for a reduction in symptoms, relative to no intervention. Effect sizes for targeted interventions were larger, with a mean effect *d* = 0.23 – 0.31 post-intervention and *d* = 0.22 – 0.34 at follow-up, indicating small-to-moderate effect sizes, relative to no intervention.

Two Cochrane Reviews, the highest standard of systematic review, have assessed the effectiveness of psychological and educational interventions at preventing depression in children and adolescents (Hetrick, Cox, Witt, Bir, & Merry, 2016; Merry et al., 2011). Merry et al. (2011) reviewed 68 trials (some with multiple interventions), of which 53 contained data suitable for meta-analysis. Thirty-one trials assessed universal prevention and 39 trials assessed targeted interventions (selective and/or indicated). The interventions were compared to placebo, another intervention, or no intervention. Participants ranged from 4-19-years-old. Two trials included only females and three included only males, with the remainder mixed gender or gender not reported. Main outcomes were: 1) the prevalence of depression in each group assessed as a dichotomous outcome using a clinical diagnostic interview or pre-designated clinical cut-off on a continuous measure of depressive symptoms and 2) severity of depressive symptoms as assessed on self-report measures. Merry et al. (2011) found a short-term efficacy for universal interventions (up to 9 months follow-up). However, only targeted interventions produced a significant effect by 12 months follow-up. For universal interventions, where risk difference was measured (risk in intervention minus risk in control, and risk defined as the proportion of participants meeting diagnostic 'caseness' in each group), a reduction in risk of depression, relative to no intervention, was found at post-treatment (RD = -0.12; 95%CI -0.20 to -0.05) and at short term follow-up (3-9 months; RD = -0.19, 95% CI -0.33 to -0.05), with no significant difference by 12-month follow-up. For targeted interventions, significant reductions in diagnosis, relative to no intervention, were found post-intervention (RD = -0.07, 95% CI -0.12 to -0.02), 3-9 month follow-up (RD = -0.06; 95%CI -0.25 to -0.04) and 12 months (RD = -0.14; 95% CI -0.24 to -0.04), indicating the preventive effects of

targeted interventions may be longer lasting than those of universal interventions. Few studies compared intervention with placebo or attention control, and these demonstrated no evidence of efficacy (Merry et al., 2011). While these effects are small, overall, they correspond to an NNT of 11 (CI 7 to 20).

While Merry et al. (2011) point out that they excluded studies which were conducted on adolescents meeting current DSM-IV criteria for current depression, the picture for exclusion based on past episodes is much less clear. Only one study out of the 63 included in the systematic review specifically reported that participants were excluded if they had experienced a past depressive episode, so it is unclear whether preventive effects are primary (first onset) or secondary (relapse prevention). While both forms of prevention are important in reducing overall disease burden, recording past episodes allows for any differential effects of an intervention on individuals with no prior history compared to those with previous experience of depression to be examined.

Hetrick et al., (2016) updated the Merry et al. (2011) review, focusing only on studies in which depression was the primary outcome. Interventions included in this review were CBT, Interpersonal therapy (IPT), and third-wave approaches (focused on process rather than content of depressogenic thoughts). The age of participants in the included trials ranged from 5 to 19-years-old. The timing of follow-up of outcome measures was divided into post-intervention, short-term (≤3 months post-intervention), medium-term (4-12 months post-intervention) and long-term (>12 months post-intervention). Across 36 trials that used diagnosis as an outcome measure, small but significant effects were found at medium-term follow-up (RD = -0.03, 95% CI -0.05 to -

0.01) but not at long-term. Overall, the risk of diagnosis reduced from 19.3% to 16.2%, which equated to an NNT of 33. However, when targeted and universal approaches were examined separately only targeted interventions showed evidence of a significant effect on diagnosis (RD -0.04, 95% CI -0.07 to -0.01) at medium-term follow-up, with no evidence of a significant impact of either approach beyond 12 months. A similar pattern of findings emerged for symptom severity (70 trials with 73 trial arms), where post-intervention severity was the primary outcome. There was evidence that targeted interventions were more effective (SMD -0.32, 95% CI -0.42 to -0.23) than universal interventions (SMD -0.11, 95% CI -0.17 to -0.05). In addition, significant effects were maintained at short to medium-term follow-up for targeted interventions but there was no evidence of an effect beyond post-intervention for the universal interventions.

A meta-review conducted by Stockings et al. (2016) investigated the efficacy of preventive interventions for depression and anxiety disorders in 5 to 18-year-olds. The review calculated combined estimates of depression and anxiety to form composite internalising disorder diagnosis or symptoms. Across one hundred and forty-six RCTs (a total of 46,072 participants), this review found evidence that preventive interventions were effective at reducing both the incidence rates and symptoms of internalising disorders. The effect size for universal interventions was larger than that found in previous reviews of prevention in children and adolescents (e.g. Hetrick et al., 2016; Merry et al., 2011). For universal interventions, incidence was significantly reduced at 6 to 9 months (RR = 0.47, 95% CI 0.37 to 0.60) and internalising symptoms were significantly reduced post-intervention (*d* = 0.15, 95% CI -0.21 to -0.08), but these effects decayed over time and there was no evidence for universal prevention at 12 months post-intervention. In addition, these positive short to

medium-term effects may be skewed by the large effect sizes for anxiety disorders in universal prevention and a lack of trials targeting anxiety disorders in selective or indicated samples (Stockings et al., 2016).

While the Stockings et al. (2016) review is the first to assess the combined effect of preventive interventions on both depression and anxiety disorders, further trials with more robust designs are needed prior to any change in practice (Merry & Hetrick, 2017). For example, where measured, effects on symptom measures reduced quickly over 6-9 months and there was a lack of longer term follow-up data so it remains unclear whether these reductions in effect size are due to a natural decay in the effect of the intervention over time, a lack of power, or both (Stockings et al., 2016). Further trials are therefore needed to better understand the longer-term impact of preventive interventions. In particular, further research is needed into the underlying mechanisms of internalising disorders and whether directly targeting these transdiagnostic mechanisms may improve preventive interventions (Merry & Hetrick, 2017).

As well as considering the efficacy of the intervention, it is also important to take in to account the optimum age at which to intervene for the best long-term outcomes. Some authors (e.g. Horowitz & Garber, 2006) have suggested that interventions should take place as early as possible, before the steep rise in new cases in later adolescence. Clearly, the earlier a preventive intervention is administered, the greater the chance of targeting individuals who have not yet crossed the threshold into a clinical episode. However, Stice et al. (2009) found greater effect sizes for samples containing a higher percentage of older adolescents. At post-test, effect sizes were small and insignificant for trials with participants below the median age (13.2 years), with moderate effect sizes

above this age (*M r* = 0.23, *p* < .001, *N* = 29). At follow-up, a tertile split revealed the largest effect size was in the top tertile (over 15.1 years). This pattern of findings could be due to older adolescents having a greater risk but could also reflect a more developed capacity for abstract reasoning, giving them greater insight into the techniques used in the interventions (Stice et al., 2009), or other factors such as increased self-motivation or recognition of need compared to younger adolescents. Similarly, Horowitz and Garber (2006) found an age effect, with interventions aimed at older adolescents having larger effect sizes post-intervention (age range across all studies 4-25 years). This age effect was no longer significant once the two trials aimed at college students were removed, indicating interventions with college students may be particularly efficacious.

Conley, Durlak, and Kirsch (2015) assessed the preventive effects of universal interventions delivered to university students, including 103 interventions with either a psychoeducational (e.g. information and group discussion about stress) or skills-based approach (e.g. CBT, mindfulness, social skills). The majority of included interventions were delivered as part of the college course or in small groups, with few delivered individually.

The supervised skills-based interventions yielded significant effects on all outcomes including reducing symptoms of depression (ES = 0.39, 95% CI 0.27-0.52), anxiety (ES = 0.55, 95% CI 0.46-0.63), and stress (ES = 0.55, 95% CI 0.44-0.66). Skills-based interventions without supervision only yielded a significant effect on anxiety symptoms (ES = 0.17, 95% CI 0.04-0.30), while psychoeducation interventions had significant effects on anxiety (ES = 0,25, 95% CI 0.11-0.38) and stress (ES = 0.13, 95% CI 0.00-0.26), but not

depression. Taken together, these findings suggest that universal interventions are effective for students, particularly those that include skills-based exercises and some form of ongoing supervision.

Conley, Shapiro, Kirsch, and Durlak (2017) conducted a meta-analysis of indicated preventive interventions for university students, including 79 trials focused on outcomes such as depression, anxiety, co-morbid depression and anxiety, and general psychological distress. Intervention approaches included cognitive-behavioural, relaxation and social skills. There was a moderate to large overall effect of indicated preventive interventions on depression (ES = 0.73, 95%CI 0.59-0.88) and anxiety (ES = 0.67, 95% CI 0.50-0.84) as a primary outcome. In addition, while only 43 of the included trials conducted follow-up assessments, there was evidence among these that positive short-term effects were maintained over the follow-up period (*M* = 35 weeks). These findings provide evidence that positive outcomes are achievable on subthreshold depression and anxiety in university students. However, only four trials included diagnostic interviews as outcome measures, so further trials assessing preventive interventions in high-risk student samples are needed to assess intervention effects on incidence.

A recent meta-analysis (Breedvelt et al., 2018) of 26 RCTs assessed the prevention of depression in young adults aged 18-25, with 25 of the trials conducted with university students as participants. Overall there was a pooled moderate effect size (*g* = 0.37, 95% CI: 0.28–0.47, NNT = 9) in favour of the interventions relative to controls in terms of reducing depressive symptoms. The overall NNT of 9 was smaller than that found in previous meta-analyses focused on younger children and adolescents (NNT = 33; Hetrick et al., 2016),

suggesting intervening during the 18-25 age range may be particularly efficient. Breedvelt et al. (2018) suggest these effect sizes may, however, reflect effects more akin to treatment than prevention due to the intensive nature of the interventions and the lack of diagnostic screening to exclude clinical cases at baseline. In addition, none of the included trials in Breedvelt et al. (2018) assessed incidence of depression at follow-up so it is unclear if these positive effects on symptoms of depression translate into a significant reduction in new cases of MDE.

Assessment tools, such as the Cochrane Collaboration's tool for assessing risk of bias in randomised trials (Higgins et al., 2011) are used within meta-analyses to assess the quality of evidence of individual RCTs, as any weaknesses in the overall design, procedure, data analysis and outcome reporting, may lead to an over- or under-estimated intervention effect (Higgins et al., 2011). Quality criteria cover domains such as allocation concealment, blinding, incomplete outcome data and selective reporting, with trials rated as high, low or unclear risk on each criterion (Higgins et al, 2011). Despite the rapidly growing number of RCTs of preventive interventions, the quality of these trials is frequently moderate to low (e.g. Breedvelt et al., 2018; Hetrick et al., 2016). Further RCTs of preventive interventions in young adults using diagnostic measures as both screening and outcome measures are therefore required to improve confidence in the estimates of intervention effects.

Although there is evidence of effectiveness of preventive interventions, particularly when targeted, effect sizes are typically small-to-moderate and longer-term effectiveness is limited (Topper et al., 2010). There is therefore scope for improving prevention at a population level, with a need for improved quality of trials, greater scalability and better targeted interventions (Topper et

al., 2010). Preventive interventions are often delivered to groups rather than in the one-to-one model that is dominant in treatment services, and can therefore reach greater numbers (Topper et al., 2010). Entire classes can be targeted within the school curriculum as an efficient way of reaching a large number of children simultaneously (Calear & Christensen, 2010). However, even group sessions have a limited reach. Alternative modes of delivery, for both acute treatment and prevention, capable of greater scalability to reach considerably larger numbers, are therefore needed (Kazdin & Blase, 2011). One such approach, reflecting rapid advances in technology, is delivering interventions via digital technologies such as the Internet.

1.7 Internet-based interventions

An important class of preventive interventions are those delivered via digital technologies, in particular via the Internet. Such interventions typically contain the same instructions and exercises that would be delivered in face-to-face sessions, in the form of psycho-educational text and interactive activities (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014). There is emergent evidence that internet-based CBT is an effective, feasible and acceptable treatment for acute depression (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Spek et al., 2007). Andrews et al., (2010) conducted a meta-analysis of 22 RCTs of computerised CBT for the treatment of major depression (MDD), GAD, social anxiety disorder, or panic disorder. There was a large overall effect size of cCBT relative to control (g = 0.88; NNT = 2.15). Andrews et al., (2018) updated this meta-analysis, with a particular focus on effectiveness in routine care. Sixty-four trials were included, comparing iCBT to waitlist, information control, usual care or placebo for the acute treatment of the same four

conditions. Across all trials, there was a large overall effect size (*g* = 0.80, 95% CI 0.68 to 0.92). This translated to an NNT = 2.34. For the MDD trials (*N* = 32), there was a moderate-to-large effect size (*g* = 0.67, 95% CI 0.51 to 0.81) with NNT = 2.78. In addition, there were small but significant increases in the effect of the intervention relative to control over time up to 18 months post-intervention.

The evidence of effective prevention using internet-based interventions is less robust, in part due to the same methodological issues outlined for face-to-face prevention studies. Very few trials of internet-based interventions have assessed the effectiveness of these interventions in preventing the incidence, as opposed to reducing the symptoms, of mental health disorders (Ebert, Cuijpers, Muñoz, & Baumeister, 2017). However, there have been some positive findings, particularly for the indicated prevention of depression. For example, in an RCT assessing the prevention of depression in 406 adults with elevated but subclinical depressive symptoms (Buntrock et al., 2016), iCBT was compared to a psychoeducation control. Analysis of disorder onset using Cox regression found a hazard ratio (HR) of 0.59 in favour of the iCBT intervention, indicating a 41% reduction in risk of MDE compared to the control condition.

Two recent meta-analyses have focused on internet-based interventions to prevent mental disorders in adult populations (Deady et al., 2017; Sander, Rausch, & Baumeister, 2016). Deady et al. (2017) included 10 trials of eHealth interventions to prevent depression or anxiety. Overall, there were significant, but small, mean differences between intervention and control. Subgroup analyses found similar effect sizes for universal interventions compared to selective or indicated. However, when assessing risk ratios, there was

insufficient evidence that these positive effects on symptoms translated into a reduction in incidence.

A range of mental disorders were examined in 17 trials reviewed by Sander et al. (2016), with the majority focused on eating disorders, depression or anxiety. All trials included measures of symptom severity. Overall, 11 trials found small-to-medium significant effects in favour of the intervention (*d* = 0.11 – 0.76; Sander et al., 2016). For depressive symptom severity, significant effects in favour of the intervention were found post-intervention and up to 6 months follow-up but no significant differences were present beyond 6 months.

Only 5 of the included trials also reported incidence data assessed by diagnostic interviews, with two finding significant effects on incidence of depression: IRR ranging from 0.09 (NNT = 9.33; Thompson et al., 2015) to 0.23 (NNT = 23.48; Imamura et al., 2015). However, this meta-analysis demonstrated that there is still a lack of trials using diagnostic interviews and, even for those that have incorporated interviews, the trial with the largest effect on incidence (Thompson et al., 2015) only measured outcomes post-intervention so, even when diagnosis is tested as an outcome, longer-term preventive effects remain unclear. More trials with longer follow-ups are therefore needed to accurately assess the impact of preventive internet interventions on incidence.

These meta-analyses generally demonstrate positive short-term effects on symptom severity, but there is limited evidence on how well these interventions perform in terms of true prevention. Firstly, there is often a lack of participant exclusion based on a ceiling cut-off on symptom measures, so samples are likely to mix both clinical and non-clinical participants, who may

react differently to the intervention (Deady et al., 2017). Secondly, the positive effects on symptom severity are generally small and it remains unclear whether these effects translate into true prevention effects (i.e. reduction in incidence) over the longer term. However, even if only small preventive effects are achieved using iCBT, the fact that the intervention can be accessed by large numbers means these interventions could produce significant preventive effects at a population level, thereby reducing the overall disease burden of depression (Deady et al., 2017).

These interventions have a range of potential advantages over traditional face-to-face sessions, including: reaching large numbers at relatively low cost; greater ease of access and convenience for the user; available at any time and place; greater autonomy for the client, anonymity, and greater time to reflect (Andersson, 2010; Muñoz et al., 2010; Richardson, Stallard, & Velleman, 2010b).

These potential benefits may appeal to universities as a means of supporting the wellbeing of the student population. Internet prevention is likely to be more accessible, scalable and cost-effective than face-to-face approaches (Mendelson & Eaton, 2018), allowing a greater number of students to receive an intervention and reducing the pressure on already overstretched treatment services.

In addition, the benefits to the client may be particularly attractive to students. Within a survey of treatment preferences for depression in primary care (Dorow, Löbner, Pabst, Stein, & Riedel-Heller, 2018), views were split on the likelihood of using internet interventions, with 38% endorsing and 42% rejecting internet interventions as a treatment option. Subgroups of patients who

were most likely to endorse internet interventions were younger, had higher levels of education and had co-morbid anxiety, suggesting this approach may be particularly helpful and relevant to university students.

The 24/7 availability allows the student more flexibility in terms of when and where to access the intervention. Competing priorities are often cited as a barrier to accessing therapy (Papadatou-Pastou, Goozee, Payne, Barrable, & Tzotzoli, 2017). The ability to access the content at any time of day or night may therefore make it easier for students to incorporate the intervention into their busy schedules and, by removing pressure to complete exercises in time for a specific appointment, may improve ability to comprehend and implement the therapeutic techniques (Andersson & Titov, 2014). A related benefit where asynchronous support is included is the inherent delay provides more time for reflection, both in terms of what the client wishes to disclose to the therapist and in interpreting and acting on the therapist's response (Hilgart, Thorndike, Pardo, & Ritterband, 2012). An understanding of one's patterns of thought, emotions and behaviour are necessary in order to gain clinical benefit from CBT interventions. Online interventions afford more time for processing the information within the intervention, self-reflection and review and may therefore encourage greater awareness and insight than face-to-face CBT (Earley, Joyce, McElvaney, Richards, & Timulak, 2017).

The Internet also offers an anonymity that cannot be achieved with face-to-face therapies. Given that there remains a level of (self-)stigma associated with mental disorders, some students may find this anonymity comforting. A survey of 200 students with elevated distress (Levin, Krafft, & Levin, 2018) found that self-stigma was a barrier to seeking professional help but was

unrelated to the intention to use self-help. These findings suggest that providing self-help interventions to university students may help to overcome self-stigma as a barrier to help-seeking. Even in web-based interventions that provide therapist support, the lack of face-to-face contact can facilitate a more open therapeutic relationship. Previous studies have found some clients find it easier to share information with their therapist via the computer than they would do in a face-to-face session (Gega, Smith, & Reynolds, 2013; MacGregor, Hayward, Peck, & Wilkes, 2009).

Students may be particularly attracted to online interventions to manage their distress. For example, with increasing levels of distress, students reported a reducing likelihood of help-seeking, but an increasing likelihood of accessing online interventions (Ryan, Shochet, & Stallman, 2010). Despite this, more recent studies show few students have experience of using online interventions.

In a large survey of students' usage of and attitudes towards online interventions, 60% were willing to use one, but only 3% had experience of using one (Dunbar, Sontag-Padilla, Kase, Seelam, & Stein, 2018). Prior experience of face-to-face therapy emerged as an important determinant of treatment preference, with students who had experience more likely to favour future face-to-face sessions, while students who had no such experience reported more reluctance to seek professional support and a preference for online support (Dunbar et al., 2018). Online therapies may therefore provide access to evidence-based interventions particularly for students who have not previously sought help.

Culjak, Kowalenko, and Tennant (2016) surveyed university students' usage and opinions of internet self-help for depression. Students rated user-

friendliness, interactivity and content as the most important features of a self-help resource. At the first timepoint (2 weeks into term), 7.18% rated self-help sites as very useful, while a larger proportion (16.31%) rated them of little use. However, increased awareness over the 8-week study period was associated with an increased willingness to use such self-help sites, suggesting that awareness-raising campaigns may increase help-seeking among students. As students often seek help only once their symptoms are having a major impact on their academic functioning (Universities UK, 2017), there is a significant potential value of anonymous, confidential, private and self-help style interventions that students may be more likely to access before symptoms become severe.

With respect to the effectiveness of web-based interventions, several meta-analyses of digital interventions have included, or been specifically targeted at, university students. A systematic narrative review of online interventions aimed at adolescents and emerging adults (12 to 25-year-olds) identified 20 trials of preventive interventions (Clarke, Kuosmanen, & Barry, 2015). The majority of these prevention studies were aimed at 18 to 25-year-olds, with eight specifically targeting university students. Across four cCBT trials rated as good quality, there were significant positive effects of the preventive intervention on symptoms of depression and anxiety (Calear, Christensen, Mackinnon, Griffiths, & O'Kearney, 2009; Clarke et al., 2009; van der Zanden, Kramer, Gerrits, & Cuijpers, 2012; Van Voorhees et al., 2008). Three trials tested cCBT for students aged 18-24, with positive effects on symptoms of both depression and anxiety post-intervention (Cukrowicz & Joiner, 2007; Kenardy, McCafferty, & Rosa, 2003; Lintvedt et al., 2013), and maintained over the course of 6 months (Kenardy, McCafferty, & Rosa, 2006). However, dropout

across the cCBT preventive interventions was high, with an average completion of 50% of modules. Early dropout was associated with higher levels of baseline depression and anxiety in several trials (Calear, Christensen, Mackinnon, & Griffiths, 2013; Kenardy et al., 2003; O'Kearney, Kang, Christensen, & Griffiths, 2009; van der Zanden et al., 2012).

Davies, Morriss, and Glazebrook (2014) conducted a meta-analysis of computer and web-based interventions aimed at depression, anxiety and general wellbeing in students. Seventeen trials were included in the meta-analysis (5 universal prevention, 11 selective/indicated prevention and 1 treatment). When compared to an inactive control, these interventions were effective with moderate to large effect sizes for depression, anxiety and stress (SMD = 0.43-0.73). In addition, no significant difference between arms was found for trials which compared web-based intervention to a comparison intervention, including face-to-face CBT. This finding may demonstrate equivalency between web-based interventions and the type of face-to-face interventions available to students (Davies et al., 2014). However, when compared to active controls, there was no evidence of effectiveness. Together, these findings suggest that web-based interventions are better than not intervening and may be as good as currently available options, but there is scope for improvement.

A meta-analysis reviewed the preventive effects of 48 digital interventions aimed at university students (Conley, Durlak, Shapiro, Kirsch, & Zahniser, 2016). The review included 22 trials of universal prevention and 26 trials of indicated prevention. The majority were unguided interventions, with 23% providing support. Half employed CBT-based techniques, with the

remainder including approaches such as mindfulness, relaxation and social skills. Outcome measures included severity of depression, anxiety and stress, general health (e.g. sleep, diet), as well as measures related to resilience, such as social and emotional skills (e.g. coping strategies), self-perception (e.g. self-esteem) and quality of interpersonal relationships. The effect sizes of multiple outcomes within trials were averaged to provide an overall effect for the intervention. Overall, there was a significant mean ES for universal interventions (ES = 0.19, 95% CI 0.11 to 0.28) and for indicated interventions (ES = 0.37, 95% CI 0.27 to 0.47), with significantly larger mean effects for indicated than for universal prevention. For indicated interventions, those with support had significantly higher ES than those without (supported: ES = 0.55, 95% CI 0.37 to 0.72; unsupported: ES = 0.28, 95% CI 0.14 to 0.40).

Few of the included trials performed follow-up assessments, but those that did demonstrated positive longer-term effects. For the eight indicated interventions that included follow-up, the ES was not significantly different from the post-intervention ES, indicating effects were maintained across the follow-up period. Only three universal interventions included follow-up, but these found ES at follow-up was significantly higher at follow-up than post-intervention, suggesting the impact of the intervention improved over time. However, one limitation of this review is that the included trials almost exclusively employed only self-report outcome measures (Conley et al., 2016). More objective measures, such as diagnostic interviews, are required to assess whether these interventions have any impact on incidence rates.

A more recent systematic review and meta-analysis of internet interventions for student mental health (Harrer et al., 2019) identified 48 studies testing 53

interventions (24 unguided, 9 included reminders, 20 guided). The majority of these trials focused on prevention. Of the included trials, 25 utilised a universal prevention approach with no preselection, 18 selected using standard cut-offs on self-report or specific risk factors and 5 were conducted with clinically diagnosed samples. The majority of trials (37) used a passive control (waitlist, no intervention control or psychoeducation without any behaviour change instructions) as a comparator, with 11 trials using active controls (placebo, diaries, or behaviour change activities). Thirty-five interventions employed CBT-based techniques, 11 were based on skills training, with the remainder using other techniques such as cognitive bias modification. Significant but small effects were found for depression (*g* = 0.18, 95% CI 0.08-0.27), anxiety (*g* = 0.27, 95% CI 0.13-0.40) and stress (*g* = 0.20, 95% CI 0.02-0.38). In terms of numbers needed to treat, these overall effect sizes equate to NNT = 9.80 for depression, NNT = 6.58 for anxiety, NNT = 8.93 for stress. In subgroup analyses, effect sizes were found to be larger for pre-selected samples and interventions that employed a CBT-based approach, were of medium length (4 to 8 weeks compared to < 4 weeks or > 8 weeks) and trials with a passive (rather than active) control arm. In contrast to previous findings that guided interventions are generally associated with larger effect sizes (Andersson & Cuijpers, 2009; Gellatly et al., 2007; Spek et al., 2007), guidance did not have a significant impact on effect sizes. Long-term outcomes were not reported in the majority of studies and, where included, length of follow-up varied so long-term effects were not pooled in this review. Further research is therefore needed to investigate whether these positive effects on depression, anxiety and stress can be further enhanced, whether they can be maintained over the longer term and whether such interventions significantly reduce incidence.

A systematic narrative review (Lattie et al., 2019) of 89 studies (22 treatment interventions; 66 preventive interventions (of which 36 were universal prevention); 1 unclear) of digital interventions for depression, anxiety or general wellbeing in university students found the majority of these studies reported effectiveness on clinical outcome measures, but high attrition and lack of continued usage of the intervention were often reported. In addition, few studies investigated the implementation of these interventions within existing university services. The potential of digital interventions to improve student mental health depends on translating the efficacy of the intervention into practice, with effective implementation and improved user experience to reduce attrition (Lattie et al., 2019).

One area that remains unclear in terms of improving preventive interventions is the inclusion of support. Meta-analyses generally show that guided iCBT outperforms unguided iCBT in terms of adherence and clinical outcomes, at least for acute treatment. For example, a meta-analysis of Internet-based and Computerised psychological treatments for depression in adults (Andersson & Cuijpers, 2009) included 12 trials, with 15 interventions (11 CBT-based, 2 Problem Solving Therapy (PST) and one using psychoeducation). Overall, the effect size was moderate (*d* = 0.41, 95%CI 0.29 to 0.54). However, subgroup analysis revealed that supported interventions produced significantly larger effect sizes (*d* = 0.61, 95% CI 0.45 to 0.77) than unsupported interventions (*d* = 0.25, 95% CI 0.14 to 0.35).

Very few trials have directly compared guided and unguided interventions to assess any additional benefits of providing guidance and a recent meta-analysis suggests the differences may be smaller than previously

found. Shim, Mahaffey, Bleidistel, and Gonzalez (2017) found nine trials with such direct comparisons. Four trials found evidence that the guided intervention was superior (Farrer, Christensen, Griffiths, & Mackinnon, 2011; Kleiboer et al., 2015; Titov, Andrews, Choi, Schwencke, & Johnston, 2009; Titov, Andrews, Choi, Schwencke, & Mahoney, 2008), but the remaining five found no significant difference, indicating similar effects can be achieved irrespective of providing support (Berger et al., 2011a; Berger, Hammerli, Gubser, Andersson, & Caspar, 2011b; Dear et al., 2015b; Kobak, Greist, Jacobi, Levy-Mack, & Greist, 2015; Santucci et al., 2014).

One proposed explanation for this disparity between guided and unguided interventions is that unguided interventions have been associated with higher drop-out rates (e.g. across 40 studies of iCBT, a mean of 74% attrition for unguided interventions, compared to 28% for guided interventions (Richards & Richardson, 2012), particularly if the intervention is provided open access (i.e. no screening or contact with researchers), with less than 1% of users completing the intervention (Christensen, Griffiths, Korten, Brittliffe, & Groves, 2004).

While support may be beneficial for acute treatment, at least in terms of encouraging adherence, the added benefit for prevention is less clear (Bolinski et al., 2018). Unguided interventions may have smaller effect sizes and a larger proportion of attrition than guided interventions, but because unguided interventions have the scope for near unlimited access, even small effects may translate to significant benefits in terms of public health (Muñoz, 2017). Unguided preventive interventions are therefore likely to be more cost-effective (Bolinski et al., 2018). In addition, as Harrer et al. (2019) found guidance did not

moderate intervention effects in student samples, it may be that students are better equipped to engage in unguided interventions, suggesting providing unguided preventive interventions in university settings has potential to be beneficial to the overall wellbeing of the student population.

A further advantage of unguided interventions is the potential to reach students who are reluctant to access face-to-face support. Of the 200 students surveyed by Levin et al. (2018), 36% reported a willingness to access professional help, while an additional 26% did not intend to access professional help but reported an intention to access at least one form of self-help, raising the overall help-seeking intentions of the sample from 36% to 62%. This suggests that help-seeking rates among students could be significantly increased by providing a wider range of self-help options in addition to formal support services. Given the burden of depression among the student population is high, even if only a minority of students were to access a self-help intervention, this still offers the potential to reduce the overall disease burden on university campuses, by engaging not only a greater number of students overall, but also providing support to a subgroup who would have remained untreated under current face-to-face approaches.

Taken together, these reviews suggest that internet interventions are effective at reducing subclinical symptoms of depression and anxiety, but with only small to moderate effects. In addition, it remains unclear whether these symptom reductions represent preventive effects as this requires assessment of incidence rates and longer follow-up periods. These findings suggest that iCBT has a positive effect on students' mental health but there is scope to improve these effect sizes and longer-term outcomes.

Preventive interventions could potentially be further improved by targeting transdiagnostic risk factors, thereby preventing several disorders with a single intervention (Nehmy, 2010). As depression and GAD are both highly prevalent and highly impactful, prevention and early intervention for these disorders is a priority. In addition, transdiagnostic interventions may be particularly valuable as co-morbidity increases the odds of significant role impairment and targeting only one disorder is unlikely to completely remove the negative impact of the co-morbid disorder (Alonso et al., 2019). A recent RCT testing a transdiagnostic intervention specifically designed for students found small but significant improvements in social anxiety symptoms and academic self-efficacy relative to no intervention (Farrer et al., 2019). The transdiagnostic intervention is aimed at a range of disorders (mood disorders, anxiety and trauma disorders, substance abuse, and eating disorders), but no significant effects were found for disorders other than social anxiety, indicating the positive effects of the intervention did not generalise across disorders. This intervention focuses on symptom clusters and specific issues relevant to students, but there was little evidence of a transdiagnostic effect.

One proposed reason for the generally small to moderate effect sizes found in prevention trials is that interventions have not been tailored towards individual presenting risk factors, with the same cognitive-behavioural intervention offered to individuals regardless of the presence or absence of cognitive risk factors (Hankin, Young, Gallop, & Garber, 2018). A more personalised approach, in which the intervention matches an individual's risk factors may result in larger preventive effects (Hankin et al., 2018). In addition, interventions may provide short-term benefit but fail to modify the underlying mechanisms (Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015), thereby leaving an

individual vulnerable over the longer-term. Directly targeting key depressogenic mechanisms is recommended to improve treatment efficacy (Watkins, 2016).

1.8 Targeting rumination for preventing depression

Topper et al. (2010) proposed repetitive negative thought (RNT), incorporating worry and rumination, as a potential target for selective prevention programmes. Worry has been defined as 'a chain of thoughts and images, negatively affect-laden and relatively uncontrollable' and 'an attempt to engage in mental problem-solving on an issue, whose outcome is uncertain but contains the possibility of one or more negative outcomes' (Borkovec, Robinson, Pruzinsky, & DePree, 1983, p.10). Rumination is defined as 'behavior and thoughts that focus one's attention on one's depressive symptoms and on the implications of these symptoms' (Nolen-Hoeksema, 1991, p.569). There is strong evidence that RNT is present across a range of disorders, including depression, generalised anxiety disorder (GAD), social anxiety and eating disorders (Ehring & Watkins, 2008; Nolen-Hoeksema & Watkins, 2011; Watkins, 2008).

Rumination is a frequently reported residual symptom of depression, with both acutely depressed and recovered individuals reporting higher levels of rumination than individuals who have never experienced depression (Roberts, Gilboa, & Gotlib, 1998). Individuals presenting with higher levels of rumination are also less responsive to medication and CBT (Ciesla & Roberts, 2007; Schmaling, Dimidjian, Katon, & Sullivan, 2002), suggesting rumination increases the risk of chronic depression.

As well as being a residual symptom, there is considerable strong evidence that rumination plays a causal role in the initial onset of a depressive

episode and the maintenance of acute symptoms (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008; Watkins, 2008). In prospective longitudinal studies, rumination predicts a) depressive symptoms over a range of follow-up periods, even after controlling for baseline symptoms severity (e.g. Abela, Brozina, & Haigh, 2002; Broderick & Korteland, 2004; Butler & Nolen-hoeksema, 1994; Nolen-Hoeksema & Morrow, 1991); b) the incidence of episodes of major depression, as well as the length of such episodes (Just & Alloy, 1997; Nolen-Hoeksema, 2000; Nolen-Hoeksema, Stice, Wade, & Bohon, 2007; Robinson & Alloy, 2003) and c) mediates the effects of other risk factors on the onset of depression (Spasojević & Alloy, 2001). RNT also predicts symptoms of other disorders, including anxiety, eating disorders and substance abuse (Nolen-Hoeksema et al., 2007).

In experimental manipulations of rumination and distraction, relative to distraction, rumination increases negative mood (Nolen-Hoeksema & Morrow, 1993), increases negative thinking (Lyubomirsky & Nolen-Hoeksema, 1995), increases recall of negative autobiographical memories (Lyubomirsky, Caldwell, & Nolen-Hoeksema, 1998), impairs concentration (Lyubomirsky, Kasri, & Zehm, 2003) and impairs problem-solving (Donaldson & Lam, 2004; Lyubomirsky & Nolen-Hoeksema, 1995; Lyubomirsky, Tucker, Caldwell, & Berg, 1999). However, the negative effects of rumination are only seen when participants are in a dysphoric state before the manipulation, demonstrating mood moderates the consequences of rumination (Watkins, 2016).

This relationship between RNT and emotional disorders is also found in children and adolescents (Abela et al., 2002; McLaughlin & Hatzenbuehler, 2009; Muris, Roelofs, Meesters, & Boomsma, 2004; Nolen-Hoeksema et al.,

2007; Schwartz & Koenig, 1996). Moreover, Hankin (2008) demonstrated that rumination is a specific risk factor for depression in adolescence, with rumination prospectively predicting fluctuations in depressive symptoms and internalising problems, but not anxious arousal or externalising problems. There is gender bias in depression rates (approximately 2:1 female: male; Kessler et al., 2005) and this is already apparent in early adolescence, with higher symptom levels seen in adolescent girls (Nolen-Hoeksema, 2001). Differences in rumination levels can partially explain this gender bias, with 27% of the association between gender and depression explained by rumination (Hankin, 2008).

Worry and rumination are commonly reported in surveys of student wellbeing, with 42.8% of student respondents ‘often’ or ‘always’ worried (Pereira et al., 2019) and indicating a tendency to internalise and have difficulty controlling emotions when faced with a setback. Two thirds of students reported dwelling on setbacks for longer than they felt they should have and over half reported a knock to their confidence as a result of a setback (McIntosh & Shaw, 2017). In addition, there was a gender imbalance for emotional control, with females scoring eight percentage points lower than males, indicating females were more likely than males to dwell on their problems.

In student samples, rumination has been found to play a role in both the onset and maintenance of depressive symptoms. Rumination prospectively predicts depressive symptoms at 6-month follow-up (Morrison & O'Connor, 2005) and the combination of rumination, stressful events and low self-esteem has been found to maintain existing depressive symptoms (Ciesla, Felton, & Roberts, 2011).

The combination of rumination and stressful events appears to be particularly deleterious for student mental health. For example, Morrison and O'Connor (2008) found high baseline rumination in combination with high levels of stress prospectively predicted a range of negative outcomes (hopelessness, dysphoria, suicidal thoughts) three weeks later. However, high trait rumination with low levels of stress predicted better outcomes, indicating that trait rumination alone does not increase distress. While this study was conducted over a short period of three weeks, a similar association between stress and rumination has been found over a one-year period (Michl, McLaughlin, Shepherd, & Nolen-Hoeksema, 2013). In this study, stressful events predicted increased rumination and rumination mediated the effect of stress on depression and anxiety at one-year follow-up.

These findings are consistent with the seminal Response Styles Theory (RST; Nolen-Hoeksema, 1991), which conceptualises rumination as a trait-like self-focused response to low mood that is stable and habitual (Nolen-Hoeksema et al., 2008; Watkins & Nolen-Hoeksema, 2014). Rumination is conceptualised as an unhelpful habit that is triggered by low moods, such as those associated with loss or stressful events.

The theory, supported by experimental evidence, proposes that rumination both worsens and prolongs low mood, with negative impacts on problem solving and a reduced ability to activate helpful behaviours (Nolen-Hoeksema, 1991; Nolen-Hoeksema et al., 2008). This fits the diathesis-stress model, in which cognitive risk factors (e.g. rumination) are particularly deleterious to mental health when triggered by stress (Morrison & O'Connor, 2005). Experimental studies have supported this diathesis-stress model, in that

rumination only shows negative consequences in the presence of low mood or stressors (Nolen-Hoeksema et al., 2008; Watkins, 2016).

In ecological momentary assessment (EMA) studies of momentary rumination, a bi-directional relationship was found with negative mood, such that rumination and negative mood worsen each other (Moberly & Watkins, 2008a; Selby, Kranzler, Panza, & Fehling, 2016; Takano, Sakamoto, & Tanno, 2013; Takano, Sakamoto, & Tanno, 2014). The relationship between stress, momentary rumination and depressive symptoms has been found in both clinical and nonclinical samples, with rumination mediating the effect of stressful events on later low mood and symptoms of depression (Genet & Siemer, 2012; Moberly & Watkins, 2008b; Ruscio et al., 2015).

As well as acting as a mediator, such momentary rumination has been found to moderate the effects of stressful events. For example, in a study of undergraduates (Connolly & Alloy, 2017), on days when students experienced a stressful event and engaged in momentary rumination, this rumination amplified the negative effects of stress on depressive symptoms. However, on days when students were exposed to stressful events but did not ruminate, or on days when they engaged in rumination but did not experience many stressors, depressive symptoms were lower, such that either stress or rumination alone did not produce deleterious effects.

Taken together, these studies in students suggest that either reducing exposure to stress, or reducing the ruminative response to stressors, will have beneficial clinical effects. While stressful events are likely to be an inevitable feature of university (Morrison & O'Connor, 2008), recent experimental and clinical studies have shown that with brief intervention, levels of rumination and

worry can be reduced (e.g. Watkins, Baeyens, & Read, 2009; Watkins & Moberly, 2009; Watkins et al., 2011; Watkins et al., 2007; Watkins et al., 2012). This suggests that rumination/worry could be a particularly promising target in improving the efficacy of preventive interventions.

One advantage of preventive interventions that target worry and rumination, rather than focusing on clinical symptoms is that this frames the therapy as a means to increase resilience and coping strategies for everyday stressors. As such, this normalises rather than medicalises common cognitive vulnerabilities (Topper et al., 2017). Such an approach may therefore encourage greater engagement from students, for whom the experience of worry and rumination is common and relatable, thereby reducing (self-)stigma as a barrier to using a preventive intervention (Topper et al., 2017).

Despite the rationale for focusing on rumination as a primary target, it is often overlooked in current treatment approaches (Watkins, 2016). In addition, there is some evidence that traditional CBT techniques may not modify rumination. For example, Haeffel (2010) tested preventive workbooks for at-risk students and found a 3-way interaction between intervention, stress and rumination, with those students who had high stress and high rumination having worse depressive symptoms after completing the traditional cognitive techniques (e.g. thought challenging) than those who had completed an adapted form of the therapy (without thought challenging) or academic skills. This pattern of findings suggests that some techniques within CBT are not effective for individuals with high levels of rumination and stress and may have an adverse effect.

Interventions that are specifically adapted to reduce rumination may therefore be particularly beneficial for individuals who are at risk of depression due to high levels of trait rumination, and particularly those who are also experiencing significant levels of stress. One recently developed intervention that aims to directly target rumination is rumination-focused cognitive-behavioural therapy (RFCBT; Watkins et al., 2007).

1.9 Rumination-Focused Cognitive-Behavioural Therapy (RFCBT)

RFCBT is an adapted form of cognitive-behavioural therapy, focusing specifically on rumination (Watkins et al., 2007). A detailed description of the underlying theories and evidence for RFCBT is provided in Chapter 2. Briefly, the intervention incorporates many elements of standard CBT (e.g. focus on the present, structured sessions, home practice, behavioural experiments) but with key differences to specifically target rumination (Watkins, 2016).

RFCBT is underpinned by theory and empirical evidence that repetitive thinking can have both unconstructive (e.g. depression, anxiety) and constructive consequences (e.g. problem solving, processing emotional events) (Watkins, 2008). Following an extensive literature review, Watkins (2008) identified key features that determine whether repetitive thinking is helpful or unhelpful: the valence of the ruminative thoughts and current mood, the context, and the level of processing (abstract vs. concrete).

The Response Styles Theory (RST; Nolen-Hoeksema, 1991) focuses on rumination in response to low mood (i.e. negative valence), with evidence that engaging in rumination can lead to depression by increasing the negative mood and inhibiting more helpful coping strategies and problem-solving (Nolen-

Hoeksema, 1991; Nolen-Hoeksema et al., 2008). However, the negative valence alone does not determine whether repetitive thought is unhelpful.

Watkins (2008) distinguishes between an abstract, evaluative processing style, as seen in RST, and a concrete, process-focused thinking style that can lead to positive outcomes. These include focusing on the task rather than evaluating oneself (Leary, Adams, & Tate, 2006), reduced overgeneralisation (Watkins, 2008), improved problem solving (Watkins & Baracaia, 2002; Watkins & Moulds, 2005) and reduced emotional reactivity to a subsequent failure event (Watkins et al., 2008).

This concrete thinking style can be trained by focusing on 'How', rather than 'Why' a stressful event occurred and recalling the step-by-step process of how it unfolded, focusing on sensory details and specific contextual details that could be triggers for engaging in a more helpful response to future stressful events (Watkins, 2016). RFCBT therefore includes exercises to increase concrete, specific, action-focused thinking, using experiential and imagery exercises to adaptively shift processing mode (including directly training concrete thinking in response to stressors, through focusing on 'How' questions and the context and sequence of a specific experience and more indirectly through increasing states that counter evaluative rumination, such as becoming absorbed in an activity and being compassionate towards oneself).

RFCBT therefore does not seek to eliminate rumination, but rather to shift towards a more helpful processing style in response to stressors. In contrast to CBT (Beck, Rush, Shaw, & Emery, 1979), RFCBT focuses much less on the content of negative thinking and challenging the veracity of individual thoughts but rather on the context and usefulness of an entire

sequence of ruminative thought, with the aim of shifting the entire process of unconstructive rumination to a more constructive thinking style.

Within RFCBT, engaging in rumination is conceptualised as a learned habitual behaviour and a form of avoidance. It is treated using techniques from Behavioural Activation (BA; Martell, Addis, & Jacobson, 2001), including Functional Analysis that analyses the specific context and function of a behaviour, with the aim of reducing behaviours that are having negative consequences and replacing these with more helpful behaviours.

RFCBT also employs approaches from the habit change literature. In order to reduce a negative habit, the first step is to identify its triggers (e.g. certain places, people, times of day, mood states) and then to make plans to either eliminate the trigger situation (Verplanken & Wood, 2006) or to engage a new, more helpful response when faced with the trigger, thereby forming new cue-response links (Verplanken & Wood, 2006). As rumination is often a response to internal states (e.g. low mood, physical symptoms of stress) removing the trigger is not always practical so RFCBT focuses mainly on changing to cue-response link.

RFCBT therefore involves techniques to increase awareness of specific triggers for rumination and making plans to practise more helpful responses to these triggers in order to counter-condition the unhelpful rumination with more adaptive responses (Watkins & Nolen-Hoeksema, 2014). These plans take the form of implementation intentions (Gollwitzer, 1999) using an IF-THEN conditional structure. This format improves goal-directed behaviour by not only specifying what behaviour to engage in, but also exactly when, where and how to implement it (Prestwich, Sheeran, Webb, & Gollwitzer, 2015).

1.9.1 Empirical evidence for RFCBT as a treatment for residual depression

RFCBT has produced positive findings in terms of treating clients with depression. An initial case series (Watkins et al., 2007) investigated the effect of individual RFCBT delivered in up to 12 hourly sessions to fourteen clients with medication-refractory depression (defined as meeting criteria for MDE in the past 18 months, but not in the past 2 months; presence of residual symptoms of depression; currently taking a therapeutic dose of antidepressant medication, including at least eight continuous weeks during MDE and for the past two months). RFCBT significantly reduced depressive symptoms pre- to post (mean reduction on BDI = 20.36 points), with 71% achieving treatment response (defined as ≥ 50% reduction in baseline depressive symptoms on HRSD) and 50% achieving full remission (defined as scoring below 8 on HRSD post-intervention and below 9 on BDI for at least 4 consecutive weeks). RFCBT also significantly reduced rumination, which was within the range seen in currently depressed patients pre-treatment and fell to within the range seen in never-depressed individuals post-treatment. Additionally, diagnoses of comorbid disorders (including social phobia, GAD and panic disorder) fell by 71% pre- to post-treatment, indicating a transdiagnostic benefit of RFCBT.

In a phase II randomised-controlled trial (Watkins et al., 2011), participants meeting criteria for medication refractory depression (defined by the same criteria as used in the case series) were randomised to receive RFCBT in addition to treatment as usual (TAU) or to receive TAU only (ongoing antidepressant medication and clinical management in outpatient settings). The addition of RFCBT to TAU significantly reduced residual depressive symptoms and enhanced remission rates compared to TAU alone. There was a large between-treatment effect size on both HRSD (d = 1.1) and BDI (d = 0.94).

Additionally, rates of treatment response (26% TAU vs. 81% RFCBT) and remission (21% TAU vs. 62% RFCBT) were significantly different. RFCBT also improved longer term outcomes with a significant reduction in 5-month relapse rates (53% TAU vs. 9.5% RFCBT). Moreover, in support of the hypothesised mechanism of change, RFCBT reduced self-reported rumination more than TAU. These changes in rumination were found to be a significant mediator of the treatment effects, although rumination was only measured concurrently so reverse causality cannot be ruled out.

1.9.2 Comparison of RFCBT to other treatments

Whilst RFCBT includes many techniques that are also found in CBT (e.g. Socratic questioning, self-monitoring, behavioural experiments, activity scheduling), these are used slightly differently as they are specifically targeted at rumination, linked to warning signs and implemented based on a formulation of the function of the rumination (Watkins, 2016). Traditional CBT (Beck et al., 1979) does not include much focus on rumination. A key technique in CBT is thought challenging, whereby evidence for and against negative thoughts is weighed up and an alternative, more realistic thought is developed. Watkins (2016) argues that this approach is not particularly effective for patients with a strong tendency to ruminate, as challenging one thought does not stop the long stream of thoughts. Watkins (2016) identifies only two situations when thought challenging is helpful for rumination: when it successfully challenges the very first thought so the stream does not have an opportunity to start, or practising thought challenging as a specific technique in response to stressful situations, so that the thought challenging becomes a new, helpful habit to replace the rumination.

The standard CBT approach of thought challenging may even be counterproductive in treating rumination, as challenging thoughts may lead to further self-evaluation and a new stream of rumination is then activated (Watkins, 2016). In addition, ruminators are likely to focus on the causes and meanings of their personal experiences and symptoms, so discussing these thoughts in detail with a therapist can keep the patient stuck in the ruminative cycle rather than encouraging more concrete, action-focused thinking that leads to positive outcomes.

RFCBT therefore involves a more behavioural than cognitive approach to shifting ruminative thoughts. As in Behavioural Activation (Martell et al., 2001), within RFCBT rumination is conceptualised as a learned habit that serves an avoidant function. Consistent with the BA approach to depression, RFCBT uses functional analysis to understand the context and function of rumination as an avoidant behaviour and replace it with more adaptive approach behaviours. In BA, rumination is only one of multiple target behaviours, whereas RFCBT explicitly focuses on rumination as the key target for treatment. In addition, RFCBT contains a novel approach not found in either CBT or BA as it is derived from previous experimental work on shifting to a more concrete, process-focused thinking style, using techniques such as concreteness, absorption and compassion (Watkins, 2016).

One other therapy that specifically aims to reduce rumination is mindfulness-based cognitive therapy (MBCT; Teasdale, Segal, & Williams, 1995). This involves meditation sessions that encourage individuals to focus on the present moment and noting thoughts, feelings and physical sensations without judgment. This non-judgment and viewing thoughts from a distance counters the abstract evaluative thinking style of depressive rumination and cultivates a

more concrete, moment-by-moment focus. However, this approach requires individuals to gradually learn to distance themselves from their depressive rumination, whereas RFCBT has a more direct emphasis on shifting to more helpful strategies with specific exercises and repeated practice (Watkins, 2016). There is therefore some overlap between mindfulness and RFCBT, in that both approaches encourage more concreteness and compassion, mindfulness is a less direct approach that involves repeatedly practising meditation in order to gain perspective on thoughts and feelings (which may be best performed when not acutely distressed). In contrast RFCBT is explicit in its aim to shift to a more concrete and compassionate response when faced with a difficult situation (i.e. when feeling distressed).

MBCT was originally designed to prevent relapse and recurrence of depression. Concerns have been raised that meditating during an acute depressive episode may be difficult, or even harmful, because of the concentration needed and the increased awareness of one's symptoms (Strauss et al. 2014). Recent evidence suggests MBCT may be effective for patients presenting to IAPT services with acute symptoms (Tickell et al., 2020) but, as effect sizes were smaller than for other treatments already provided by IAPT, Tickell et al. (2020) recommended MBCT be provided as a complement to existing acute treatments to improve longer term symptom management. In contrast, because RFCBT is designed to directly target elevated rumination, irrespective of symptoms of depression, it can be used throughout the course of depression (i.e. for prevention, acute episodes, and relapse prevention).

1.10 RFCBT and prevention

Topper, Emmelkamp, Watkins, & Ehring (2017) adapted RFCBT for use as a preventive intervention for adolescents and young adults, with two different modes of delivery: internet-based RFCBT (i-RFCBT) and group-delivered RFCBT, compared to waiting list control.

The i-RFCBT intervention is described in detail using the TIDieR checklist (Hoffmann et al., 2014) in Chapter 2. Briefly, i-RFCBT consists of six modules, each taking around an hour to complete for each session and 1-to-2 weeks practice in-between sessions. It includes psycho-education, mood diaries, on-line experiential exercises using audio-recordings, pictures, and video vignettes of students' experiences of the therapy.

Participants in the prevention trial were high school and university students (*N* = 251) aged 15-22, selected for elevated worry and rumination (scoring on top quartiles of respective measures: ≥ 50 on Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990); ≥ 40 on Ruminative Response Scale of the Response Styles Questionnaire (RRS; Nolen-Hoeksema & Morrow, 1991) but no current diagnosis of major depression or generalised anxiety disorder (assessed using cut-offs on self-report measures). Eligible participants were randomised to i-RFCBT, group RFCBT or waitlist control and self-report outcome measures were conducted post-intervention (6 weeks) and at 3- and 12-month follow-ups. Randomisation was stratified by gender and educational level. Stratification by gender reflects the known gender differences (approximately 2:1 female: male) for worry and rumination and the incidence of depression in adolescence (Nolen-Hoeksema et al., 2008). Stratification by educational level (high school vs. university) was

used to control for developmental differences, particularly as the transition between the two is a high-risk period. Stressful life events were significantly higher in the control arm than either intervention arm, so the main analyses controlled for any potential impact by including number of events as a covariate.

Relative to the control arm, both interventions significantly reduced RNT (*d* = 0.53 to 0.89) as well as symptoms of depression and anxiety (*d* = 0.36 to 0.72) post-intervention. These beneficial effects were maintained across the follow-up period, with no significant differences between the outcomes of the two RFCBT interventions. Incidence rates were also estimated using clinical cut-offs on the symptom measures. Both interventions significantly reduced the incidence of both MDE (15.3% group; 14.7% i-RFCBT) and GAD (18.0% group; 16.0% i-RFCBT) relative to controls (32.4% MDE; 42.2% GAD). Change in rumination was a significant mediator of these intervention effects.

These findings provide further evidence that rumination increases the risk of depression and anxiety, given that incidence rates in the control group are considerably higher than the reported prevalence rates in adolescents and young adults (19%; McManus et al., 2016). In addition, these findings support the efficacy of RFCBT to reduce rumination and worry and that targeting rumination may have preventive effects in adolescents and young adults. The pattern of findings is also consistent with the hypothesis that rumination is a transdiagnostic risk factor, as effects were found for both depression and anxiety.

The Topper et al. (2017) trial provides preliminary evidence for the efficacy of RFCBT as a targeted preventive intervention. However, diagnostic status was only assessed using clinical cut-offs on self-report measures, which

are more likely to result in false positives (Topper et al., 2017). Diagnostic interviews are more conservative as it is possible for individuals to score above the cut-off but not fulfil all the diagnostic criteria. A further limitation of self-report is that the resulting incidence rates only include point prevalence, rather than retrospective incidence as the periods between follow-up assessments are not captured. Similarly, because of the lack of a retrospective measure, Topper et al. (2017) were unable to assess whether participants had a history of depression and it is therefore unclear whether the intervention had differential effects in terms of preventing first onset or relapse/recurrence. Diagnostic interviews are therefore able to provide a more accurate measure of both incidence/recurrence and the time to onset.

1.11 Aims of the PhD

The aim of the studies reported in this thesis are to replicate and extend the Topper et al. (2017) trial in order to assess the efficacy of internet-based rumination-focused cognitive-behavioural therapy (i-RFCBT) in the treatment and prevention of depression in UK university students. Given the evidence that university students are a particularly high-risk subgroup, the thesis aims to test whether i-RFCBT is acceptable and efficacious in this specific population.

1.11.1 Study 1: Audit and open multiple baseline case series (Chapter 3)

While there is evidence for the efficacy of RFCBT for the treatment and prevention of major depression, the intervention has not previously been implemented in a routine clinical setting. The first study (Chapter 3) therefore consists of a service audit and an open multiple baseline case series to test the effectiveness of i-RFCBT as delivered in the Wellbeing Services at the University of Exeter. Within this setting the intervention is provided as a guided

treatment for acute symptoms of depression and/or anxiety for students actively seeking help. As an audit of the implementation of i-RFCBT within the Wellbeing Services, standardised measures that are routinely collected and recorded for service monitoring purposes will be collected. This data concerns service usage data (numbers accessing the intervention) and anonymised pre-intervention and post-intervention scores for depression and anxiety (PHQ-9 and GAD-7). This audit will test the hypothesis that i-RFCBT will be efficacious in treating acute symptoms of depression and anxiety within a routine clinical service. In addition to the overall service audit, individual consent will be sought to participate in a multiple baseline case series, in which weekly scores will be collected to measure change in symptoms and rumination over time.

While the students attending the Wellbeing Services will receive i-RFCBT as a treatment for acute depression or anxiety, the remaining studies reported in this thesis sought to assess the acceptability and efficacy of i-RFCBT as a preventive intervention for HE students.

1.11.2 Study 2: Qualitative analysis of the acceptability of i-RFCBT for prevention (Chapter 4):

As the literature has highlighted an issue with high drop-out rates with internet-based interventions (Richardson et al., 2010b; Waller & Gilbody, 2009), Study 2 (Chapter 4) sought to investigate the relevance and acceptability of internet-based approaches for prevention for a high-risk UK university sample as well as obtain specific feedback on the i-RFCBT intervention.

1.11.3 Study 3: RESPOND (REducing Stress and Preventing Depression feasibility RCT for internet-RFCBT) (Chapters 5 and 6)

The primary aim of the RESPOND trial is to replicate the Topper et al. (2017) findings comparing guided i-RFCBT to care as usual, while addressing the identified limitations by including the gold standard diagnostic interview to increase accuracy in determining current and past diagnostic status, and to allow for stratification on history of depression. To achieve this, the well-validated Structured Clinical Interview for DSM-IV (SCID-I; First et al., 2002) is included.

As a secondary aim, we will also explore the feasibility and acceptability of an unguided version of i-RFCBT to prevent depression. The Topper et al (2017) trial used guided i-RFCBT. However, prevention requires widespread dissemination. As guided interventions are necessarily limited by clinician availability, we therefore also aim to assess the potential for i-RFCBT to be delivered as an unguided self-help intervention. As this format is previously untested, a quasi phase-II pilot feasibility study, comparing unguided i-RFCBT to usual care aims to assess acceptability and estimate effect sizes of this intervention.

CHAPTER 2: Description of Internet-based rumination-focused cognitive-behavioural therapy (i-RFCBT)

The aim of this chapter is to provide a more complete description of web-based rumination-focused cognitive-behavioural therapy (i-RFCBT) than provided in the individual study chapters. Because the quality of published intervention descriptions is generally poor, the Template for Intervention Description and Replication (TIDieR) checklist (Hoffmann et al., 2014) has been developed to improve the reporting of interventions. The aim of this checklist is to provide sufficiently detailed descriptions for researchers to conduct replication studies and for clinicians and patients to implement interventions correctly. The checklist consists of twelve items relating to the why, what, who, how, where, when, how much and how well of delivering a clinical intervention.

This thesis reports on two variants of web-based rumination-focused cognitive-behavioural therapy intervention (i-RFCBT): one guided (supported by a therapist) and the other unguided (self-administered). As the two variants are almost identical in content, this chapter first describes the guided version in detail (Section 2.1). Section 2.2 then provides a separate description of unguided i-RFCBT, specifically identifying where the two versions differ. In both sections, each TIDieR checklist item and a brief description of these (Hoffmann et al., 2014) is provided as a subheading, followed by a description of the relevant elements of guided/unguided i-RFCBT. Finally, Section 2.3 summarises the studies undertaken to assess i-RFCBT. As the participants in these studies were all university students and i-RFCBT was tested as both a treatment and a preventive intervention, the term student rather than patient/client is used throughout this chapter to describe the users of i-RFCBT.

2.1. Guided i-RFCBT

2.1.1 Brief name

Guided internet-based rumination-focused cognitive-behavioural therapy (i-RFCBT) consists of the key treatment components of face-to-face RFCBT, adapted for web-based online delivery, with therapist support.

2.1.2 Why - Rationale of key elements of the intervention

Rumination plays an important role in the onset and maintenance of depression (Nolen-Hoeksema et al., 2008; Watkins, 2008). It also remains elevated after remission from depression (Riso et al., 2003; Roberts et al., 1998) and is associated with poorer response to antidepressant medication and cognitive therapy (Ciesla & Roberts, 2002; Schmaling et al., 2002), increasing the risk of relapse. As well as playing a significant role in depression, there is evidence that rumination is a transdiagnostic process, involved in the development of other disorders such as generalised anxiety disorder (GAD) and eating disorders (Ehring & Watkins, 2008; Watkins, 2008). Even in the absence of a diagnosable disorder, depressive rumination can cause significant distress, with negative consequences such as self-criticism, lack of motivation and hopelessness (Watkins, 2016). Despite these negative consequences, standard therapeutic approaches often neglect rumination (Watkins, 2016).

As outlined in Chapter 1, there are several key reasons for targeting rumination in university students: a) students frequently report high levels of worry and dwelling on problems (McIntosh & Shaw, 2017; Pereira et al., 2019) b) in a student sample, rumination prospectively predicted depressive symptoms 6 months later (Morrison & O'Connor, 2005) and c) rumination

interacts with the effects of other risk factors (e.g. stressful events, low self-esteem) on concurrent and future symptoms of depression (Ciesla et al., 2011; Connolly & Alloy, 2017; Michl et al., 2013). As a risk factor that is highly prevalent and highly impactful among university students, an intervention which directly targets rumination has the potential to significantly reduce depression among this population.

Rumination-focused cognitive-behavioural therapy (RFCBT) (Watkins, 2016; Watkins et al., 2007) was designed to specifically target depressive rumination. Directly targeting rumination has a number of theoretical benefits. First, as rumination is a transdiagnostic process, multiple disorders can be treated with a single intervention (Topper et al., 2010). Second, reducing rumination can also improve longer term outcomes by reducing both an important distressing residual symptom, reducing the risk of relapse, and preventing first onset of clinical disorders in at-risk populations (Watkins, 2016).

RFCBT was originally developed as a face-to-face intervention. A detailed description is provided by Watkins (2016). RFCBT is underpinned by the key principles of CBT (e.g. Socratic questioning, self-monitoring, behavioural experiments) but with several key adaptations, informed by theory and empirical findings (Watkins, 2016). Firstly, RFCBT normalises rumination and teaches individuals to distinguish between pathological rumination and more helpful repetitive thinking in response to a difficult situation. The Control Theory account of state rumination (Martin & Tesser, 1996) hypothesises that rumination is triggered by unattained goals and can be either constructive or unconstructive depending on whether it helps an individual to move closer to their goal or only emphasises the discrepancy between one's current situation

and the desired goal. Rumination will therefore persist until the goal is either reached or no longer valued, for example by being replaced by a new goal (Martin & Tesser, 1996). Rumination can be particularly persistent when goals are difficult to achieve, are in conflict with another goal or are poorly defined, such that the individual is unclear how to achieve the goal (Martin & Tesser, 1996).

One factor that determines whether or not the ruminative response is helpful is the processing mode adopted during repetitive thinking. Watkins (2008) reviewed the evidence for both unconstructive and constructive consequences of repetitive thought. The main unconstructive consequences identified from the literature were common mental disorders (depression and anxiety) and physical illness. In contrast repetitive thought could lead to positive outcomes such as processing and recovering from a traumatic experience, planning, recovery from depression and treatment seeking for health complaints. Based on an extensive review of the literature, Watkins (2008) identified common elements of both the structure and process of repetitive thought that determine whether it is constructive or unconstructive: valence of thought content and overall mood, the situation in which the thoughts occur, and level of processing (abstract vs. concrete).

In terms of valence, the most prominent theory of rumination, the Response Styles Theory (RST; Nolen-Hoeksema, 1991) emphasises the negative consequences of rumination that occurs in response to low mood. There is evidence that depressive rumination leads to clinical depression by amplifying negative mood, interfering with problem-solving abilities and reducing helpful behaviours (Nolen-Hoeksema, 1991; Nolen-Hoeksema et al., 2008).

Watkins (2008) proposed the elaborated control theory to explain the combination of structure and process in determining whether RT has constructive or unconstructive consequences. More specifically, engaging in abstract, evaluative processing in response to a stressful situation is most likely to lead to unconstructive consequences. This is analogous to depressive rumination in RST, which focuses on the causes and implications of one's low mood. However, the elaborated control theory is also able to explain why RT can have constructive consequences, for example adopting a concrete, process-focused style during a difficult situation encourages effective problem-solving.

In terms of level of processing, Watkins (2008) presents evidence for distinct forms of rumination with either unconstructive or constructive consequences. Unconstructive rumination is characterised by an abstract, evaluative thinking style, asking 'Why?' a difficult event happened, whereas constructive repetitive thought is concrete, specific and process-focused, asking 'How?' a stressful event happened. A more concrete thinking style can be trained by recalling a stressful event and focusing in detail on the direct experience of the event (i.e. sensory detail and the distinctive features of the event); reflecting on how an event unfolded (in as much detail as possible, as if watching a film frame-by-frame) and any triggers or turning points that could be used to inform future plans for how to manage such difficult situations in the future (Watkins, 2016).

Concrete thinking in response to a difficult situation has several advantages over abstract thinking. Firstly, concrete thinking improves one's ability to focus on the immediate needs of the task rather than self-evaluative

thoughts (Leary, Adams, & Tate, 2006). Secondly, concrete thinking reduces overgeneralisation from one failure to judging oneself as a failure (Watkins, 2008), with such overgeneralisations shown to increase risk of depression (Carver, 1998). In experimental studies, concrete thinking, when compared to abstract thinking, also improves problem solving (Watkins & Baracaia, 2002; Watkins & Moulds, 2005) and repeated practice of concrete thinking reduces emotional reactivity to a subsequent failure event (Watkins et al., 2008). RFCBT therefore aims to shift an individual's thinking style from abstract to concrete when faced with difficult situations. This shift in processing style differentiates RFCBT from standard CBT, which challenges the content of individual thoughts (Beck, Rush, Shaw, & Emery, 1979).

While this elaborated control theory is able to consolidate elements of both RST and the control theory, it does not explain how state episodes of depression are linked to trait rumination. Watkins and Nolen-Hoeksema (2014) propose a habit-goal framework, which includes the three principles of habitual behaviour outlined by Wood and Neal (2007), namely (a) that habits are triggered by context, (b) that this triggering is not affected by goals, and (c) that habits develop slowly and are therefore resistant to change.

Within RFCBT, rumination is therefore also conceptualised as a learned habit (Watkins & Nolen-Hoeksema, 2014). A habit is "a behavior that has a history of repetition, is characterized by a lack of awareness and conscious intent, is mentally efficient, and is sometimes difficult to control" (Verplanken, Friborg, Wang, Trafimow, & Woolf, 2007, p. 526). While state episodes of rumination may initially be triggered by goal discrepancy (Martin & Tesser, 1996), the ruminative response can become habitual if it occurs frequently and

in the same context, such that an association is formed between the context (e.g. a particular location, time of day, mood) and the ruminative response (Watkins & Nolen-Hoeksema, 2014). The habitual rumination then becomes triggered automatically by the environmental or internal context (e.g., sad mood), regardless of any goal discrepancies (Watkins & Nolen-Hoeksema, 2014).

The behavioural activation (BA) approach (Martell et al., 2001) also views rumination as a learned behaviour that serves particular functions. One such hypothesised function is that of avoidance of distress, such that the rumination becomes negatively reinforced (Martell et al., 2001).

Depressive rumination is therefore conceptualised as a habitual behaviour that serves an avoidant function. Consistent with the BA approach to treating rumination (Martell, Dimidjian, & Herman-Dunn, 2013), RFCBT treats rumination as an internal behaviour, targeted using the same BA principles applied to overt behaviours. Specifically, this involves the use of functional analysis to understand the context and function of rumination and then replacing this ruminative behaviour with a more adaptive behaviour that serves the same function but without the negative consequences of rumination (Watkins, 2016).

Changing habits requires an awareness of the triggers of the habitual behaviour and making plans to do something differently, either by changing the environmental context which triggers the habitual behaviour (Verplanken & Wood, 2006), or counterconditioning an alternative, more helpful response to those trigger situations (Wood & Neal, 2007). While changing environmental context may be possible for some external triggers, longer-lasting change is

likely to be achieved by altering the context-response linkage. The techniques within i-RFCBT are therefore designed to train new, helpful responses to the cues that ordinarily trigger rumination, which with repeated practise form a new context-response link.

Within i-RFCBT, the use of implementation intentions (Gollwitzer, 1999) in the form of IF-THEN plans is used to countercondition more helpful responses. These implementation intentions are shown to increase goal-directed behaviour, as the superordinate goal only specifies what to do, whereas the subordinate implementation intention identifies precisely where, when and how a target behaviour will be implemented (Prestwich, Sheeran, Webb, & Gollwitzer, 2015). The IF-THEN conditional format of implementation intentions is also an important feature, as it both increases the saliency of opportunities to act (the 'If' section of the plan) and serves to strengthen the link between the situation and the planned response (cue-response linkage), such that when that situation is encountered the response can occur relatively automatically, without much conscious effort (Webb & Sheeran, 2007). Stronger habits also require stronger implementation intentions to overcome the original response (Gollwitzer, 2014). One approach to creating stronger implementation intentions is through immersive experiential exercises, which have been shown to strengthen the cue-response linkage (Knauper et al., 2011). I-RFCBT therefore includes several experiential audio exercises which aim to strengthen implementation intentions by acting as a mental rehearsal, imagining responding to a trigger situation in the desired way.

The advantages of using concrete thinking in response to difficulties also extend to the IF-THEN implementation intentions used in the intervention.

Experimental studies (Wieber, Sezer, & Gollwitzer, 2013) have shown that a 'Why' mindset hinders implementation intentions, as thinking about reasons for the behaviour interrupts the automaticity of the cue-response linkage. Encouraging a concrete thinking style, as incorporated in RFCBT, should therefore also improve the effectiveness of the implementation intentions by making a highly detailed and specific plans of when, where, how and with whom (but not why) the desired behaviour will be carried out.

I-RFCBT contains the same therapeutic components as face-to-face RFCBT, adapted for internet-based delivery. This adaptation was made because internet-based delivery has the potential to greatly increase the accessibility of psychological interventions and offers a range of advantages to users, clinicians and funders, such as: availability at any time; greater autonomy for user; less time consuming for therapist; more time for reflection; reduced stigma compared to visiting a therapist; reduced cost (Andersson, 2010; Muñoz et al., 2010; Richardson et al., 2010b)

2.1.3 What (Materials used in the intervention or training of providers)

The intervention consists of 6 internet-delivered modules, split into smaller sessions (separate webpages) so that the materials are presented in easier-to-manage chunks that can be completed in 10-to-15 minutes. Each module includes text instructions and psycho-education as well as images and a range of interactive features. These include video case studies of two students (played by actors) discussing their experiences of worry, rumination and using the i-RFCBT techniques; audio exercises; reflective writing exercises; mood rating scales and questionnaires. Conditional feedback is built into the interactive exercises to highlight techniques that were particularly helpful e.g. if

mood ratings showed a marked improvement after an exercise compared to the rating before the exercise.

Symptom monitoring is completed at the end of each module, using standard questionnaires to assess depression (The Patient Health Questionnaire; PHQ-9; Kroenke et al., 2001) and anxiety (The Generalised Anxiety Disorder Screener; GAD-7; Spitzer, Kroenke, Williams, & Löwe, 2006). To ensure safety, conditional feedback acknowledging risk is built in to the PHQ-9 questionnaire (presented if PHQ-9 item 9 re suicide risk is scored 2 or 3). This feedback recommends the student to contact their GP or to access emergency services if the need is urgent. It also provides contact details for support organisations.

Consistent with the conceptualisation of rumination as a learned habit, measures also record the strength of ruminative habit each week to assess whether this weakens across the course of the intervention. These measures are: The Habit Index of Negative Thinking (HINT; Verplanken et al., 2007) and The Ruminative Habit (RH) scale, adapted from the Self-Report Habit Index (SRHI; Verplanken & Orbell, 2003) as well the generalisation subscale from a standardised measure of overgeneralisation (The Attitudes Towards Self scale; ATS; Carver, 2013). From module 3 onwards the strength of healthy habits is also measured using the same items as the HINT but applied to the IF-THEN plans, administered during the reflection section at the start of each module.

2.1.4 What (Procedures used in the intervention, including enabling or support)

The modules consist of the same overall series of activities: reflection on homework exercises; introduction of new techniques and practising these live

during the session; planning how to implement the new techniques as homework and, finally, scheduling a specific time to complete the next module. A more detailed description of the techniques included in each individual module follows:

Module 1

The first module serves to socialise the student into the treatment model, providing a rationale for focusing on worry, rumination and avoidance, and an introduction to the distinction between unhelpful and helpful responses. Students conduct an analysis of three specific stressful events (related to work/university; family; friends/partner) to better understand their triggers and responses to stressful situations as well as differentiate between more versus less helpful ways of responding. This uses techniques from face-to-face RFCBT (Watkins, 2016) consisting of elements of the ABC analysis (identifying antecedents, behaviours and consequences) as well as the CUDOS analysis, identifying the Context (where and when rumination occurs); Usefulness (did the rumination lead to positive outcomes); Development (when the rumination first started) and alternative OptionS (what are the alternatives to rumination that have produced more positive consequences). The CUDOS approach focuses on the variability of rumination to highlight effective and ineffective ways of responding to the same stressful situation.

Questionnaires are used to identify common experiences of worry, rumination (e.g. “Do you spend a lot of time thinking about yourself and how you feel?”) and overgeneralisation (e.g. “Does a single mistake make you feel like a complete failure?”) to both normalise these experiences and highlight that such responses are likely to increase stress.

The final session covers rumination as an unhelpful habit and the need to increase awareness of triggers as a first step to change. This is achieved through completion of a Mood Diary both in session and as daily homework for the first two weeks, comparing recent situations where the student felt bad to situations where they felt better (identifying specific trigger situations; strength of emotion during the situation; whether rumination occurred in response to the negative situation; consequences of responses to the situations).

Module 2

The second module serves to deepen the understanding of the consequences and causes of worry and rumination. Students endorse questionnaire items of commonly reported negative consequences (e.g. “It makes it hard for me to concentrate”; “It is tiring and de-motivating”), in line with the behavioural activation (BA) approach, using negative consequences to demonstrate how pathological rumination exacerbates the original problem (Martell et al., 2013). While the BA approach focuses on the negative consequences, i-RFCBT differs by also highlighting specific situations where there may be positive consequences (e.g. “It has helped me with problem solving.”) to help make the distinction between unhelpful and helpful bouts of repetitive thought as, under the right circumstances, thinking about one’s problems can be helpful.

Questionnaires are also used to identify triggers for rumination, with items listing common situations (e.g. “When I’m under pressure”) and settings (e.g. “When I’m alone”) as well as internal warning signs in the form of physical symptoms (e.g. “increased heart rate”); actions (e.g. “I start putting things off”) and thinking (e.g. “I start asking “Why me?”). Where possible, students are

encouraged to change these environmental contexts e.g. if rumination is triggered at a certain time of day, such as lying in bed in the morning, a behavioural experiment can be conducted to test whether changing one's morning routine reduces the rumination. However, as rumination is often triggered by internal cues, such as feeling stressed, a simple change to the environmental context is not always feasible and rumination must be counter-conditioned with IF-THEN plans to practise new, more helpful responses.

Four alternative responses are introduced: slowing things down (focusing on one task at a time rather than trying to do too much at once); being more active (using physical activity as an alternative to sitting still and ruminating); breaking things down (working on small steps rather than feeling overwhelmed by a large project) and opposite action (choosing to behave in a way directly opposed to one's internal feelings). The opposite action serves to replace avoidant behaviours (e.g. withdrawing when feeling sad) with more helpful approach behaviours (e.g. engaging in a positive activity).

Module 3

The third module covers relaxation and concreteness. These are practised using experiential auditory exercises and behavioural experiments, with physical feelings and emotions rated before and after the auditory exercises to assess how helpful the technique was. Firstly, the relaxation audio exercise focuses on slowing breathing and progressive muscle relaxation before opening awareness outwards to the wider environment, with the aim of helping students to manage physical symptoms of stress and to become grounded in the present moment. An IF-THEN plan is generated to use the relaxation audio exercise in response to physical warning signs.

Concreteness training aims to shift processing style through the use of audio exercises. This involves a Why-How behavioural experiment to highlight the differences between thinking about a stressful situation in an abstract, evaluative way (e.g. thinking 'Why did this happen to me?') versus thinking about the same situation in a concrete, specific way (e.g. 'How did this happen?'). Finally, the relaxation and concreteness techniques are combined to encourage a relaxed state before thinking about a personally stressful situation in a more concrete way, consisting of prompts to focus on the context in which the situation occurs, to notice sensory-perceptual details and to ask helpful "How?" questions such as "How did this happen?" "How can I start to tackle this problem?".

Module 4

This module builds on earlier functional analysis, helping students to understand why they worry and ruminate. Free text questions assess potential advantages of rumination e.g. "Which bad things do you avoid by worrying or ruminating?" and fixed questionnaires also assess common reasons for worry and rumination (e.g. "To avoid the risk of failure or embarrassment"). These questions are used to further distinguish unhelpful and helpful thinking about difficulties. Three rules-of-thumb are provided to identify when rumination may be unproductive: rumination on unanswerable questions; rumination that lasts more than 30 minutes and rumination that does not lead to a specific plan or action.

As rumination can interfere with full engagement or enjoyment of activities, absorption is introduced as a means to become fully immersed in activities (Watkins, 2016). This involves a focus on the process of the activity

rather than on evaluating one's performance. Absorption is encouraged through an experiential audio exercise, comparing the differences between thoughts, feelings, actions and focus of attention when absorbed versus not absorbed in an activity. The absorption audio is then used repeatedly in homework practice to: encourage a more concrete thinking style (focusing on the details and sensory experiences of the situation); as a way to increase focus and motivation before engaging in an activity and as a guide to identifying specific absorbing activities to practise. Students are asked to schedule one absorbing activity for their weekly homework.

Module 5

Module five focuses on self-compassion. High ruminators often use negative and critical self-talk, sometimes in an attempt to motivate themselves, and can find self-compassion challenging (Watkins, 2016). Barriers to self-compassion include finding it strange or unfamiliar to talk to oneself kindly and worrying that one will lose motivation and be less effective. The compassion exercises therefore begin with imagining talking compassionately towards a friend or family member, noticing the content of the speech and tone of voice, before practising using this same compassionate talk to oneself. Some concrete steps are provided: to normalise the situation; focus on any progress already made; highlight past successes; put the situation in perspective and encourage oneself to take the next step to move forward. To facilitate the use of compassionate self-talk, students are asked to plan specific phrases to use in upcoming stressful situations, break down the task to identify the smallest amount of self-compassion they would be willing to try, and to weigh up the pros and cons of being compassionate versus being self-critical. Self-compassion

also involves identifying activities to increase (e.g. taking exercise, getting more sleep) or decrease (e.g. drinking less alcohol, having a less pressured schedule), to take better care of oneself. Plans are made to build in more self-compassionate activities.

Module 6

As rumination often affects interpersonal relationships. the final module introduces the importance of assertiveness. Students identify a situation where they failed to be assertive, read a list of tips to behave more assertively (e.g. focus on one's own values and feelings; be calm, clear and direct and to seek and give feedback) and make an IF-THEN plan to implement these behaviours. The final session encourages students to reflect on their experiences over the course of the intervention, identify which techniques were most helpful and make plans to continue implementing these as relapse prevention.

Support provided

Students were supported by a clinician who provided asynchronous written feedback within the secure internet platform at the end of each completed module. The therapist received notification of a completed module, logged in to the platform to view the student's responses, provided written feedback and the student then received notification that feedback was available. Additionally, any risk reported was followed up with an email and, if necessary, a telephone call to assess the level of risk and obtain appropriate clinical support for the student, in line with the departmental risk protocol.

Template feedbacks provided clinicians with model responses for common difficulties, which the therapist then tailored to individual students,

providing a personalised response. The feedback served to acknowledge and normalise any challenges, highlight successes and suggest refinements to plans. The aim of the feedback was therefore to motivate the student, increase the chances that the intervention will be successful and help the student to feel supported by conveying a sense of warmth and empathy. As well as receiving feedback at the end of each module, students were able to send direct messages to their therapist within the platform.

2.1.5 Who provided (expertise, background, training)

The guided support was provided by qualified clinicians, either psychological wellbeing practitioners (PWPs), or clinical psychologists. Clinicians were provided with specific training by the developer of RFCBT (EW), involving one to two-day workshops covering the rationale and content of i-RFCBT to ensure therapists followed the treatment model. In addition, these workshops also involved detailed training and practice in providing effective feedback for several case examples. The first two feedbacks were also checked by EW prior to being sent to students. This feedback training is necessary to ensure therapists are able to convey nonspecific therapeutic factors, such as empathy and optimism in writing (Watkins, 2016). Ongoing supervision was also provided by EW to begin with and continued by an experienced RFCBT clinician (JC).

2.1.6 How (mode of delivery and whether intervention was provided to individuals or groups)

The intervention was accessed individually by participants, via the internet. The internet treatment was delivered on a secure internet platform using software owned, programmed, and hosted by Minddistrict

(https://www.minddistrict.com), using a research licence purchased from Minddistrict by the research team. The specific content (e.g. text, images, interactive exercises), developed by the research team led by Edward Watkins, was entered into the platform using its Content Management System (CMS) by the research team.

2.1.7 Where (location and infrastructure)

The intervention was accessed on a secure, password protected website. The website is not publicly accessible. Access was therefore limited only to those specifically participating in the research or being treated at the University's Wellbeing Centre. Access was granted by a link sent by email, inviting the student to set up a personal account. To ensure confidentiality, only individual students, their therapist and the research team were able to access an individual's responses. Once a student had set up their personal account, including selecting a personal password, they were able to access the intervention on any internet connected device.

2.1.8 When and How Much (number of sessions, scheduling, duration, intensity, dose)

i-RFCBT is split into six modules, each taking 1-2 hours to complete on screen, with homework tasks set at the end of each module. To make this more manageable, each module is split into 4 to 5 separate webpages (sessions) which can be completed in 15-20 minutes. Responses are saved each time the student moves to the next webpage. Students were encouraged to complete modules over the course of one to two weeks in order to allow sufficient time for homework practice. Students were only able to move to the next module once their therapist had provided feedback, typically within 2 working days.

Therapists received an email when a module was submitted to aid timely responses.

2.1.9 Tailoring (any personalisation of the intervention, describing what, why, when, and how.)

Although the content and presentation of each module was identical for each participant, some tailoring occurred in the feedback from the therapist through the personalisation of the template responses (as described in 2.1.4). However, this individualisation was constrained by the templates to ensure any responses remained faithful to the treatment model.

2.1.10 Modifications (any changes to the intervention during the study, describing what, why, when, and how).

No changes to the content were made during the delivery of the intervention.

2.1.11 How well – planned (assessment of adherence or fidelity; how assessed and by whom and any strategies used to improve fidelity)

Treatment fidelity was ensured through identical content and a fixed module order. The only element that differed between participants was the feedback provided by clinicians. To ensure this remained faithful to the treatment model, early feedbacks (a minimum of 3 per therapist) were checked by EW or an experienced RFCBT clinician (JC). Ongoing supervision was also provided to discuss specific cases, and a random sample of later feedbacks were checked to ensure therapists remained on model.

To increase adherence, the intervention asks students to plan homework and schedule a time and place to complete the next module. Student log-ons

were monitored by the therapist and reminder emails sent if there was no log-on for over a week.

2.1.12 How well - actual (to what extent intervention was delivered as planned)

Actual treatment adherence is reported separately in an audit and case series of guided i-RFCBT with the University of Exeter's Wellbeing Services (Chapter 3) and a randomised controlled trial of guided i-RFCBT versus usual care to prevent depression (RESPOND, Chapters 5 and 6).

2.2 Unguided i-RFCBT

2.2.1 Brief name

Unguided internet-based rumination-focused cognitive-behavioural therapy contains the same components as guided i-RFCBT, adapted for delivery without therapist support.

2.2.2 Why - Rationale of key elements of the intervention

The rationale for the content of unguided i-RFCBT is the same as that described for guided i-RFCBT. We developed an unguided version of i-RFCBT for two main reasons. Firstly, demand for Wellbeing Services at university is growing (Thorley, 2017; Williams et al., 2015) but there remains a considerable treatment gap (54% of students needing support did not access it; NUS, 2015), indicating the need for more accessible and highly scalable interventions within universities. Secondly, prevention is a key priority for reducing the disease burden of depression (Andrews et al., 2004; Topper et al., 2010; WHO, 2017). To achieve this, widespread coverage is needed as large numbers are required to demonstrate a significant reduction in the incidence of depression (Muñoz et

al., 2010). Guided internet interventions have a wider reach than traditional face-to-face models, but the need for therapist involvement necessarily limits their scalability. While unguided interventions generally have lower effect sizes than guided, at least for current depression (Andersson & Cuijpers, 2009; Gellatly et al., 2007; Spek et al., 2007), their potential for almost limitless coverage could still produce significant reductions in the disease burden of depression (Cuijpers, Riper, & Andersson, 2015). The unguided version of i-RFCBT was therefore developed as a potential means of increasing the scalability of i-RFCBT, specifically within Higher Education.

2.2.3 What (Materials used in the intervention or training of providers)

The techniques and content of unguided i-RFCBT are identical to guided i-RFCBT, with some minor changes to ensure it is appropriate for use without a therapist. Firstly, any reference to the therapist was removed. Secondly, some questionnaires were added to the reflection section at the start of each module listing commonly identified difficulties with using the techniques. Example items for each technique are: relaxation: “I didn’t like focusing on my bodily sensations”; concreteness: “I can see the difference between abstract and concrete thoughts but I found it difficult to keep my thoughts concrete.”; absorption “I didn’t know what activity to focus on”; or compassion: “I know what I would say to a friend but I find it hard to say the same to myself.” If students endorsed these items, conditional feedback was presented to normalise the difficulty and offer tips for overcoming these challenges.

2.2.4 What (Procedures used in the intervention, including enabling or support)

As an unguided intervention, no enabling or support was provided. However, for safety reasons, in the trial of unguided i-RFCBT (RESPOND, Chapters 5 and 6) responses to the PHQ-9 questionnaires were monitored weekly, to check for reported risk. The same automatic conditional feedback (see Section 2.1.3) was inbuilt and any reported risk followed up by a trial therapist in the same way as described in Section 2.1.4.

2.2.5 Who provided (expertise, background, training)

No support was provided for unguided i-RFCBT.

2.2.6 How (mode of delivery and whether intervention was provided to individuals or groups)

As with guided i-RFCBT, unguided i-RFCBT was accessed individually via the internet.

2.2.7 Where (location and infrastructure)

Unguided i-RFCBT was accessed using the same secure, password protected platform as guided i-RFCBT. Unguided participants were sent a link from the research team to set up their personal account and were then able to access the intervention via the internet at their convenience. Only the individual participant and the research team were able to access individual accounts.

2.2.8 When and How Much (number of sessions, scheduling, duration, intensity, dose)

Unguided i-RFCBT contains the same six modules (also split into shorter sessions) as guided i-RFCBT (see 2.1.8). Unguided participants were able to log on at any time. Each module is automatically unlocked on completion of the previous module such that access to modules is not restricted, but modules must still be completed sequentially, in the predefined order. Users were therefore able to choose their own pace but advised to spend 1-2 weeks on each module to ensure sufficient time for practice.

2.2.9 Tailoring (any personalisation of the intervention, describing what, why, when, and how.)

Except for the conditional feedback built in to the intervention (see 2.2.3), the presented content of unguided i-RFCBT was identical for all students.

2.2.10 Modifications (any changes to the intervention during the study, describing what, why, when, and how)

No changes were made during the delivery phase. The PHQ-9 was replaced by the PHQ-8 (Kroenke et al., 2009), which contains the same items as the PHQ-9 except for the risk question, at the end of the RESPOND trial. This was in order that participants, including the usual care group, could continue to access the intervention after the trial without any therapist monitoring for risk.

2.2.11 How well – planned (assessment of adherence or fidelity; how assessed and by whom and any strategies used to improve fidelity)

Treatment fidelity was ensured through a fixed module order and identical content for each student. In contrast to the guided students, no reminders were sent but, as described in 2.1.11, students were asked to make homework plans and schedule the next module to increase adherence.

2.2.12 How well - actual (to what extent intervention was delivered as planned)

Actual treatment adherence to unguided i-RFCBT is reported in the RESPOND trial outcomes (Chapter 6).

2.3 Summary of empirical studies to assess i-RFCBT as an intervention for UK university students

The two interventions described in this chapter were investigated in several different contexts. These studies are reported in the following Chapters 3 to 6 of the thesis. Firstly, the effectiveness of guided i-RFCBT within the University's Wellbeing Services was tested by conducting an audit of outcomes for all users as well as an open multiple baseline case series on a consenting subsample (Chapter 3). Secondly, an online focus group investigated students' opinions of i-RFCBT as a potential preventive intervention (Chapter 4). Finally, the RESPOND trial (Chapters 5 and 6) consisted of: (a) a phase III randomised-controlled trial to test whether guided i-RFCBT would prevent the onset of depression, relative to usual care and (b) a quasi-phase II pilot trial comparing unguided i-RFCBT to usual care to assess the feasibility and estimate effect sizes for a fully powered trial.

CHAPTER 3: Audit and open multiple baseline case series

3.1 Preface

This chapter describes an audit and open multiple baseline case series to test the effectiveness of guided i-RFCBT as delivered in routine clinical services within the University of Exeter.

A paper reporting the study is currently under review:

Cook, L. & Watkins, E.R. (under review). Internet-based rumination-focused cognitive-behavioural therapy (i-RFCBT) in a university Wellbeing Service: a service audit and open multiple baseline case series.

This Chapter is principally based on this submitted paper.

While there is considerable evidence of the clinical effectiveness of digital interventions, these positive findings have not successfully translated into routine clinical settings (Mohr, Riper, & Schueller, 2018). Failures in intervention design, research methodology and implementation have led to a considerable research to practice gap (Mohr et al., 2018). Similarly among student samples, while there is increasing evidence of the efficacy of iCBT in reducing symptoms of depression, anxiety, when evaluated using RCTs (Davies et al., 2014; Farrer et al., 2013; Harrer et al., 2018; Nguyen-Feng, Greer, & Frazier, 2017), very few effectiveness trials have been conducted within existing university support services (Dear et al., 2019). Even when interventions produce clinical benefits in research settings, effect sizes are generally small and there may be methodological issues (e.g. high attrition and small sample sizes) and demographic differences between research participants and clinical patients (e.g. research participants may have lower symptom, research may employ

convenience samples as opposed to the active help-seekers found in treatment services), so without more effectiveness studies, it is unclear whether any positive research findings will translate to routine care (Dear et al., 2019).

In an effectiveness trial conducted over four years (*N* = 1081) within a university counselling service, Dear et al. (2019) found large effects of an iCBT intervention on symptoms of depression (Cohen's *d* = 0.81) and anxiety (Cohen's *d* = 0.94). Satisfaction ratings were also high. In addition, these positive clinical outcomes and satisfaction ratings were not significantly different across several referral pathways (triage by specially trained staff, direct referral by in-house counsellor, self-referral), despite differences in uptake, attrition and clinician involvement, indicating the intervention is effective across different contexts (Dear et al., 2019). This demonstrates the potential for iCBT to increase the accessibility to evidence-based interventions on university campuses, with students able to access the intervention via the counselling centre or via self-referral, while maintaining positive clinical outcomes (Dear et al., 2019).

Dear et al. (2019) suggest the positive outcomes of their implementation trial may be due to the iCBT intervention being offered as one of a range of treatment options within the counselling services, as opposed to a replacement for face-to-face therapy, a first step towards face-to-face therapy or as an intervention likely to benefit everyone. Students were therefore able to actively choose iCBT if they thought it was appropriate for their individual circumstances and therefore a self-selecting subsample of the students attending the service.

Records of usage of online support such as self-management apps, peer support and out of hours services within university Wellbeing services are patchy, which could indicate an overreliance on the traditional face-to-face

treatment modality (Thorley, 2017). With demand for treatment increasing, there is a need to broaden the range of services to improve student wellbeing (Thorley, 2017).

The Wellbeing Services at the University of Exeter sought to offer i-RFCBT as a treatment option from January 2014 and this study reports an audit of this implementation of numbers using i-RFCBT, and pre- to post-intervention scores for depression and anxiety to test the hypothesis that i-RFCBT will be efficacious in treating acute symptoms of depression and anxiety within a routine clinical service. With additional consent, individuals' weekly scores throughout the intervention are also analysed in a multiple baseline case series to test change in depression, anxiety and rumination over time.

Internet-based rumination-focused cognitive-behavioural therapy (i-RFCBT) in a university Wellbeing Service: a service audit and open multiple baseline case series

Lorna Cook* & Edward Watkins

* Corresponding author: Lorna Cook, lzc204@exeter.ac.uk

SMART Lab, Mood Disorders Centre, School of Psychology, University of Exeter, EX4 4QG, UK

Acknowledgements

We are grateful to Josie Bannon, Jenny Cadman and Sarah Lane for providing the therapy as well as Mark Sawyer, Head of Wellbeing Services, for implementing the therapy and permitting access to service users.

Ethical statement: The study was approved by the Ethics Committee of the School of Psychology, University of Exeter as well as the Data Protection Officer at the Wellbeing Services, University of Exeter.

Conflicts of interest: The authors have no conflicts of interest to disclose.

Financial support: This work was supported by University of Exeter, UK, through a matched funded PhD studentship to a successful Wellcome Trust Capital Bid.

3.2 Abstract

Background: Depression and anxiety are common disorders among university students. There are challenges in the availability of and engagement with face-to-face therapies for students, to which the internet may provide a valuable alternative.

Aims: This audit and case series investigates the effectiveness of internet-based rumination-focused cognitive-behavioural therapy (i-RFCBT) in the Wellbeing Services at the University of Exeter.

Method: 108 students were treated with up to 6 sessions of i-RFCBT. Twenty-six participants with elevated symptoms of depression and/or anxiety provided session-by-session scores in an open multiple baseline case series.

Results: Both depressive and anxious symptoms reduced significantly from assessment to end of treatment. i-RFCBT also produced a significant reduction in rumination. Using standardised clinical cut-offs, 62.5% of the case series participants achieved recovery for depression and 52.2% for anxiety.

Conclusion: These findings provide preliminary evidence for i-RFCBT as an efficacious treatment for depression and anxiety in university students that may increase accessibility to wellbeing services.

Key learning aims

(1) To understand why the university student population is not well catered for by face-to-face CBT.
(2) To understand the potential role of internet treatments in overcoming this treatment gap.

(3) To learn about a novel approach to treating depression and anxiety by targeting maladaptive rumination.

Keywords

Student mental health; Cognitive Behavioural Therapy (CBT); Rumination; Depression; Anxiety; Internet-Delivery

3.3 Introduction

Depression and anxiety are common disorders (Kessler et al., 2005). Initial onset is often early in life, with cases of depression rising steeply from the age of 14 (Hankin et al., 2015) and the median onset of anxiety disorders occurring at 19 years (McEvoy, Grove, & Slade, 2011). Early onset of anxiety and depression is linked to poorer long-term outcomes and greater risk of chronicity (Pine, Cohen, Gurley, Brook, & Ma, 1998). Recently, the UK Adult Psychiatric Morbidity Survey (McManus, Bebbington, Jenkins, & Brugha, 2016) found an increasing prevalence of depression and anxiety disorders in 16-24-year-olds, from 15% in 1993 to 19% in 2014. Within this age range, there is a particular concern about mental health whilst at university, with a five-fold increase in disclosure of a mental health condition to higher education institutions (HEIs) over the past ten years (Thorley, 2017).

A recent meta-analysis found an overall weighted mean prevalence of depression of 30.6% in undergraduates across 24 studies (range 10%-85%) (Ibrahim, Kelly, Adams, & Glazebrook, 2013) (see also Bewick, Gill, Mulhern, Barkham, & Hill, 2008 who reported prevalence of 29% across 4 UK HEIs), which suggests increased prevalence of depression relative to the general population of young adults, where it is estimated to range from 10.8% to 22% in community samples of 20-24 year olds (Aalto-Setälä, Marttunen, Tuulio-Henriksson, Poikolainen, & Lönnqvist, 2001; Newman et al., 1996). Potential reasons for increased rates of depression among undergraduate students include the specific challenges and lifestyle changes associated with university, such as leaving home for the first time, forming new social relationships, independent learning, and changes in sleep patterns (National Institute of Mental Health, 2003).

The experience of mental health difficulties during university is linked to negative outcomes including poorer academic performance (Hysenbegasi, Hass, & Rowland, 2005) and higher drop-out rates (Eisenberg, Golberstein, & Hunt, 2009). Nonetheless, with appropriate support, students experiencing psychiatric problems are able to successfully engage with their studies and perform well at university (Collins & Mowbray, 2005). However, the university student population is considered a distinct group that is not necessarily well-catered for in standard NHS services, in part due to the academic calendar and difficulty integrating care in both the home and university locations (Randall & Bewick, 2015). Many UK universities now provide counselling and wellbeing services, including psychological therapies, such as cognitive-behavioural therapy (CBT), with increasing demand placing pressure on these services (Williams et al., 2015). However, in a survey of 1093 students, 54% of those needing treatment did not access university services and 33% reported not knowing where to access support if needed (National Union of Students, 2015). There is therefore a need for increased availability to manage demand and for improvements in accessibility of support services to engage those students not currently receiving treatment.

One means of increasing availability and engagement in students may be internet-based interventions, which can reach larger numbers of patients at lower costs than traditional face-to-face therapy (Andersson, 2010). They may also reach people who have not previously engaged with face-to-face therapy (Christensen, Griffiths, & Jorm, 2004). Potential advantages include greater flexibility and autonomy, with patients able to access the therapy at a time and place that suits them; not needing a scheduled therapy appointment time; more time for reflection on content of the treatment and increased anonymity, which

may help to avoid the stigma of visiting a therapist or wellbeing service centre (Andersson, 2010; Muñoz, Cuijpers, Smit, Barrera, & Leykin, 2010; Richardson, Stallard, & Velleman, 2010). This flexibility may be particularly advantageous to students as they are able to continue accessing the therapy outside term-time. There is also evidence of equivalence in outcomes between internet-based and face-to-face treatments (Andersson, 2010; Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010).

In addition to adapting treatment delivery, adapting treatment content may also improve outcomes. Given the high rates of co-occurrence of depression and anxiety disorders (Fava et al., 2000), one recommended approach is to focus on transdiagnostic processes, rather than disorder-specific interventions (Craske, 2012). One such process is repetitive negative thought (RNT), incorporating both worry and rumination. RNT has been shown to play a role in both the onset and maintenance of a range of psychological disorders, including depression and anxiety (Ehring & Watkins, 2008; Nolen-Hoeksema & Watkins, 2011; Watkins, 2008). RNT has also been linked to less effective therapy (Ciesla & Roberts, 2002), suggesting interventions specifically targeting RNT may produce improved outcomes. Morrison and O'Connor (2005) found rumination was a predictor of change in depression scores in undergraduate students over a six-month period and argued that therapy for students could be enhanced by focusing on rumination as well as depression and anxiety.

One such therapy designed to specifically target rumination is rumination-focused cognitive-behavioural therapy (RFCBT; Watkins, 2016; Watkins et al., 2007). Theoretical models (Watkins, 2008) and experimental findings propose that repetitive thought (RT) has distinct processing modes, which each have distinct consequences. Unconstructive RT, such as

depressive rumination, is characterised by an abstract processing mode, focusing on the meaning and implications of negative events. Conversely, constructive RT is concrete, specific and action-focused, focusing on how (rather than why) an event happened (Watkins, 2008). In experimental studies, inducing a concrete processing mode improved problem solving (Watkins & Baracaia, 2002; Watkins & Moulds, 2005) and reduced emotional reactivity in response to a failure experience (Watkins, Moberly, & Moulds, 2008), relative to an abstract mode. RFCBT therefore aims to shift individuals from an abstract to a concrete mode of RT, in order to reduce unconstructive rumination. In support of this, concreteness training for dysphoric and depressed participants reduced rumination and symptoms of depression in both a proof-of-principle study and randomised-controlled trial (RCT) (Watkins, Baeyens, & Read, 2009; Watkins et al., 2012).

Pathological rumination is also conceptualised as a mental habit (Watkins & Nolen-Hoeksema, 2014). To change this mental habit, RFCBT uses functional analysis to help patients identify triggers for rumination, distinguish between unconstructive and constructive rumination, and trains users to practise more functional responses. It also uses experiential and imagery exercises to adaptively shift processing mode (including concreteness, absorption, compassion). In contrast to standard CBT, which challenges the content of specific thoughts, RFCBT seeks to change the process of thinking (Watkins et al., 2007). Relatedly, rumination is conceptualised as a form of avoidance (Borkovec, Alcaine, & Behar, 2004; Watkins, 2008). Behavioural activation principles (Martell, Addis, & Jacobson, 2001) are incorporated in RFCBT, replacing avoidance behaviour with more appropriate approach behaviours.

In an RCT (Watkins et al., 2011) in adult patients with medication-refractory residual depression, the addition of RFCBT to treatment-as-usual (TAU, antidepressant medication) reduced depressive symptoms more than TAU alone, with improvements in remission rates (62% vs. 21%) and reduction in 5-month relapse rates (9.5% vs. 53%). Changes in rumination scores were found to be a significant mediator of these treatment effects.

These positive treatment and relapse prevention effects led to an adaptation of RFCBT for online use (Topper, Emmelkamp, Watkins, & Ehring, 2017). An RCT tested the intervention in 15-22-year-olds with elevated worry and rumination and found both therapist-supported internet-RFCBT (i-RFCBT) and group RFCBT reduced symptoms of depression and anxiety relative to usual care control (*d* = 0.36 to 0.72). Cumulative incidence rates at 12-month follow-up were lower in both intervention groups for depression (14.7% internet; 15.3% group) and generalised anxiety disorder (GAD; 16.0% internet; 18.0% group) compared to usual care control (32.4% depression and 42.2% GAD). Consistent with the hypothesis that the key mechanism of the intervention was change in rumination, reductions in RNT were found to mediate the effect of condition on incidence at 12-month follow-up.

Based on these positive effects in adolescents and young adults, it was hypothesised that i-RFCBT would also be useful for treating acute symptoms of depression and anxiety in university students within a Wellbeing service. The Wellbeing Services at the University of Exeter offer confidential therapeutic and practical advice and support to students, for common mental health disorders, such as anxiety and depression, as well as for stress that may impact on academic progress. To this end, whilst the Improving Access to Psychological Therapies (IAPT) minimum data set assessments are used to measure

symptom levels, there is no minimum symptom threshold for receiving support. Therapies include CBT, counselling, and Mindfulness delivered via face-to-face, telephone, group and online settings. In the 2014/15 academic year, approximately 1600 students were treated (representing 8% of total University of Exeter student population). Demand for the service has increased by 60% since 2010 (Wellbeing Services, University of Exeter, 2016, personal communication), indicating the need for alternative efficient means of delivering therapy.

The current research investigates the use and outcomes of i-RFCBT within the Wellbeing Services at the University of Exeter over a 30-month period, from the introduction of i-RFCBT in the service in January 2014 to June 2016, in two ways: (a) a general audit of use and outcomes of the intervention during this period; (b) a multiple baseline case series of those participants who consented to provide their weekly scores.

3.4 Method

3.4.1 Participants

I-RFBCT service evaluation. Students presenting at the Wellbeing Services were assessed by staff at the Wellbeing Services and offered i-RFCBT as one of a range of treatment options. One hundred and eight students selected i-RFCBT as their treatment of choice.

Case series participants. Students choosing i-RFCBT were additionally asked by their therapist to participate in the case series by providing written consent to share their treatment data with the research team. This information was normally provided during the assessment interview. Where this was not possible, retrospective consent was sought during or after treatment.

Participants' treatment was unaffected by their decision to participate in the study as the research sought only to access the data already being collected.

Thirty-two students returned written consent to participate in the open case series. Of these, 3 students were excluded as they did not complete any modules and no follow-up data was available. The case series investigated whether i-RFCBT would be useful for treating acute symptoms. For this reason, only those meeting caseness on at least one measure (PHQ ≥10 or GAD ≥8) were included in the analyses. On this basis, three were excluded for being below caseness on both measures. The final case series sample therefore consisted of 26 participants (11 male, 15 female) with an age range of 19 to 30 (*M* = 21.58, *SD* = 2.94). Of these, 23 participants were undergraduate students and 3 postgraduate students. Participants were from the full range of colleges at the university: 6 from Life and Environmental Sciences; 5 from Humanities; 4 from Engineering, Mathematics and Physical Sciences; 3 from the Business School; 3 from the Medical School and 3 from Social Sciences and International Studies. Two students were studying in multiple colleges with a Flexible Combined Honours.

3.4.2 Intervention

Internet-based RFCBT (i-RFCBT) consists of six modules, each taking around one hour to complete. Each module follows a basic structure consisting of reflection on the previous week, introduction and practice of new techniques and then formulation of plans to practise and implement these techniques in the coming week. The therapy incorporates a range of interactive tools, including psycho-education, mood diaries, on-line experiential exercises using audio-recordings, pictures, and video vignettes of students' experiences of the therapy. Unhelpful RNT is conceptualised as a mental habit, requiring repeated

practice of an alternative, more helpful response to replace negative rumination (Watkins & Nolen-Hoeksema, 2014). To achieve this, users first need to become aware of their triggers or warning signs and then make specific plans to respond differently to the trigger in order to override the habitual ruminative response (Watkins, 2016). These plans are informed by the research into implementation intentions in the form of If-Then plans of the form “If situation X occurs then I will do Y” (Gollwitzer, 1999; Gollwitzer & Sheeran, 2006) as these have been shown to both increase the saliency of trigger situations (cues) as well as strengthen the link between the cue and response, making the desired response more likely to be triggered automatically by the specified context (Webb & Sheeran, 2007). The alternative strategies include: being more active; slowing things down; breaking tasks down; opposite action; relaxation; concrete thinking; becoming absorbed; self-compassion and assertiveness. The therapy is supported by qualified clinicians (psychological wellbeing practitioners, PWPs) within the Wellbeing Services in the form of asynchronous written text feedback delivered within the internet platform at the end of each module. This feedback consists of highlighting positives as well as identifying areas for focussing on in the next module. While patients complete modules at their own pace, they are encouraged to spend one to two weeks on each module to allow sufficient time for practice. Subsequent modules can only be accessed once the therapist has provided feedback. A more detailed description of the intervention following the TIDIeR checklist format (Hoffmann et al., 2014), is provided in Table 3.1.

Table 3.1. Description of internet RFCBT (i-RFCBT) on TIDIeR criteria.

TIDIeR Checklist item	Description
1. Brief name	Internet-based rumination-focused cognitive-behavioural therapy (i-RFCBT)
2. Why (rationale)	The intervention was developed from theory and evidence that (a) rumination is an unhelpful mental habit and the intervention therefore utilises techniques to identify cues for rumination, and repeatedly rehearse alternative responses to these cues to change the habit (Watkins & Nolen-Hoeksema, 2014); (b) processing style (concrete, action-focused vs. abstract, evaluative) influences whether thinking is helpful or not and therefore teaches participants to change thinking style (Watkins, 2008; Watkins et al., 2012).
3. What (materials)	The intervention consists of psycho-education, video case studies, images, audio-exercises, a mood diary, self-monitoring questionnaires and free text questions within a secure internet platform. Specific content in each module is as follows: <u>Module 1</u> Introducing worry, rumination and avoidance as unhelpful habits through text and video examples; free text questions to identify personal stressful situations to spot warning signs and triggers for rumination; mood diary to increase awareness of rumination. <u>Module 2</u> Questionnaires to identify common warning signs and consequences of worry and rumination; introducing IF-THEN implementation intention plans to break the rumination habit (linking a more helpful response to a specific warning sign); suggested strategies include: slowing things down (focusing on one task at a time); becoming more active; breaking tasks into smaller steps; opposite action (acting differently to your emotions e.g. engaging in a calming activity when feeling anxious). <u>Module 3</u> Relaxation audio exercise as an alternative to rumination; behavioural experiment (using audio recordings) to compare effects of abstract versus concrete thinking; audio exercise to practise concrete thinking in response to a personal situation; adding IF-THEN plans for useful techniques. <u>Module 4</u> Understanding reasons for worry and rumination (e.g. motivating self, trying to problem solve, avoiding risk of failure); introducing 3 rules-of-thumb to identify when rumination is unhelpful (unanswerable questions, thinking longer than 30 minutes without progress, thinking

		that leads to more thinking rather than plans or actions); behavioural experiment using audio exercises to compare experience of being fully absorbed ('flow' experiences) versus not being absorbed; identifying and scheduling absorbing activities; adding IF-THEN plans for useful techniques. <u>Module 5</u> Experiential audio exercise to increase self-compassion comparing critical self-talk versus talking in a friendly way to a friend; practising applying friendly talk to self; identifying activities to increase or decrease to be kinder to oneself; adding IF-THEN plans for useful techniques. <u>Module 6</u> Tackling rumination about interpersonal relationships by becoming more assertive; reflection on which techniques were most useful and making concrete plans for relapse prevention.
4.	What (procedure)	Exercises completed online at the user's convenience. Daily practice encouraged to ensure techniques applied to real life situations. Support delivered in the form of asynchronous written text feedback within the internet platform at the end of each module. This feedback consists of highlighting positives as well as acknowledging any challenges in implementing the techniques and making recommendations for adapting plans to increase the chances of successful implementation.
5.	Who delivered	Psychological wellbeing practitioners (PWPs) employed by the University of Exeter Wellbeing Services. All staff delivering i-RFCBT received specialist training in supporting i-RFCBT delivered by its developer (EW) and less experienced staff received ongoing supervision from an experienced i-RFCBT clinician.
6. 7.	How Where	Internet-delivered. Access to secure password protected site granted by PWP at the Wellbeing Services and then accessible remotely at any time or location convenient to user.
8.	When and how much	Six modules of 1-2 hours (split into 15-20-minute sessions), with homework tasks between modules. Recommended pace of one to two weeks per module to allow sufficient practice. Subsequent modules can only be accessed once therapist provides feedback. Feedback typically within 2 working days of completing module.
9.	Tailoring	No tailoring included in the modules but a limited amount is incorporated into the therapist's feedback. The feedback follows a template model which is adapted to reflect the individual patient's responses. Any free form text in the feedback reinforces the therapeutic model e.g. encouraging patients to make their IF-THEN plans more concrete and specific.
10.	Modificat-ions	Not applicable

11.	How well (planned)	The online content is identical for each patient ensuring treatment fidelity. Template responses are provided for the therapists to format their feedbacks, with some scope for individualisation to each patient. Patient compliance was defined as completing a minimum of 4/6 modules. Reminders sent to patients if not logged on for more than a week.
12.	How well (actual)	Supervision by more senior staff until each therapist felt confident with writing the feedbacks ensured the therapist content remained on model. Overall compliance rates of 47.2% among audit sample and 62.5% among case series sample.

3.4.3 Measures

The following measures, which form part of the minimum data set across IAPT services, were administered at the initial assessment session and built into each treatment module to assess progress:

The Patient Health Questionnaire (PHQ-9; Kroenke, Spitzer, & Williams, 2001) is a nine-symptom measure of depressive symptoms, designed to measure both severity and diagnostic status of depression. Scores range from 0-27, with higher scores indicating greater severity. The PHQ-9 is a reliable and valid measure of severity of depressive symptoms (Kroenke et al., 2001). A cut-off ≥ 10 on the PHQ-9 has 88% sensitivity and 88% specificity for diagnosing major depression (Kroenke et al., 2001).

The Generalised Anxiety Disorder Screener (GAD-7; Spitzer, Kroenke, Williams, & Löwe, 2006) is a standardised self-report measure of symptoms of anxiety. Scores range from 0-21 and higher scores indicate more severe symptoms. Spitzer et al., (2006) demonstrated good validity and reliability of the GAD-7. A cut-off ≥ 8 on GAD-7 is representative of a likely diagnosis of GAD (Kroenke, Spitzer, Williams, Monahan, & Löwe, 2007).

3.4.3.1 Additional measures in case series sample

Further measures built in to the intervention platform were analysed to assess change in rumination and habits across the course of treatment.
Rumination and overgeneralisation measures

The Habit Index of Negative Thinking (HINT; Verplanken, Friborg, Wang, Trafimow, & Woolf, 2007) assesses the degree to which negative thinking is a habit, with 12-items asking whether negative self-thoughts (here defined as "worry and rumination") over the last two weeks occurred frequently (e.g., 'I do every day'), without intention, started without conscious awareness (e.g., 'I start doing before I realize I'm doing it') and were difficult to control, each scored on a five-point scale from 0 (Strongly disagree) to 4 (Strongly agree), with higher scores indicating more habitual negative thinking. Two original items relating to the extent to which negative thinking was seen as a self-descriptive trait were removed as we were focused on assessing change in ruminative habit, resulting in a 10-item scale, with scores ranging from 0 to 40.

The Ruminative Habit (RH) scale was adapted from the Self-Report Habit Index (SRHI; Verplanken & Orbell, 2003), a well-established measure of habit strength, which can be applied to a range of target behaviours to examine the habitual nature of rumination. It consists of 8 items assessing frequency, rated from 1 (not at all) to 5 (multiple times daily), repetitiveness (e.g. 'When I worry or ruminate, it seems as if I come back to the same or similar ideas again and again', rated from 1 (almost never) to 5 (almost always), and automaticity (e.g. 'What amount of conscious attention did the worry or rumination require to start?', rated from 1 (almost no attention) to 5 (constant attention), providing

total scores ranging from 8 to 40. Higher scores reflect a stronger habit of rumination.

The Attitudes Towards Self scale (ATS; Carver, 2013) generalisation subscale consists of 4 items assessing the tendency to generalise from a single failure to one's sense of self-worth (e.g. 'When even one thing goes wrong, I begin to wonder if I can do well at anything at all'), scored from 1 (I agree a lot) to 5 (I disagree a lot). Reverse coding gives scores ranging from 4 to 20, with higher scores indicating greater levels of generalisation.

3.4.4 Case series Design

The study was an open case series investigating the efficacy of i-RFCBT in terms of symptom changes pre- to post-treatment within a university wellbeing centre. The differing start-points across the academic year and varying lengths of time that students spent on the waiting list prior to commencing treatment provided a quasi-random multiple baseline design. With varying lengths of baseline periods, if reductions in symptoms are found only once treatment begins and not during the waiting list period, there is greater confidence that these symptom reductions are due to the therapy and not simply due to other factors such as maturation, history, regression to the mean or spontaneous remission over time (Hayes, 1981; Kazdin, 2003).

3.5 Results

3.5.1 Adherence and accessibility

Audit sample. Of six modules, participants completed a mean number of 3.19 (*SD* = 2.35). We operationalised compliance as completing at least four out of six modules, consistent with other studies (Cook & Watkins, 2016). Fifty-one participants (47.2%) were treatment compliers. To explore whether

baseline severity was linked to dropout among the audit sample, Mann-Whitney U tests were conducted to compare baseline symptom severity between compliers and non-compliers. Baseline symptom severity was not significantly different between those who complied (completed at least 4 modules) and those who did not (including those who did not start therapy): Baseline PHQ (U = 1206, p = .76, r = .003) and Baseline GAD (U = 1121, p = .38, r = .009).

Case series sample. In order not to inflate the adherence rates, these are calculated for all thirty-two consenting participants. The intervention was generally well adhered to with participants completing a mean of 3.81 out of 6 modules (SD = 2.01) and 20/32 (62.5%) were treatment compliers. The intervention was not limited to the university setting, with 45 modules from a total of 118 (38.14%) completed outside term-time, demonstrating the flexible accessibility of internet-based interventions.

To test the representativeness of the case series sample, Mann-Whitney U tests compared baseline symptom severity for participants who were included in the case series sample and those only included in the audit sample. No significant differences were found between the case series and audit sample for either Baseline PHQ (U = 626.5, p = .31, r = -0.11) or Baseline GAD (U = 607.5, p = .23, r = -0.13).

3.5.2 Clinical outcomes

Pre-treatment scores were taken during the assessment session with the PWP. The PHQ-9 and GAD-7 are administered at the end of each module. The last recorded symptom scores in the i-RFCBT platform were taken as post-treatment outcome (equivalent to recording symptoms at the last attended session in face-to-face therapy), as no in-person post-treatment assessment was conducted with the PWP. Normality of scores were assessed using the

Shapiro-Wilk test. Response to treatment was assessed using either a paired-samples t-test or Wilcoxon matched pairs test as appropriate, comparing symptoms at assessment with those at end of treatment. Although diagnostic status was not formally assessed, the guidelines for cut-offs (≥10 PHQ, ≥ 8 GAD) were used to assess clinical caseness for major depression and GAD respectively.

Audit sample. Twenty-three participants did not complete the first module and assessment data for three participants could not be accessed, and, therefore, the audit of pre-post treatment scores was conducted on eighty-two participants. I-RFCBT was associated with a significant reduction in symptoms of depression and anxiety (see Table 3.2). In order to investigate the role of treatment compliance, we tested whether there was a relationship between number of modules completed and change score. There was a significant positive relationship between number of modules and change in depression, such that those who completed more modules demonstrated a greater reduction in symptoms (r_S = .48, N = 82, p <.001). A similar positive correlation was found for number of modules completed and change in anxiety symptoms (r_S = .53, N = 82, p < .001) [1].

Using the standard cut-offs on the PHQ-9 and GAD-7, at initial assessment, 45 (54.9%) participants met caseness for major depression and 62 (75.6%) for GAD. Of these, 26 (57.8%) no longer met caseness for depression

[1] Similarly, using baseline adjusted ANCOVAs, those who complied (≥4 modules) had significantly lower post-treatment scores than those who did not comply for both depression ($F_{1,79}$ = 18.55, p < .001; M = 6.5, SE = .65 and M = 10.93, SE = .79 respectively) and anxiety ($F_{1,79}$ = 23.74, p < .001; M = 6.29, SE = .58 and M = 10.78, SE = .71 respectively).

and 30 (48.4%) no longer met caseness for GAD at end of treatment. Using the IAPT definition (Community and Mental Health team, 2015, 2016) of recovery as being above caseness on at least one measure (PHQ-9 and/or GAD-7) at baseline and below caseness on both at end of treatment, this equates to recovery rates of 46.7% for depression and 40.3% for anxiety. Thirteen participants (15.6%) crossed the threshold in the other direction (subclinical to clinical) on one or both measures (9 on PHQ only; 2 on GAD only and 2 on both). Of these, none completed the therapy and 76.9% completed less than four modules.

As the audit sample consisted of a mix of participants who did/did not meet caseness, we examined these two subgroups separately to determine if baseline severity influenced outcome. We found significant improvements, with moderate to large effect sizes, in symptoms only for those who met caseness at assessment (see Table 3.2).

Table 3.2. Depressive and anxiety scores pre- and post-treatment for 82 audit participants.

		Scores Pre-RFCBT		Scores Post-RFCBT		Analysis		
	N	Mean	SD	Mean	SD	*Z*	*p*	*r*
PHQ9	82	11.62	5.33	8.28	5.34	-4.39	<0.001	0.34
GAD7	82	10.93	4.71	8.10	4.84	-4.05	<0.001	0.32
PHQ9(≥10)	45	15.53	3.56	9.53	5.01	-5.02	<0.001	0.53
PHQ9(<10)	37	6.86	2.44	6.76	5.40	-0.23	0.821	0.03
GAD7(≥8)	62	12.92	3.38	9.06	4.82	-4.36	<0.001	0.39
GAD7(<8)	20	4.75	2.15	5.10	3.57	0.47	0.637	0.07

Note: PHQ9, Patient Health Questionnaire; GAD7, Generalised Anxiety Disorder Screener. Effect size $r = Z/\sqrt{N}$, where 0.1 denotes a small effect, 0.3 a medium effect and 0.5 a large effect.
Analysis on full sample, then split by meeting caseness on PHQ9 and GAD7 at baseline.

Case series sample. GAD7, HINT and ATS were not normally distributed. Response to treatment was assessed using a paired-samples t-test for PHQ9 and RH and a Wilcoxon matched pairs test for the non-normal measures, comparing symptoms at assessment with those at end of treatment. Among the case series sample, treatment with i-RFCBT was associated with a significant reduction in both depressive and anxious symptoms, with moderate to large effect sizes (see Table 3.3). Additionally, in support of the hypothesised mechanism of change, there was also a significant mean reduction in levels of rumination, with large effect sizes (see Table 3.3).

All participants met caseness for major depression and/or GAD at initial assessment: 16 (61.5%) for major depression and 23 (88.5%) for GAD. Of these, 12 (75%) no longer met caseness for depression at termination of treatment and 14 (60.9%) no longer met caseness for GAD. Using the IAPT definition of recovery (Community and Mental Health team, 2015, 2016), recovery rates among the case series sample were 62.5% for depression and 52.2% for GAD. Only one participant crossed the threshold in the other direction on PHQ9, although this shift represented an overall increase of only one point.

Table 3.3. Depressive, anxiety, rumination and overgeneralisation scores pre- and post-treatment for 26 case series participants.

	Scores Pre-RFCBT		Scores Post-RFCBT		Analysis		
	Mean	SD	Mean	SD	*t/Z*	*P*	*r/d*
PHQ9	12.69	5.58	7.46	4.33	5.02[a]	<0.001	0.98[a]
GAD7	11.85	4.55	7.23	4.36	-3.48[b]	0.001	0.48[b]
RH	30.00	3.36	23.12	6.33	5.31[a]	<0.001	1.04[a]
HINT	34.12	4.20	24.77	8.67	-3.99[b]	<0.001	0.55[b]
ATS	17.62	2.16	12.88	3.05	-4.25[b]	<0.001	0.59[b]

Note: PHQ9, Patient Health Questionnaire; RH, Ruminative Habit scale; GAD7, Generalised Anxiety Disorder Screener; HINT, Habit Index of Negative Thinking; ATS, Attitudes Towards Self scale

[a]Analysed using paired-samples t-test with effect size *d*; [b]analysed using Wilcoxon matched pairs test, with effect size *r*. Effect size *d* = paired mean/paired SD, where *d* = 0.2 denotes a small effect, *d* = 0.5 a medium effect and *d* = 0.8 a large effect. $r = Z/\sqrt{N}$, where 0.1 denotes a small effect, 0.3 a medium effect and 0.5 a large effect.

Change in scores across treatment phase in multiple baseline case series

To assess the effect of i-RFCBT, the multiple-baseline graphs are inspected in terms of timing and magnitude of symptom changes. On visual inspection of the graphs (see Figure 3.1), the trend for the majority of participants is for symptoms to remain stable or slightly increase across the baseline period. Across participants there was a reduction in symptoms only once treatment began, despite the baseline period varying from 1 week to 17 weeks. In most cases, improvement in symptoms occurred only after the first treatment session, perhaps reflecting hope and optimism in the intervention, and showed further decreases over time. These changes in symptoms of depression and anxiety followed a similar trajectory across participants. For some participants, the trajectory was not smooth, with the majority of spikes in symptoms occurring in module 3. This may be due to increased monitoring of rumination in the first two weeks, increasing awareness of symptoms. Additionally, changes in anxiety and depression symptoms tended to occur in

parallel, suggesting that an intervention focusing on rumination was associated with concurrent reductions in both anxiety and depression. The observation that improvement only occurred once treatment commenced across a range of participants, baseline lengths, and at different times of the year (see assessment dates in Figure 3.1) increases the generalisability of findings and reduces the likelihood that the observed improvements are due to spontaneous remission, maturation or timing effects (such as exam or holiday periods), repeated testing and other common threats to internal validity.

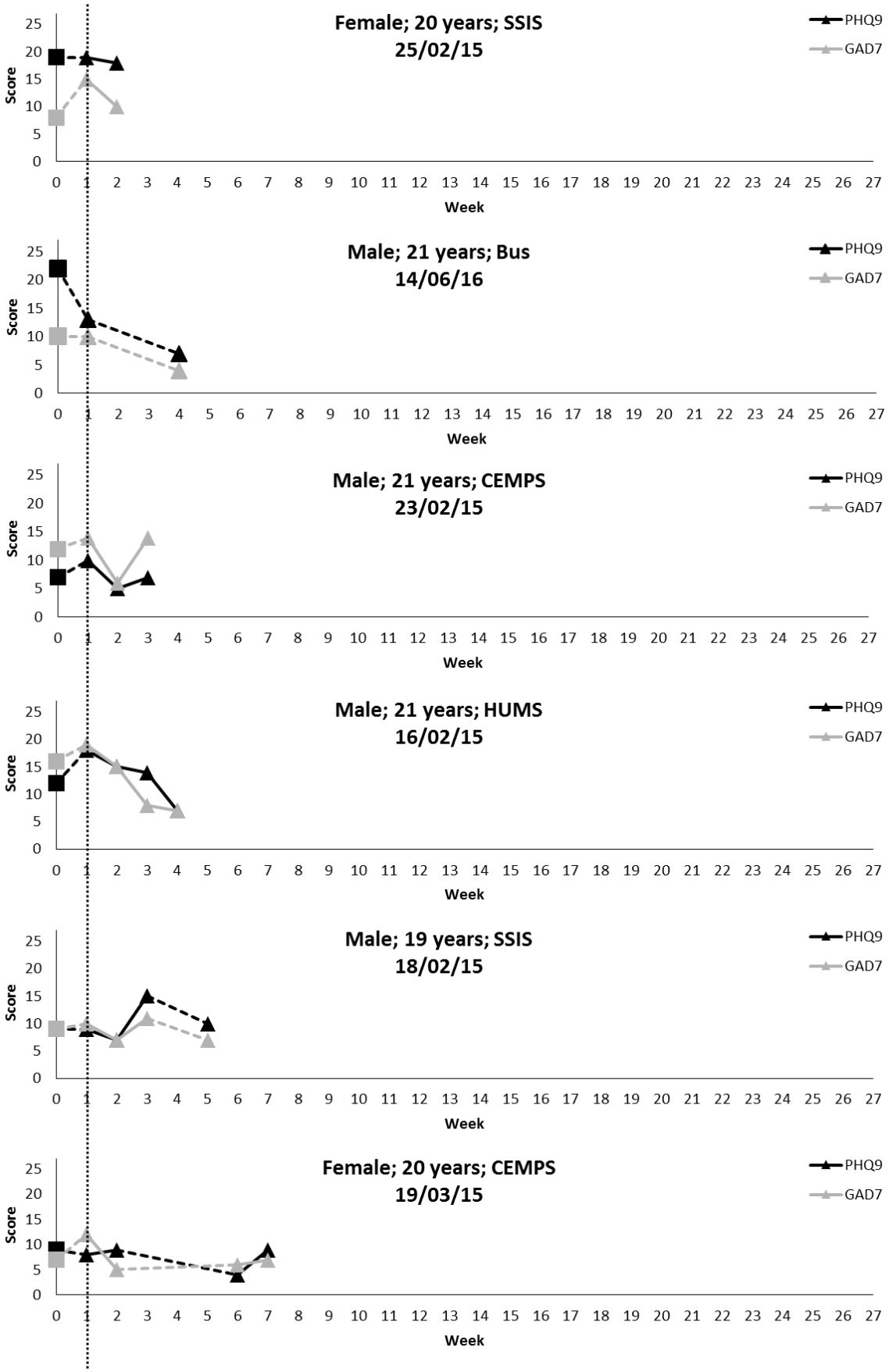


Figure 3.1(a)-(e). Depressive (PHQ) and anxious (GAD) symptoms across weeks for 26 students.

Note: In all graphs, assessment sessions are marked with squares and treatment sessions with triangles. The dotted vertical lines indicate the end of the baseline/commencement of treatment period. *Note*: Bus, The Business School; CEMPS, College of Engineering, Mathematics and Physical Sciences; CLES, College of Life and Environmental Sciences; HUMS, College of Humanities; FCH, Flexible Combined Honours; Med, Medical School; SSIS, College of Social Sciences and International Studies; PG, postgraduate.

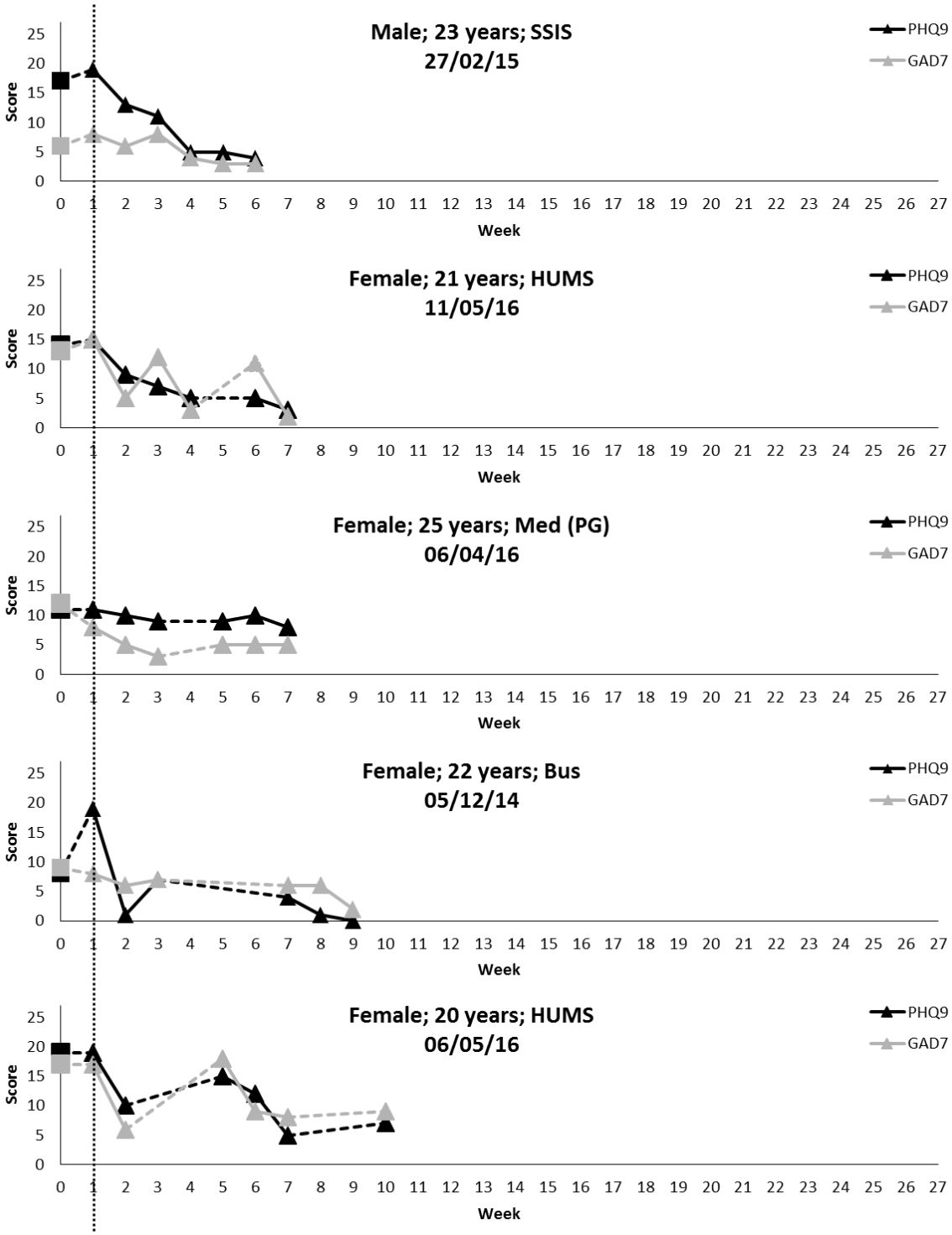

Male; 23 years; SSIS
27/02/15
Female; 21 years; HUMS
11/05/16
Female; 25 years; Med (PG)
06/04/16
Female; 22 years; Bus
05/12/14
Female; 20 years; HUMS
06/05/16
PHQ9
GAD7
Score
Week

Figure 3.1(b).

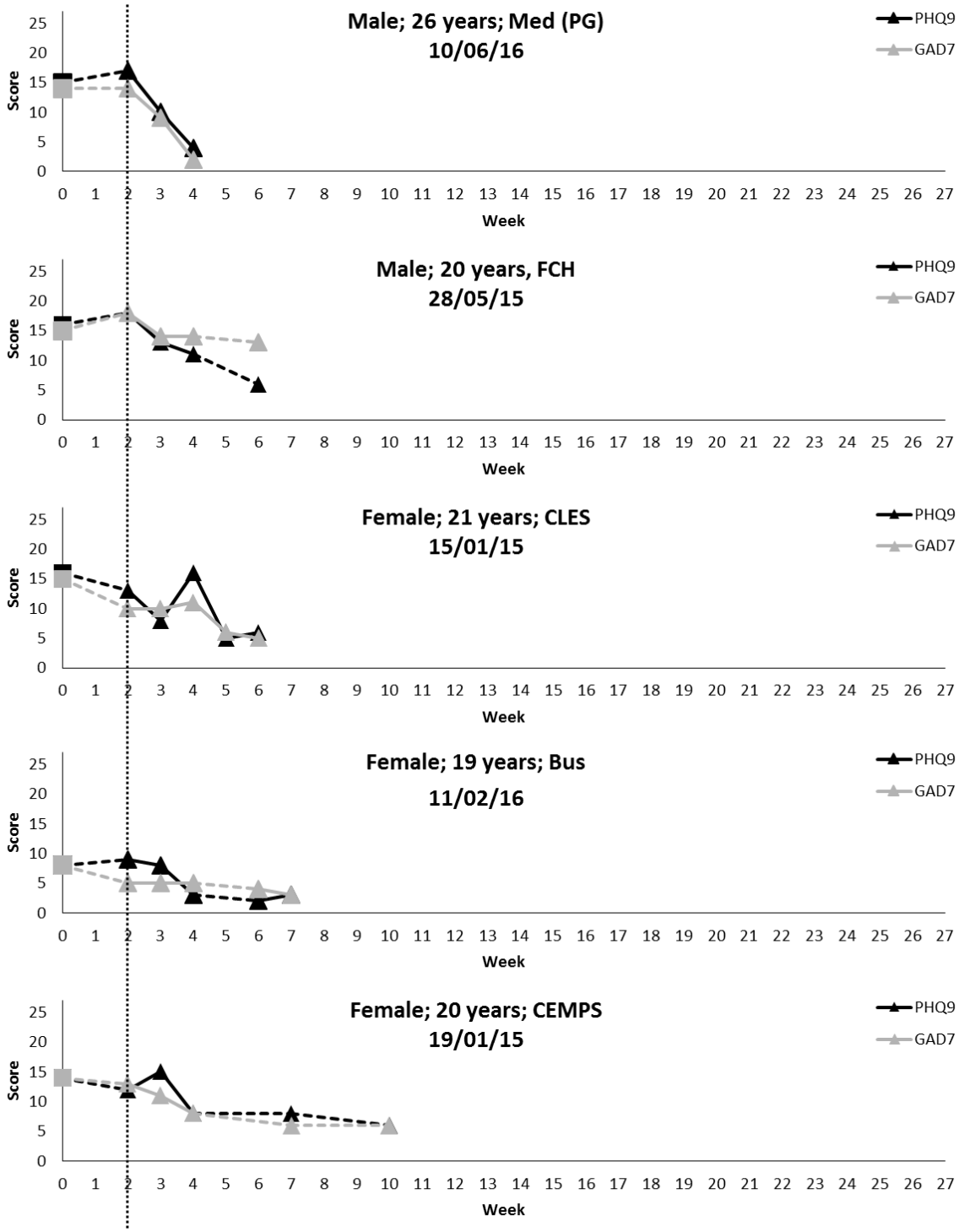

Male; 26 years; Med (PG)
10/06/16
Male; 20 years, FCH
28/05/15
Female; 21 years; CLES
15/01/15
Female; 19 years; Bus
11/02/16
Female; 20 years; CEMPS
19/01/15
PHQ9
GAD7
Score
Week

Figure 3.1(c).

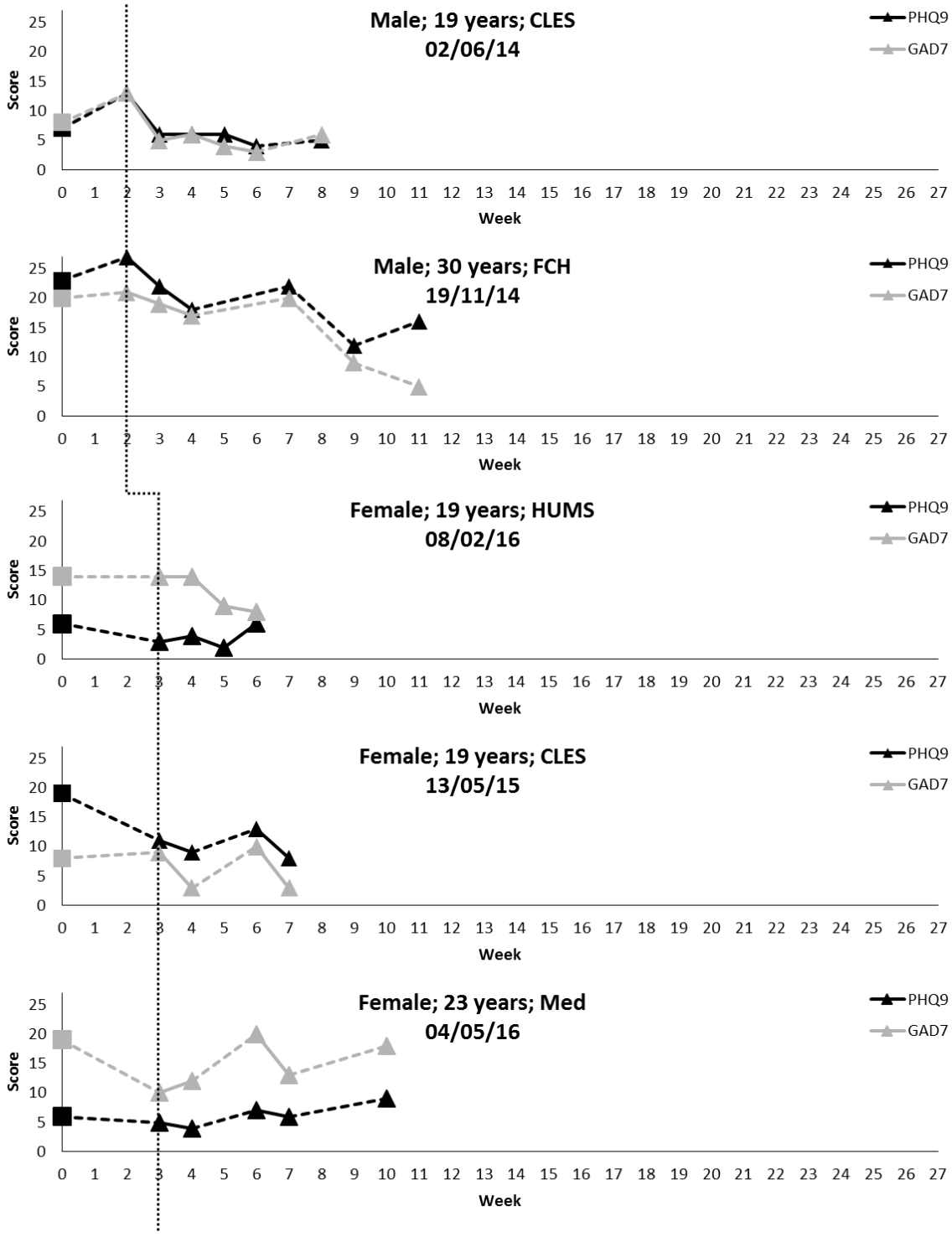

Male; 19 years; CLES
02/06/14
Male; 30 years; FCH
19/11/14
Female; 19 years; HUMS
08/02/16
Female; 19 years; CLES
13/05/15
Female; 23 years; Med
04/05/16
PHQ9
GAD7
Score
Week

Figure 3.1(d).

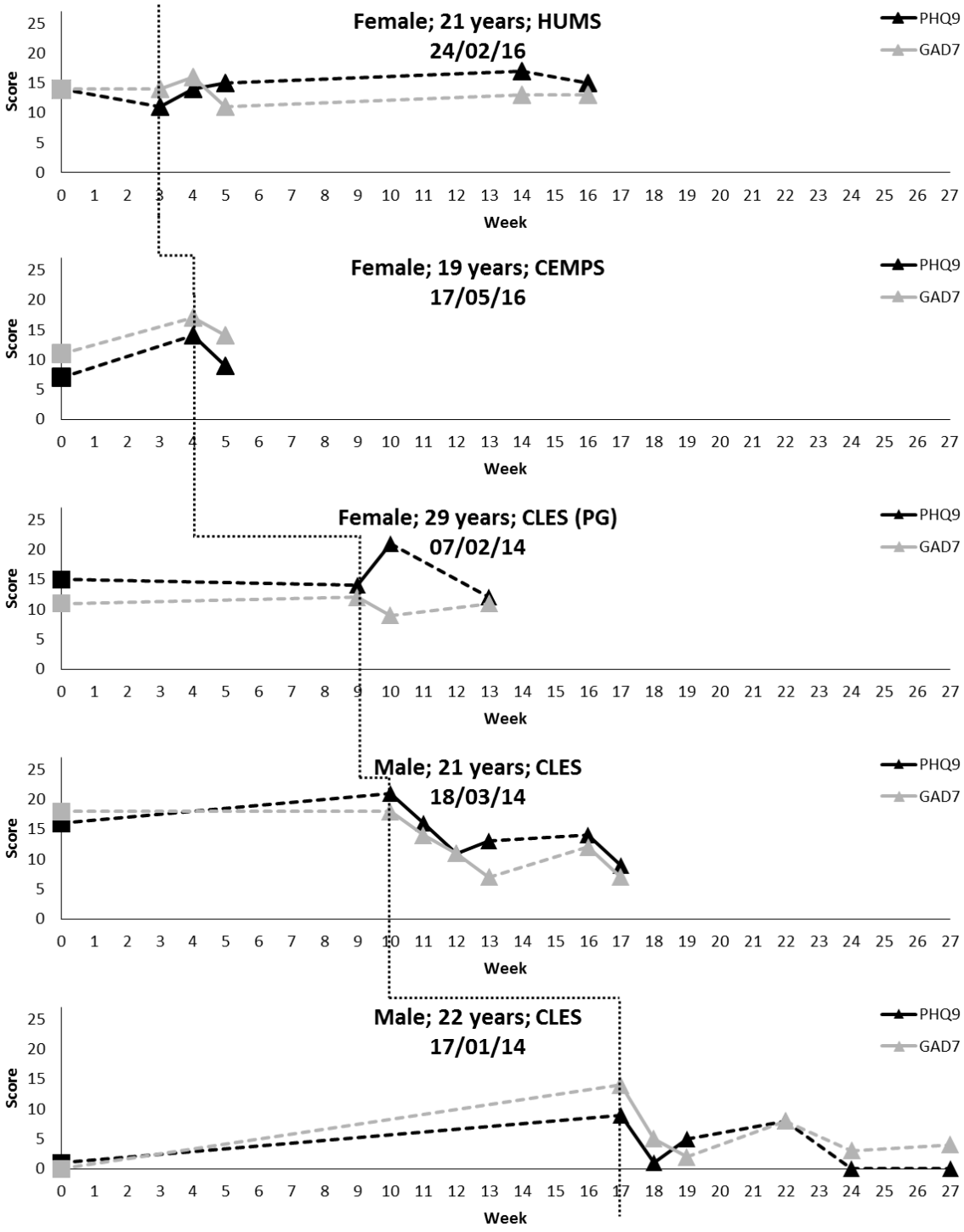

Female; 21 years; HUMS
24/02/16
Female; 19 years; CEMPS
17/05/16
Female; 29 years; CLES (PG)
07/02/14
Male; 21 years; CLES
18/03/14
Male; 22 years; CLES
17/01/14
PHQ9
GAD7
Score
Week

Figure 3.1(e).

3.6 Discussion

The aim of the study was to investigate the use and outcomes of a novel internet-based rumination-focused treatment for acute symptoms of depression and anxiety in a university wellbeing service. Significant improvements in symptoms were found in both the audit and case series samples. Additionally, these improvements were found across a range of baseline periods, times of year, subjects studied and initial symptom levels. These findings suggest that an internet treatment focusing on reducing rumination is able to produce positive outcomes for both depression and anxiety in a diverse university student population. This is consistent with previous research suggesting that rumination plays a role in the maintenance of symptoms (for reviews see Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008; Watkins, 2008).

Compliance rates among the current audit sample were 47.2%. This is lower than those reported in a recent meta-analysis of RCTs of supported internet-based cognitive-behavioural therapy (iCBT), which found 65.1% of iCBT users completed the intervention (van Ballegooijen et al., 2014), with 67.5% completing at least 80% of the content. However, few studies have tested iCBT in routine clinical settings. Two studies of an iCBT intervention for mixed anxiety and depression (the Worry and Sadness Program; Newby et al., 2013) found considerably higher completion rates when the intervention was delivered in a controlled research setting (89%) than when delivered in primary care (41.2%). This demonstrates that there are challenges in translating positive research findings into real world settings and the setting may explain the low compliance levels in the audit sample. Participants were offered i-RFCBT as one of several treatment options including face-to-face treatment, and therefore

may not have been as interested or motivated as someone specifically self-selecting to take part in a research trial of internet therapy.

Within the audit sample, baseline symptom severity was not linked to compliance, but post-treatment scores were significantly lower for those who complied. While we do not have interim scores for the audit sample, and therefore cannot be certain what the pattern of change was, this suggests participants whose symptom severity remained high were more likely to drop out early.

Compliance rates were higher in the case series sample, at 62.5%, suggesting that the sub-sample who actively chose to participate in the research may have been more motivated to complete the therapy, more consistent with the rates found in RCTs. Completion of more sessions (i.e., greater compliance) was linked to greater reductions in symptom levels, suggesting a potential dose-response relationship. Reasons for non-compliance should therefore be investigated in future studies in order to improve outcomes.

Recovery rates of 46.7% for depression and 40.3% for anxiety across the audit sample are comparable to the IAPT outcomes over the same period. For 2014/15 overall IAPT recovery rates were 44.6% for depression and 47.8% for anxiety/stress related disorders and in 2015/16, 46.7% and 48.8% for depression and anxiety/stress related disorders respectively (Community and Mental Health team, 2015, 2016). Within the case series subsample, recovery rates were even higher with 62.5% recovery for depression and 52.2% recovery for anxiety. Additionally, the recovery rates for i-RFCBT compare favourably with post-treatment recovery rates in a recent trial of internet-based CBT for university students. Mullin et al. (2015) trialled a transdiagnostic internet-based therapy for anxiety and depression, which included psycho-education and case

studies adapted specifically for university students. Using the standard cut-offs for caseness on PHQ9 and GAD7 to identify a clinical subsample, they found post-treatment recovery rates of 25% for depression and 44% for anxiety. However, longer term outcomes for this clinical subsample were good, increasing to 90% for depression and 78% for anxiety at 3-month follow-up. This suggests a follow-up assessment of the longer-term effects of i-RFCBT may be beneficial in future research.

A minority of participants worsened during the course of i-RFCBT. Given that recovery rates across the audit sample are comparable to IAPT outcomes, this may simply reflect individuals who are non-responsive to psychological treatment. However, it could also suggest a subgroup for whom either this particular intervention, or internet-based therapy in general, is not suitable.

A key limitation of the study is the lack of a control group and the lack of randomisation to treatment versus control. Without this it cannot be definitively argued that the reduction in symptoms is due to the treatment, rather than a measured or unmeasured confound, and causal inferences cannot be made. However, it is promising that a similar pattern of results was seen across a range of baseline lengths (between 1-17 weeks) and across the academic year (between term 2 of 2013/14 and term 3 of 2015/16), covering a range of challenges faced by the students, not simply confined to exam periods. This reduces the likelihood that other factors such as time of year, history or maturation are the reason for these changes. Additionally, the symptoms tended to remain stable or increase over the waiting list period, suggesting any improvements are less likely to be due to spontaneous remission. Furthermore, the sample comprised an almost equal number of males and females, an age range of 19-30, and students from all 6 academic colleges, demonstrating a

diverse range of subjects studied. This suggests the treatment effect can be generalised across genders, ages and academic subjects, suggesting that i-RFCBT could be beneficial for a variety of students.

I-RFCBT is one of a range of available treatments provided by the Wellbeing Centre. It is unclear how the outcomes compare to other treatments, as the Data Protection Officer only granted access to pre-and post-treatment scores for those students who had selected i-RFCBT. We cannot therefore benchmark the i-RFCBT treatment effects against other approaches offered in the Wellbeing Services. Future research in university settings should investigate how i-RFCBT compares to current face-to-face approaches, as this would provide a more robust investigation of its effectiveness than the within-person changes measured in the current study.

One area for further investigation is the mechanism of change. As the intervention targets rumination, we asked the Wellbeing Services to include a measure of rumination in the pre- and post-treatment assessments. However, the therapists reported that the assessment session already includes substantial information gathering and giving and it would not be practicable to add any questionnaires to the assessment battery. Rather, students who disclosed worry or rumination as a difficulty during their assessment session were offered i-RFCBT as a treatment option. Further studies of i-RFCBT in a clinical setting should include formal measures of repetitive negative thought (RNT), both pre- and post-intervention in order to test the effects of i-RFCBT on RNT in a real-world setting. Several measures of RNT have been used in RCTs of i-RFCBT (Cook, Mostazir, & Watkins, 2019; Topper et al., 2017): the Perseverative Thinking Questionnaire (PTQ; Ehring et al., 2011); the Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990)

and the Ruminative Response Scale of the Response Styles Questionnaire (RRS; Nolen-Hoeksema & Morrow, 1991). Building these measures into the therapy platform, administered before the first module and in each treatment module would provide pre-post RNT scores without adding further questionnaires to the in-person assessment session.

A key potential advantage of internet-based therapy for students compared to other treatment options provided in the Wellbeing Centre is that accessibility is not limited to term-time. This has the potential to improve continuity of care and increase the numbers of students who could be treated concurrently, thereby reducing waiting lists, which tend to expand quickly during term-time. In support of this, among the case series sample, over one third of modules were completed outside term-time. Furthermore, there is no need to schedule appointments, increasing flexibility for both student and therapist. This reduces the administrative burden on the service and removes the time lost to missed appointments. Additionally, the time needed to provide feedback for each module is reduced relative to face-to-face appointments by the use of template responses that are tailored to the individual.

Another limitation concerns the potential sampling bias of the case series participants. While 108 students were referred for i-RFCBT, only 32 consented to their data being included, despite this requiring no changes to their therapy. Of these, 3 were subsequently excluded for low baseline scores and a further 3 for not logging into the platform. One reason for this relatively low consent rate is that the therapy assessment session only lasted 30 minutes, during which time the therapist must gather information and offer treatment options to the student. Therapists reported that they often did not have sufficient time to explain the research in detail during this session and that, if consent wasn't

obtained during the assessment session, it was unlikely to be returned at a later date. While there was no difference on baseline symptom severity, the lack of retrospective consent suggests that the final sample may consist of those who had more positive attitudes prior to starting treatment and were more willing to engage.

A key potential advantage of internet-based therapy for students compared to other treatment options provided in the Wellbeing Centre is that accessibility is not limited to term-time. This has the potential to improve continuity of care and increase the numbers of students who could be treated concurrently, thereby reducing waiting lists, which tend to expand quickly during term-time. In support of this, among the case series sample, over one third of modules were completed outside term-time. Furthermore, there is no need to schedule appointments, increasing flexibility for both student and therapist. This reduces the administrative burden on the service and removes the time lost to missed appointments. Additionally, the time needed to provide feedback for each module is reduced relative to face-to-face appointments by the use of template responses that are tailored to the individual.

Future research should investigate whether such adaptations to the therapy or its implementation within the service may be needed to engage a greater number of students. As there is limited time in the assessment session for the therapist to explain both the RFCBT rationale and the internet-based approach, students for whom either the internet approach or focus on rumination was not appropriate may have chosen this treatment but then elected not to start it. Providing materials prior to the assessment that briefly explain the rationale and the practicalities of i-RFCBT may help to socialise students to the therapy and increase engagement.

In addition, a considerable proportion did not complete a minimum of 4 modules. It may be that earlier modules were less relevant to some individuals and providing the modules in a flexible order may help students to engage more with the intervention and providing information on i-RFCBT prior to the assessment appointment. It may be that those students who dropped out early did not find the earlier techniques helpful, so providing the modules in a flexible order might produce earlier symptom change and encourage users to persist with later modules.

Widespread implementation of internet therapy within university settings would require buy-in from policy makers and clinical staff. In a European survey (Topooco et al., 2017), only 47% of care providers and policy makers recommended iCBT and only for mild cases of depression. These stakeholders were concerned about losing the benefits of face-to-face contact and had reservations about whether a positive therapeutic alliance could be formed online. Information packs could therefore be provided to explain the benefits of providing internet interventions such as i-RFCBT for university services (e.g. more joined up care across the academic year, reduced waiting times, a lower threshold for treatment). In addition, all therapists should be provided with specific training in writing the feedbacks to allay concerns about developing a therapeutic alliance in writing.

In conclusion, these findings suggest that i-RFCBT may be beneficial in reducing symptoms of depression and anxiety in university students. Internet delivery has the potential to transcend geographical barriers and the challenges of term-time only appointments, ensuring continuity of care as the therapy can also be provided during holiday periods. Given the challenges in terms of availability and accessibility of current face-to-face treatment models, these

findings are promising and provide preliminary evidence that i-RFCBT could provide an effective alternative to face-to-face therapy for university students experiencing anxiety and depression.

Further reading

Watkins, E. R. (2016). *Rumination-focused Cognitive Behavioural Therapy for Depression*. New York: Guilford Press.

3.7 References

Aalto-Setälä, T., Marttunen, M., Tuulio-Henriksson, A., Poikolainen, K., & Lönnqvist, J. (2001). One-month prevalence of depression and other DSM-IV disorders among young adults. *Psychological Medicine, 31*(5), 791-801. doi:10.1017/s0033291701004081

Andersson, G. (2010). The promise and pitfalls of the internet for cognitive behavioral therapy. *BMC Medicine, 8*, 82. doi:10.1186/1741-7015-8-82

Andrews, G., Cuijpers, P., Craske, M. G., McEvoy, P., & Titov, N. (2010). Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis. *PloS one, 5*(10), e13196. doi:10.1371/journal.pone.0013196

Bewick, B. M., Gill, J., Mulhern, B., Barkham, M., & Hill, A. J. (2008). Using electronic surveying to assess psychological distress within the UK student population: a multi-site pilot investigation. *E-Journal of Applied Psychology, 4*(2). doi:10.7790/ejap.v4i2.120

Borkovec, T. D., Alcaine, O. M., & Behar, E. (2004). Avoidance theory of worry and generalized anxiety disorder. In R. G. Heimberg, C. L. Turk, & D. S. Mennin (Eds.), *Generalized anxiety disorder: Advances in research and practice* (pp. 77–108). New York, NY: Guilford.

Carver, C. S. (2013). *Attitudes Toward Self (ATS). Measurement Instrument Database for the Social Sciences*. Retrieved from http://www.midss.org/content/attitudes-toward-self-ats

Christensen, H., Griffiths, K. M., & Jorm, A. F. (2004). Delivering interventions for depression by using the internet: randomised controlled trial. *BMJ, 328*(7434), 265. doi:10.1136/bmj.37945.566632.EE

Ciesla, J. A., & Roberts, J. E. (2002). Self-directed thought and response to treatment for depression: A preliminary investigation. *Journal of Cognitive Psychotherapy, 16*(4), 435-453. doi:10.1891/jcop.16.4.435.52528

Collins, M. E., & Mowbray, C. T. (2005). Higher education and psychiatric disabilities: national survey of campus disability services. *American Journal of Orthopsychiatry, 75*(2), 304-315. doi:10.1037/0002-9432.75.2.304

Community and Mental Health team. (2015). *Psychological Therapies, Annual Report on the use of IAPT services - England, 2014-15*. Leeds: Health and Social Care Information Centre Retrieved from http://digital.nhs.uk/catalogue/PUB19098.

Community and Mental Health team. (2016). *Psychological Therapies: Annual report on the use of IAPT services. England, 2015-16*. Leeds: NHS Digital Retrieved from http://digital.nhs.uk/catalogue/PUB22110.

Cook, L., & Watkins, E. (2016). Guided, internet-based, rumination-focused cognitive behavioural therapy (i-RFCBT) versus a no-intervention control to prevent depression in high-ruminating young adults, along with an adjunct assessment of the feasibility of unguided i-RFCBT, in the REducing Stress and Preventing Depression trial (RESPOND): study

protocol for a phase III randomised controlled trial. *Trials, 17*, 1. doi:10.1186/s13063-015-1128-9

Craske, M. G. (2012). Transdiagnostic treatment for anxiety and depression. *Depression and Anxiety, 29*(9), 749-753. doi:10.1002/da.21992

Ehring, T., & Watkins, E. R. (2008). Repetitive Negative Thinking as a Transdiagnostic Process. *International Journal of Cognitive Therapy, 1*(3), 192-205. doi:10.1521/ijct.2008.1.3.192

Eisenberg, D., Golberstein, E., & Hunt, J. B. (2009). Mental Health and Academic Success in College. *The B.E. Journal of Economic Analysis & Policy, 9*(1). doi:10.2202/1935-1682.2191

Fava, M., Rankin, M. A., Wright, E. C., Alpert, J. E., Nierenberg, A. A., Pava, J., & Rosenbaum, J. F. (2000). Anxiety disorders in major depression. *Compr Psychiatry, 41*(2), 97-102. doi:10.1016/S0010-440X(00)90140-8

Gollwitzer, P. M. (1999). Implementation Intentions: Strong Effects of Simple Plans. *American Psychologist, 54*, 493-503. doi:10.1037/0003-066X.54.7.493

Gollwitzer, P. M., & Sheeran, P. (2006). Implementation Intentions and Goal Achievement: A Meta-analysis of Effects and Processes. *Advances in Experimental Social Psychology, 38*, 69-119. doi:https://doi.org/10.1016/S0065-2601(06)38002-1

Hankin, B. L., Young, J. F., Abela, J. R., Smolen, A., Jenness, J. L., Gulley, L. D., . . . Oppenheimer, C. W. (2015). Depression from childhood into late adolescence: Influence of gender, development, genetic susceptibility, and peer stress. *Journal of Abnormal Psychology, 124*(4), 803-816. doi:10.1037/abn0000089

Hayes, S. C. (1981). Single case experimental design and empirical clinical practice. *Journal of Consulting and Clinical Psychology, 49*(2), 193-211. doi:10.1037//0022-006x.49.2.193

Hoffmann, T. C., Glasziou, P. P., Boutron, I., Milne, R., Perera, R., Moher, D., . . . Michie, S. (2014). Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ, 348*, g1687. doi:10.1136/bmj.g1687

Hysenbegasi, A., Hass, S. L., & Rowland, C. R. (2005). The impact of depression on the academic productivity of university students. *The Journal of Mental Health Policy and Economics, 8*(3), 145-151.

Ibrahim, A. K., Kelly, S. J., Adams, C. E., & Glazebrook, C. (2013). A systematic review of studies of depression prevalence in university students. *Journal of Psychiatric Research, 47*(3), 391-400. doi:10.1016/j.jpsychires.2012.11.015

Kazdin, A. E. (2003). *Methodological issues and strategies in clinical research 3rd ed*. Washington D.C.: American Psychological Association.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry, 62*(6), 593-602. doi:10.1001/archpsyc.62.6.593

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: validity of a brief depression severity measure. *Journal of General Internal Medicine, 16*(9), 606-613. doi:10.1046/j.1525-1497.2001.016009606.x

Kroenke, K., Spitzer, R. L., Williams, J. B., Monahan, P. O., & Löwe, B. (2007). Anxiety disorders in primary care: prevalence, impairment, comorbidity,

and detection. *Annals of Internal Medicine, 146*(5), 317-325. doi:10.7326/0003-4819-146-5-200703060-00004

Martell, C. R., Addis, M. E., & Jacobson, N. S. (2001). *Depression in context: Strategies for guided action*. New York: Norton.

McEvoy, P. M., Grove, R., & Slade, T. (2011). Epidemiology of anxiety disorders in the Australian general population: findings of the 2007 Australian National Survey of Mental Health and Wellbeing. *Australian and New Zealand Journal of Psychiatry, 45*(11), 957-967. doi:10.3109/00048674.2011.624083

McManus, S., Bebbington, P., Jenkins, R., & Brugha, T. (2016). *Mental health and wellbeing in England: Adult Psychiatric Morbidity Survey 2014*. Leeds, UK: NHS Digital Retrieved from https://digital.nhs.uk/catalogue/PUB21748.

Morrison, R., & O'Connor, R. C. (2005). Predicting psychological distress in college students: the role of rumination and stress. *Journal of Clinical Psychology, 61*(4), 447-460. doi:10.1002/jclp.20021

Mullin, A., Dear, B. F., Karin, E., Wootton, B. M., Staples, L. G., Johnston, L., . . . Titov, N. (2015). The UniWellbeing course: A randomised controlled trial of a transdiagnostic internet-delivered cognitive behavioural therapy (CBT) programme for university students with symptoms of anxiety and depression. *Internet Interventions, 2*(2), 128-136. doi:10.1016/j.invent.2015.02.002

Muñoz, R. F., Cuijpers, P., Smit, F., Barrera, A. Z., & Leykin, Y. (2010). Prevention of major depression. *Annual Review of Clinical Psychology, 6*, 181-212. doi:10.1146/annurev-clinpsy-033109-132040

National Institute of Mental Health. (2003). *Depression and college students*. (NIH Publication No. 15-4266). Bethesda, MD: NIMH Retrieved from https://www.nimh.nih.gov/health/publications/depression-and-college-students/index.shtml.

National Union of Students. (2015). *Lost in transition? – provision of mental health support for year olds moving to further and higher education.* Paper presented at the All Party Parliamentary Group on Students, London, UK.

Newman, D. L., Moffitt, T. E., Caspi, A., Magdol, L., Silva, P. A., & Stanton, W. R. (1996). Psychiatric disorder in a birth cohort of young adults: prevalence, comorbidity, clinical significance, and new case incidence from ages 11 to 21. *Journal of Consulting and Clinical Psychology, 64*(3), 552-562. doi:10.1037//0022-006x.64.3.552

Nolen-Hoeksema, S., & Watkins, E. R. (2011). A Heuristic for Developing Transdiagnostic Models of Psychopathology: Explaining Multifinality and Divergent Trajectories. *Perspectives on Psychological Science, 6*(6), 589-609. doi:10.1177/1745691611419672

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking Rumination. *Perspectives on Psychological Science, 3*(5), 400-424. doi:10.1111/j.1745-6924.2008.00088.x

Pine, D. S., Cohen, P., Gurley, D., Brook, J., & Ma, Y. (1998). The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. *Archives of General Psychiatry, 55*(1), 56-64. doi:10.1001/archpsyc.55.1.56

Randall, E. M., & Bewick, B. M. (2015). Exploration of counsellors' perceptions of the redesigned service pathways: a qualitative study of a UK university

student counselling service. *British Journal of Guidance & Counselling, 44*(1), 86-98. doi:10.1080/03069885.2015.1017801

Richardson, T., Stallard, P., & Velleman, S. (2010). Computerised cognitive behavioural therapy for the prevention and treatment of depression and anxiety in children and adolescents: a systematic review. *Clinical Child and Family Psychology Review, 13*(3), 275-290. doi:10.1007/s10567-010-0069-9

Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of Internal Medicine, 166*(10), 1092-1097. doi:10.1001/archinte.166.10.1092

Thorley, C. (2017). *Not by degrees: Improving student mental health in the UK's universities*. London: IPPR Retrieved from http://www.ippr.org/research/publications/not-by-degrees.

Topper, M., Emmelkamp, P. M., Watkins, E., & Ehring, T. (2017). Prevention of anxiety disorders and depression by targeting excessive worry and rumination in adolescents and young adults: A randomized controlled trial. *Behaviour Research and Therapy, 90*, 123-136. doi:10.1016/j.brat.2016.12.015

van Ballegooijen, W., Cuijpers, P., van Straten, A., Karyotaki, E., Andersson, G., Smit, J. H., & Riper, H. (2014). Adherence to Internet-based and face-to-face cognitive behavioural therapy for depression: a meta-analysis. *PloS one, 9*(7), e100674. doi:10.1371/journal.pone.0100674

Verplanken, B., Friborg, O., Wang, C. E., Trafimow, D., & Woolf, K. (2007). Mental habits: metacognitive reflection on negative self-thinking. *Journal of Personality and Social Psychology, 92*(3), 526-541. doi:10.1037/0022-3514.92.3.526

Verplanken, B., & Orbell, S. (2003). Reflections on Past Behavior: A Self-Report Index of Habit Strength. *Journal of Applied Social Psychology, 33*(6), 1313-1330. doi:10.1111/j.1559-1816.2003.tb01951.x

Watkins, E. R. (2008). Constructive and unconstructive repetitive thought. *Psychological Bulletin, 134*(2), 163-206. doi:10.1037/0033-2909.134.2.163

Watkins, E. R. (2016). *Rumination-focused Cognitive Behavioural Therapy for Depression*. New York: Guilford Press.

Watkins, E. R., Baeyens, C. B., & Read, R. (2009). Concreteness training reduces dysphoria: proof-of-principle for repeated cognitive bias modification in depression. *Journal of Abnormal Psychology, 118*(1), 55-64. doi:10.1037/a0013642

Watkins, E. R., & Baracaia, S. (2002). Rumination and social problem-solving in depression. *Behaviour Research and Therapy, 40*(10), 1179-1189. doi:10.1016/s0005-7967(01)00098-5

Watkins, E. R., Moberly, N. J., & Moulds, M. L. (2008). Processing mode causally influences emotional reactivity: distinct effects of abstract versus concrete construal on emotional response. *Emotion, 8*(3), 364-378. doi:10.1037/1528-3542.8.3.364

Watkins, E. R., & Moulds, M. (2005). Distinct modes of ruminative self-focus: impact of abstract versus concrete rumination on problem solving in depression. *Emotion, 5*(3), 319-328. doi:10.1037/1528-3542.5.3.319

Watkins, E. R., Mullan, E., Wingrove, J., Rimes, K., Steiner, H., Bathurst, N., . . . Scott, J. (2011). Rumination-focused cognitive-behavioural therapy for residual depression: phase II randomised controlled trial. *The British Journal of Psychiatry, 199*(4), 317-322. doi:10.1192/bjp.bp.110.090282

Watkins, E. R., & Nolen-Hoeksema, S. (2014). A habit-goal framework of depressive rumination. *Journal of Abnormal Psychology, 123*(1), 24-34. doi:10.1037/a0035540

Watkins, E. R., Scott, J., Wingrove, J., Rimes, K., Bathurst, N., Steiner, H., . . . Malliaris, Y. (2007). Rumination-focused cognitive behaviour therapy for residual depression: a case series. *Behaviour Research and Therapy, 45*(9), 2144-2154. doi:10.1016/j.brat.2006.09.018

Watkins, E. R., Taylor, R. S., Byng, R., Baeyens, C., Read, R., Pearson, K., & Watson, L. (2012). Guided self-help concreteness training as an intervention for major depression in primary care: a Phase II randomized controlled trial. *Psychological Medicine, 42*(7), 1359-1371. doi:10.1017/S0033291711002480

Webb, T., & Sheeran, P. (2007). How do implementation intentions promote goal attainment? A test of component processes. *Journal of Experimental Social Psychology, 43(2)*, 295-302. doi:10.1016/j.jesp.2006.02.001

Williams, M., Coare, P., Marvell, R., Pollard, E., Houghton, A.-M., & Anderson, J. (2015). *Understanding provision for students with mental health problems and intensive support needs*. (IES project code: 00099-3782). Brighton, UK: IES Retrieved from http://www.hefce.ac.uk/pubs/rereports/year/2015/mh/.

CHAPTER 4: Qualitative analysis of the acceptability of i-RFCBT for prevention

4.1 Chapter overview

This chapter reports a qualitative study to assess the acceptability of i-RFCBT for the prevention of depression in high-ruminating undergraduates. While the findings from the audit and case series indicate that i-RFCBT has a positive treatment effect, when delivered as a guided intervention to students with clinical levels of depression or anxiety, delivering the intervention only via treatment services restricts accessibility and scalability, which are key benefits of internet compared to face-to-face intervention. In order to alleviate the personal distress associated with depression, as well as the pressures on overstretched treatment services, there is also a need to focus on prevention and building resilience among the student body through timely interventions when students first show symptoms rather than waiting until a crisis (Student Minds, 2014; Universities UK, 2017). Topper et al. (2017) demonstrated that i-RFCBT could be an effective preventive intervention in adolescents and young adults, but it remains unclear whether this intervention would be acceptable to similarly high-ruminating university students in the UK.

This chapter recapitulates the key arguments for prevention in university students and reports an online focus group conducted with high-ruminating students, seeking opinions on the benefits and barriers to using an online preventive intervention as well as the acceptability of i-RFCBT.

4.2 Introduction

Improving the mental health of university students is increasingly identified as a priority (Thorley, 2017; Universities UK, 2018). Anonymised data from primary care records at 12 medical practices indicate depression is the most commonly diagnosed student mental health condition in the UK (8.4% of student-patients), followed by anxiety (7.4% of student-patients) (Thorley, 2017). Across a sample of 13,984 first-year students in 8 countries, 12-month prevalence rates were 18.5% for Major Depressive Disorder (MDD) and 16.7% for Generalised Anxiety Disorder (GAD; (Auerbach et al., 2018). There is also evidence that rates are increasing, with a five-fold increase in disclosures of mental health disorders to UK higher education institutions (HEIs) in the past 10 years (Thorley, 2017). However, prevalence data relies on people receiving and disclosing a formal diagnosis and there is evidence that prevalence rates amongst students may be considerably higher. For example, a survey of four UK HEIs found 29% of students scoring in the clinical range for psychological distress (Bewick, Gill, Mulhern, Barkham, & Hill, 2008).

Students face many novel experiences and responsibilities at university, that may be both exciting and challenging, such as: leaving home for the first time; more self-directed study; forming new friendships and changes in routine, in particular to sleep patterns (National Institute of Mental Health, 2003). Significant life transitions, such as moving to a new city and starting university, are opportunities for growth (Praharso, Tear, & Cruwys, 2017) but such periods can also be significant stressors and are associated with increases in psychological distress and the onset of depression (Hammen, 2005; Paykel, 2003). Mental health difficulties negatively impact academic performance (Hysenbegasi, Hass, & Rowland, 2005) and increase risk of drop-out from

university (Eisenberg, Golberstein, & Hunt, 2009). However, with appropriate support, students with mental health difficulties can succeed academically (Collins & Mowbray, 2005).

UK universities now provide in-house support services for mental health difficulties, largely wellbeing and counselling services (Universities UK, 2018). Demand for these services is increasing (Williams et al., 2015). Despite this increase in demand, there remains a considerable treatment gap, with 54% of students reporting mental health problems not seeking support (NUS, 2015). Studies investigating the barriers to help seeking suggest that students place a greater importance on attitudinal than structural barriers to treatment (Ebert et al., 2019), with 'preference to handle problem alone' the most frequently reported reason (56.4%), followed by 'wanting to talk to friends/relatives instead' (48%) and 'being too embarrassed' (32.2%). Other reported barriers include lack of time; minimising the severity of symptoms; lack of anonymity and viewing stress as normal during college (Downs & Eisenberg, 2012; Eisenberg, Speer, & Hunt, 2012; Lintvedt, Sørensen, Østvik, Verplanken, & Wang, 2008). Of those students who do access support, only half access university support services (NUS, 2015).

One approach to addressing this unmet need may be the use of computerised (cCBT) or internet-based cognitive-behavioural therapy (iCBT). For consistency, these interventions are collectively referred to as iCBT throughout this chapter. Reviews suggest that guided iCBT is both effective and feasible in treating common mental health disorders such as depression and anxiety (Andrews et al., 2018; Andrews et al., 2010; Spek et al., 2007), with attrition rates comparable to face-to-face interventions (Christensen, Griffiths, & Farrer, 2009). Online therapies may provide an alternative for such students

who do not access face-to-face therapies (Day, McGrath, & Wojtowicz, 2013). Benefits that may be particularly attractive to students include greater flexibility and autonomy, being able to access content at a time and place of their own choosing, more time for self-reflection and greater anonymity, which could reduce any concerns about visiting university wellbeing centres. (Andersson, 2010; Muñoz et al., 2010; Richardson et al., 2010b). Additionally, the lack of geographical barrier means students would be able to continue accessing the intervention and receiving written support outside term time, thereby receiving joined up care throughout the academic year (Universities UK, 2018).

Despite the theoretical benefits of iCBT for students, a study examining university students' attitudes towards iCBT before this approach became more commonly adopted, found low levels of credibility, expectancy of improvement and likelihood of using a computerised therapy (Mitchell & Gordon, 2007). Students rated computerised therapy as impersonal and generic, not tailored to individual needs and with an overwhelming amount of content that would be difficult to complete without additional support. Only 9.8% of 122 students identified iCBT as their preferred treatment. Despite this small percentage, participants who favoured iCBT preferred self-guided therapy for reasons of privacy and accessibility, suggesting that self-administered iCBT has the potential to reach students who would not normally access face-to-face interventions (Mitchell & Gordon, 2007), and given the wider reach that can be achieved with self-administered interventions this could provide significant public health benefits.

Recent studies suggest students' attitudes towards internet interventions have improved, highlighting factors such as anonymity, privacy and lack of stigma as benefits of iCBT (Chan, Farrer, Gulliver, Bennett, & Griffiths, 2016).

Flexibility is also important as students have a particularly variable timetable so may be unable to attend a regular weekly appointment (Fleischmann et al., 2017). Students value being able to access interventions outside normal working hours, particularly during the night (Chan et al., 2016).

The use of evidence-based techniques, engaging content, and having an online supporter can also improve user engagement and treatment satisfaction (Eells, Barrett, Wright, & Thase, 2014; Richards & Timulak, 2012). While most students appreciated having an online supporter, the feedback did not necessarily meet their needs due to being too generic or scripted (Fleischmann et al., 2017). Students particularly value online supporters when they respond in a personal way, as this helps to tailor the intervention (Walsh & Richards, 2016).

Despite these positive attitudes, academic stress is a significant factor in students disengaging from iCBT or dropping out of research trials altogether (Doherty, Coyle, & Sharry, 2012; Sharry, Davidson, McLoughlin, & Doherty, 2013). Consistent with this finding, lack of time and having a number of competing priorities are commonly reported as barriers (Fleischmann et al., 2017; Richards & Timulak, 2012; Walsh & Richards, 2016). These barriers could be heightened at certain times of the academic year, such as during exams, suggesting that interventions for students need to be particularly sensitive to these external pressures (Richards & Timulak, 2012). Greater understanding of students' attitudes towards iCBT are therefore needed to ensure internet interventions are adequately adapted to their specific needs (Davies et al., 2014), as positive attitudes towards iCBT not only increase engagement, but are associated with greater improvements in clinical outcomes (Schröder et al., 2018).

As well as developing technological solutions to overcome the limited resources of Wellbeing services, prevention has been highlighted as a priority to increase wellbeing among students (Thorley, 2017), thereby reducing the need for acute treatment. Qualitative studies of iCBT to date have largely focused on treatment rather than prevention (Earley et al., 2017). However, attitudes may differ when using an intervention for prevention. For example, users who are currently well may be less motivated to invest significant time and effort in completing an intervention (Ebert et al., 2017).

Fleishmann et al.'s (2017) intervention targeted stress in students but participants were not selected as being subclinical for depression, so it is unclear if the users viewed the intervention as a treatment or prevention. One recent study of adults with subclinical symptoms of depression (Earley et al., 2017) reported benefits were similar to those found in treatment studies, including increased accessibility, flexibility, gaining awareness and insight, increased wellbeing and supportive feedback (Earley et al., 2017). The main criticisms also reflected those highlighted in treatment studies, such as difficulties with navigation and lack of identification with the case studies. Some participants also reported that the feedback felt scripted and needed further individualisation. However, further qualitative research is needed to ensure iCBT is acceptable for prevention.

Given that moving to university is a significant life transition, the student population as a whole is considered at risk of depression and may therefore benefit from a universal prevention approach to increase general wellbeing and resilience (Universities UK, 2018). However, certain subgroups within the student population are at greater risk due to specific risk factors, such as rumination, and may therefore have the greatest need and most to gain from a

preventive intervention. Such a targeted approach prioritises those most at risk by identifying and mitigating against these risk factors (Topper et al., 2010). Rumination predicts depressive symptoms in students over 6 months (Morrison & O'Connor, 2005) and also interacts with other risk factors (low self-esteem and stressful life events) to maintain depressive symptoms (Ciesla et al., 2011). As well as maintaining existing symptoms, a ruminative response to stressful events prospectively predicts the onset of depressive symptoms (Connolly & Alloy).

One intervention that directly targets this risk factor is rumination-focused cognitive-behavioural therapy (RFCBT; Watkins, 2016; Watkins et al., 2007). While grounded in the principles of CBT, RFCBT contains several novel elements. Firstly, RFCBT builds on theory and empirical evidence that there are distinct forms of rumination in response to negative situations, with either unconstructive or constructive consequences (Watkins, 2008). Unconstructive rumination is characterised by abstract, global and evaluative thoughts whereas constructive rumination is more concrete, specific and process focused. Experimental studies have shown that the more concrete style has a number of benefits including increased problem solving (Watkins & Baracaia, 2002; Watkins & Moulds, 2005) and less emotional reactivity in response to failure (Watkins et al., 2008). RFCBT therefore differs from standard CBT, which seeks to challenge the content of individual negative thoughts, by shifting thinking style. Secondly, pathological rumination is conceptualised as a learned habit (Watkins & Nolen-Hoeksema, 2014) and a form of avoidance (Borkovec et al., 2004; Watkins, 2008) and RFCBT incorporates BA principles, such as functional analysis, to replace maladaptive rumination with more adaptive approach behaviours (Martell et al., 2001).

In a randomised-controlled trial (Topper et al., 2017), i-RFCBT was compared to group-delivered RFCBT and waiting list control, in a sample of 251 15-22-year-olds with elevated repetitive negative thought (RNT, incorporating worry and rumination). Both interventions reduced symptoms of depression and anxiety, relative to the control arm (*d* = 0.36 to 0.72). Using cut-offs on continuous measures as a proxy diagnosis, cumulative incidence rates at 12-month follow-up were lower in both intervention groups than controls for depression (14.7% internet; 15.3% group; 32.4% control) and generalised anxiety disorder (GAD; 16.0% internet; 18.0% group; 42.2% control). Moreover, in support of the hypothesised mechanism of change, reductions in rumination mediated these clinical outcomes.

Topper et al. (2017) originally aimed to recruit secondary school students (aged 15-19) but the upper age was increased to 22, to include undergraduates. Given their positive outcomes in adolescents and undergraduates, we hypothesised that the same i-RFCBT intervention may be effective at preventing depression in UK undergraduates experiencing high levels of worry and rumination.

Previous studies suggest university students may have specific benefits and barriers in using iCBT (Fleischmann et al., 2017; Richards & Timulak, 2012). Prevention is a priority among students (Thorley, 2017) but few studies have assessed the acceptability of preventive interventions using qualitative methods (Earley et al., 2017). We therefore wanted to qualitatively assess the acceptability of iCBT for the prevention of depression in a high-risk undergraduate sample and to examine opinions on the benefits and barriers of accessing internet-based interventions, relative to face-to-face interventions. As i-RFCBT is previously untested in the UK, a key question was the acceptability

of this intervention in particular and obtaining specific feedback on barriers and facilitators to its use, with reference to content, design and delivery. NICE guidelines recommend supported iCBT for mild to moderate depression (National Institute of Clinical Excellence, 2009). However, there is less evidence as to the relative benefits of guided versus unguided iCBT for prevention, and unguided preventive interventions are significantly more scalable at a public health level. A further question was therefore the acceptability of an unguided self-help variant of i-RFCBT, which was the variant that participants viewed.

4.3 Methods

4.3.1 Design

The study used an asynchronous online focus group and a Framework analysis approach. The Framework approach is appropriate for answering a range of questions and incorporates both a priori and emergent coding to form a final analytic framework (Ritchie & Spencer, 1994). It was chosen because it was consistent with the study aims to evaluate a novel intervention by exploring both previously identified benefits and barriers as well as exploring potential new insights specific to i-RFCBT.

Focus groups have been used to explore participants' experiences on a specific topic, with the group dynamics encouraging a wide range of views through debate between participants (Kitzinger, 1995). The online format was chosen for several reasons. Firstly, an initial recruitment for a face-to-face focus group yielded no responses, which led us to hypothesise that highly worried/ruminative students may be reluctant to speak in a group setting. Secondly, with increasing use of the internet for communication, particularly among young people, the use of online focus groups is increasingly popular

(Fox, Morris, & Rumsey, 2007; Williams, Clausen, Robertson, Peacock, & McPherson, 2012).

The online focus group format may provide benefits over face-to-face groups for the exploration of sensitive topics. Participants may be more willing to disclose personal experiences due to the increased anonymity compared to face-to-face focus groups (Williams et al., 2012). Additionally, with this anonymity participants are more likely to express negative opinions online than they would be face-to-face (Williams et al., 2012), providing a wider range of opinions.

Online focus groups may be conducted in a synchronous or asynchronous format. Synchronous discussions, run in real time, more closely mirror face-to-face interaction but participants must all attend at a given time and the speed of conversation can encourage shorter answers, lacking in richness (Smithson, 2008). An asynchronous focus group (where participants are able to log on at any time, read others' comments and contribute their own responses) was chosen for the current study to both increase convenience for participants and provide a longer period to reflect on responses, potentially increasing the richness of the data (Williams et al., 2012).

4.3.2 Participants

Participants were undergraduate students at the University of Exeter, aged 18-24, selected as being at risk for depression because of elevated worry and rumination. This was defined as meeting criteria for elevated RNT (Topper et al., 2017): ≥ 50 on the Penn-State Worry Questionnaire (PSWQ; Meyer et al., 1990) and/or ≥ 40 on the Ruminative Response Scale (RRS; Nolen-Hoeksema & Morrow, 1991). As a prevention study, participants were only included if they

also did not meet diagnostic criteria for a current major depressive episode (MDE) and, to ensure safety, did not present with active suicide risk.

4.3.3 Recruitment and screening procedure

Participants were recruited through the University of Exeter psychology research portal and given £10 remuneration or course credit for taking part. The screening procedure consisted of two steps: completion of self-report measures to confirm elevated RNT and measure depressive symptoms, followed by a clinical interview to check diagnostic status for current and past MDE. The study was approved by the University of Exeter Psychology Ethics Committee.

4.3.4 Self-report measures

Twenty-seven students expressed interest in the study and were sent the initial screening questionnaires by email: RRS (Nolen-Hoeksema & Morrow, 1991), PSWQ (Meyer et al., 1990), and the 8-item Patient Health Questionnaire (PHQ-8; Kroenke et al., 2009). The 8-item version is the same as the PHQ-9 (Kroenke et al., 2001) with the suicide question removed and has satisfactory validity and reliability (Pressler et al., 2011). This measure provided an initial screen of depressive symptoms, but participants were invited to attend the diagnostic interview regardless of their severity score on the PHQ-8, to confirm eligibility. Fourteen participants (52%) returned completed questionnaires. All these respondents met the initial screening criteria for elevated rumination (≥40 RRS) or worry (≥ 50 PWSQ) and were invited to undergo the diagnostic interview. One student with a PHQ-8 score indicating likely depression declined the interview and was sent contact details of support services. Thirteen undergraduate students consented to the diagnostic interview, conducted either in person or by telephone.

4.3.5 Diagnostic interview

The diagnostic interview assessed current and past MDE, using the relevant depression modules of the Structured Clinical Interview for DSM-IV (SCID-I; First et al., 2002). Consent to interview included agreement to any significant disclosure of risk being shared with their GP. In the event of disclosure, this was assessed using a well-established protocol to determine level of risk and seek clinical support as appropriate. No participants interviewed met criteria for current MDE or disclosed any risk. Thirteen undergraduates were therefore eligible for the study and were provided with more detailed information about the study and returned written consent to participate.

4.3.6 Intervention

Internet-based RFCBT (i-RFCBT) includes the same techniques as face-to-face RFCBT (Watkins, 2016; Watkins et al., 2011; Watkins et al., 2007), adapted for online delivery. The intervention is described in full according to TIDieR guidelines (Hoffmann et al., 2014) in Chapter 2. Briefly, the unguided version (Cook & Watkins, 2016) viewed by participants contains the same modules used by Topper et al. (2017), adapted for use as a self-help intervention. It consists of six modules of 1-2 hours, split into shorter sessions (single webpages) that each take 15-20 minutes to complete. Each module follows a basic structure consisting of: reflection on the previous week, introduction and practice of new techniques, and formulation of plans to practise and implement these new techniques in daily life. Unguided users can access all modules sequentially but are advised to spend one to two weeks on each to allow sufficient time for practice.

Consistent with the conceptualisation of pathological rumination as a learned habit (Watkins & Nolen-Hoeksema, 2014), the techniques are used in response to situations that would ordinarily trigger rumination, thereby counter-conditioning the habitual rumination with a new, more helpful response. This counter-conditioning takes the form of implementation intentions, or If-Then plans: “If I encounter situation X, Then I will do Y” (Gollwitzer, 1999; Gollwitzer & Sheeran, 2006). The alternative responses covered in i-RFCBT include: being more active, slowing things down, breaking tasks down, opposite action, relaxation, concrete thinking, becoming absorbed, self-compassion and assertiveness.

The intervention incorporates a range of interactive tools to deliver and reinforce the key techniques of RFCBT (Watkins et al., 2011; Watkins et al., 2007), including mood diaries, on-line experiential exercises using audio-recordings, images, and video case studies of students’ experiences of the therapy. Individual audio exercises are downloadable for further practice, while the content of each module is accessible as a pdf file. In addition, the website contains a screen reader so users can listen to, rather than read, the text content.

4.3.7 Focus group procedure

Access to unguided i-RFCBT was provided two weeks in advance of access to the focus group to allow participants time to explore the intervention. Participants were asked to read through the intervention with a view to providing their opinion on its structure and content.

After two weeks, participants were provided with log-in details for the asynchronous online focus group and asked to select a pseudonym to preserve

anonymity. The online focus group was conducted on a secure password-protected online forum, using Vanilla Forums 2.0.18.8 software. It was hosted on the University of Exeter server only accessible to the researchers, invited participants and the departmental IT technician. Participants were also asked not to discuss any of the comments posted with anyone outside the research study.

The focus group consisted of 23 questions, divided into 9 topic groups (see Appendix 2 for full interview schedule). Questions moved from general opinions on benefits and barriers to internet versus face-to-face therapy to specific features of content, design and delivery of iCBT with specific reference to i-RFCBT intervention. In order for self-help materials to be engaging, they must be considered readable, have a good design, personal relevance and be practical (Williams & Morrison, 2010). Content should be evidence-based, convey common therapeutic factors such as empathy and warmth and reflect the user's experience through the use of relevant case examples (Richards & Farrand, 2010). Specific questions addressed these domains, using recommendations for assessing internet interventions in particular (Kerr, Murray, Stevenson, Gore, & Nazareth, 2006), focusing on the clarity of the language used; overall tone of the intervention; visual appearance of the site; interactive features, including audio exercises and video case studies; ease of navigation and the perceived safety and trustworthiness of the site. Participants were also asked about the relevance and helpfulness of the specific RFCBT techniques as well as the practicality of completing a module weekly or fortnightly as the burden of academic work may be a barrier to engagement (Richards & Timulak, 2012). As deadlines may improve the effectiveness of self-help CBT (Nordin, Carlbring, Cuijpers, & Andersson, 2010), we asked

participants to consider if deadlines would increase motivation to complete modules. Although participants only viewed the unguided i-RFCBT, the focus group questions explained that there is also a guided version of i-RFCBT so that opinions could be gathered on the relative benefits and barriers of the two different formats.

All questions in the focus group were available simultaneously, although as some questions were contingent on others, participants were advised to work through them in the order they appeared on Vanilla Forums. Although participants accessed the forum at different times and over a period of one month, some interaction between participants was achieved as comments could be posted either as a direct reply to the original question or as a reaction to another participant's comment. The content of the online focus group was moderated by LC, with participants able to contact LC directly if they had any concerns regarding posts. No posts were reported or deemed inappropriate by the researcher and none required removal from the site.

4.3.8 Analysis

Responses were analysed using a Framework approach (Ritchie & Spencer, 1994) that provides a systematic procedure for analysing qualitative data and consists of five key stages: familiarisation; identifying a thematic framework; indexing; charting; mapping and interpretation. While these stages have distinct features, the approach is not prescriptive and does not follow a simple linear course, with multiple iterations and reworking of previous ideas required (Ritchie & Spencer, 1994). Initial coding of the raw data was conducted by LC. This initial coding was highly descriptive and based on a priori concepts. Through a process of iterative revisions and discussions with an experienced

qualitative researcher (PF) and the developer of RFCBT (EW), emergent patterns and interpretations informed the development of themes and subthemes. Additionally, themes and subthemes were derived independently by a second coder with clinical experience of supporting CBT (LO). Any disagreements served to further refine themes and subthemes through discussion (Barbour, 2001) until consensus on the final framework was reached. In addition, as focus groups can overemphasise consensus among participants (Barbour, 2008), to further increase rigour, disconfirming cases or comments were actively sought and used to refine emergent subthemes (Barbour, 2005). To increase transparency, illustrative quotes, including examples of disconfirming comments, are provided for each subtheme verbatim.

4.3.8.1 Self-reflection

The research team each brought a different perspective to the analyses and group meetings provided opportunity to discuss different aspects of the data that we felt was relevant. I was initially drawn to this topic due to personal experience of CMDs and have used both face-to-face CBT in IAPT services and MoodGYM as an unguided intervention. I was therefore drawn to the benefits of unguided therapy and, initially noted only the differences between face-to-face and unguided internet therapy in the data. However, discussion with PF highlighted the benefits of guided therapy for increasing adherence and forming a therapeutic alliance. A further area of discussion was around the specific content of i-RFCBT. In initial analyses, I had identified specific techniques that participants had liked but was unsure how these fitted together. As EW developed the intervention, he was able to identify that it was the range of

techniques that was important, as this allowed users to try different approaches and then focus on those that were the most helpful.

4.4 Results

Only nine of the thirteen participants logged on to the focus group site and posted comments for subsequent analysis (see Table 4.1 for baseline characteristics). No significant differences were found in baseline symptom severity between those who did or did not post comments. The number of comments from each participant ranged from 5 to 25.

Table 4.1. Demographic characteristics and symptom levels of focus group participants.

ID	Gender	Age	Ethnicity	Past MDE	RRS	PSWQ	PHQ8
P01	F	21	East Asian	No	41	46	6
P02	F	19	Caucasian	No	41	61	0
P03	F	19	Caucasian	Yes	55	59	12
P04	M	18	East Asian	No	46	40	2
P05	F	18	Caucasian	No	31	69	2
P06	F	21	East Asian	Yes	58	53	10
P07	F	19	Caucasian	Yes	44	77	4
P08	F	18	Caucasian	Yes	49	62	5
P09	F	19	East Asian	Yes	59	46	6

Note: PHQ-8: Patient Health Questionnaire (8-item version);
PSWQ: Penn State Worry Questionnaire; RRS: Ruminative Response Scale.

Five main themes were identified: ‘Benefits of iCBT’; ‘Attitudes towards support’; Positive aspects of platform design and delivery’; ‘Improvements to design and delivery’ and ‘Positive aspects of i-RFCBT content’. Five of the main themes comprise several subthemes (see Table 4.2).

Table 4.2. Key themes and sub-themes describing undergraduate students' opinions of internet therapies with specific reference to i-RFCBT.

Major Themes	Subthemes	Disconfirming Cases
Benefits of internet therapy	Convenience Easier to express feelings	
Attitudes towards support	Preference for and benefits of face-to-face support Benefits of guided iCBT	
Positive aspects of platform design and delivery	Design Video case studies Security	Prefer written transcripts Easier log-in wanted
Improvements to design and delivery to increase usability and personalisation	Shorter, clearer sections Simpler, more flexible navigation	
Positive aspects of i-RFCBT content	Range of helpful techniques A reassuring tone	

4.4.1 Theme 1: Benefits of internet therapy

This theme refers to the perceived benefits of accessing CBT via an internet platform (iCBT), as opposed to attending face-to-face appointments. The theme encompasses both practical and therapeutic benefits.

4.4.1.1 Subtheme 1: Convenience

This subtheme reflects the advantages of being able to access the content at one's own convenience. In particular, participants appreciated being able to access the content at any time of the day:

"It is 24/7, people can log in at anytime they want." (P01)

"I really liked that you could do it any time." (P03)

The inclusion of audio exercises and a screen reader made it easier to fit the intervention around other daily activities, thereby saving time:

> *"It is so sweet that I can 'listen' to the website…when I'm cooking or washing".* (P01)

Students also expressed a desire to be able to access the intervention 'on the move', thereby further integrating the intervention into their daily routines:

> *"I would appreciate if I could download the audio as mp3 documents and review via a mp3 player."* (P01)

> *"I agree with P01 as this would mean that you could listen to it anytime, instead of just when you have access to a computer."* (P08)

4.4.4.2 Subtheme 2: Easier to express feelings

This second subtheme concerns the disinhibiting effect that iCBT may have, encouraging greater self-reflection and disclosure of personal information. Firstly, participants felt a sense of comfort and control from not having to attend appointments:

> *"it's very comforting to be able to do it in a familiar environment."* (P02)

> *"…for people who struggle with anxiety or depression, sometimes you can just 'not be in the mood' to talk, which makes it hard when having to talk about how you feel at a scheduled time. Being able to think about things when you want to (not when you have to) is great."* (P03).

As well as removing the time pressure of appointments, the written nature of the intervention also encouraged self-reflection, allowing users to explore their feelings in greater depth and express themselves more easily:

"…we can talk more and express better comparing with face to face conversation." (P04)

"I agree with P04 that people may express better in online intervention because they can think twice before they post their opinions on the net…Unlike face-to-face invention, you can be mindful about your words and have a deeper and thorough expression on the internet." (P06)

This written format also removed some of the social barriers that may have inhibited users from accessing face-to-face interventions, such as concerns about confidentiality, feeling uncomfortable talking to someone about one's difficulties, or fears of being judged, thereby providing a greater freedom to disclose sensitive information:

"…it is much more confidential and we are not afraid of share the truth online" (P04)

"Sometimes they are not comfortable to have a face to face talk, internet-based intervention makes them more open to face their problems." (P01)

"I myself struggle a bit with social interactions, so I found it really useful to be able to talk about my worries without worrying too much about being judged." (P02)

4.4.2 Theme 2: Attitudes towards support

This theme captures students' opinions regarding the practical and therapeutic benefits of human support. Two distinct forms of support are discussed in separate subthemes: face-to-face sessions and guided iCBT.

4.4.2.1 Subtheme 1: Preference for and benefits of face-to-face support

Participants highlighted some positive features of face-to-face sessions that they felt were lacking in iCBT. During these sessions, therapists are able make use of more than just the client's words to understand their experiences:

> *"Through the internet-based intervention, the therapist cannot observe the patient's facial expression and body language - these are very important clues…sometimes patient may reveal their true feelings via non-verbal language during the face-to-face interactions."* (P06)

As well as the therapist being able to make use of nonverbal cues, the interactive and fluid nature of spoken conversation provides greater opportunity to ask probing questions to help the client frame their thoughts:

> *"I'm a verbal processor, so it helps to have people pick up on what I say and then ask me a follow-up question. You largely lose this online. With internet-based intervention you need to know how you feel, and understand what the questions are asking. It is a lot easier to clarify both of these in a face-to-face setting."* (P03)

Some participants felt face-to-face interaction may help to build a more successful therapeutic alliance and may even be vital to some individuals:

> *"...you also lose the rapport between the patient and the therapist as there is no face to face interaction- people may feel more supported by talking to an actual person."* (P05)

> *"Perhaps I'm behind the times but for me it just couldn't compete with talking to a real-life therapist*." (P07)

4.4.2.2 Subtheme 2: Benefits of guided iCBT

Participants identified some difficulties with self-management that impacted on their engagement with the unguided intervention. These included forgetting to log in, or not finding enough time to complete the intervention alongside competing priorities:

> *"Although it is good that you can work through at your own pace it is very easy to forget to do it or not be able to find time to do it..."* (P05)

> *"It is also very easy for me to leave the treatments behind when I am busy."* (P06)

Participants felt a supporter might help to provide structure, deadlines and monitoring and encouraging regular usage:

> *"I think the guided method could be useful to give the intervention in a more structured timeframe, allowing users to work towards specific goals each week with the help of a coach, deadlines may be useful for keeping people on track and encouraging them to engage with it more!"* (P05)

As well as encouraging use of the intervention, the presence of a supporter may enhance the user experience by transforming one-sided unguided iCBT into a two-way interaction:

> *"it is a bit odd to write to a machine that you already knew that it cannot response."* (P01)

> *"It would be nice to have the option for guided therapy as well, as some people benefit from more of an interaction."* (P03)

This human interaction may serve to validate the user's experience, helping them to feel someone cares about their situation:

> *"…support is also very important in the internet-based intervention...It would be helpful if therapist can provide consolation for patient who is likely to experience worry and stress."* (P06)

4.4.3 Theme 3: Positive aspects of platform design and delivery

This theme covers the positive characteristics of the design and delivery of the internet platform, incorporating aspects of the visual appearance, multimedia and the website's security. While these comments refer specifically the i-RFCBT platform, these are general features that could be applied to other internet interventions for students.

4.4.3.1 Subtheme 1: Design

This subtheme refers to the overall impression of the visual appearance of the site. Comments suggest students prefer a minimalist graphic design as this enhanced credibility and allowed users to focus on the content rather than being distracted by the design:

> *"I like it, clean and clear."* (P01)

> *"It was pretty spartan, but I think that was actually a benefit as it made it seem more professional/clinical."* (P02)

> *"The pictures break the page up, make the text more accessible and are quite neutral colours but I think that a few more might be too many as this takes attention away from the tasks themselves."* (P08).

P09 offered a more nuanced response. Whilst she also liked the simplicity of the design, she felt more variety was needed to maintain interest:

> *"Layout was simple, clean and effective, but very quickly became boring and tiring. Some changes in positioning of texts, images and questions once in a while would have helped make the page more visually engaging."* (P09)

4.4.3.2 Subtheme 2: Video case studies

This subtheme refers to presenting case studies in a video format. The positive comments identified two specific ways in which these videos might increase engagement with the intervention. Firstly, the video format, as opposed to written case studies, reduced reading fatigue, while reinforcing the text content:

> *"The videos were a pleasant surprise, as they provided me a break from having to read everything!"* (P09)

> *"I thought that in the beginning exercises, the videos were good at maintaining interest as they broke up long pages of text and showed how the topic was relevant."* (P08)

However, P07 acted as a disconfirming case. The video format was a barrier to her being able to engage with the case studies as she found them a chore to watch:

> *"I just find them time-consuming (i.e. you have to listen to the whole thing to find out whether it's relevant)…I find them a waste of my time. If participants are feeling stressed I don't think feeling like they have to sit and watch these will help."* (P07)

Secondly, the views on the specific content of the videos appeared to fall along a continuum from positive, through ambivalent, to negative, depending on how personally relevant the characters were. For those who viewed the characters positively, these helped to contextualise the intervention and to normalise their personal difficulties, thereby providing a sense of felt identification with the intervention:

> *"I liked the use of videos as helpful pointers/real life examples."* (P04)

> *"Actually I like the videos, the stories from others make me feel that I'm not the only one who has those difficulties. It gave me the feeling of being recognised."* (P01)

One participant was ambivalent. She liked the use of videos but found the examples weren't necessarily personally relevant:

> *"The videos were good, though not always applicable to me directly."* (P02)

Finally, one participant found the videos difficult to engage with as the case study was very different to her own experiences:

> *"The videos with Emma were quite specific; she talked a lot about her experiences going out or talking to boys, which didn't really translate to me."* (P03)

Participants who did not identify with the videos suggested changes to the content and format to ensure wider appeal:

> *"Perhaps people sharing experiences that are more generalisable would be beneficial."* (P03)

"I personally don't like videos although I suspect i'm in a minority…Perhaps include a transcript of the video content for anyone like me who'd like to skim to see if it's relevant rather than sit through the video?" (P07)

4.4.3.3 Subtheme 3: Security

Given the sensitive nature of responses entered into an online intervention, security was important to users:

"Because of the particularity of this website, remaining confidential is very important at least for me." (P01).

A sense of anonymity from using unguided interventions may increase perceived security:

"I felt very safe with the anonymity and security of the site." (P03).

"I think I'd feel more secure using the unguided therapy, but either way it wouldn't concern me too much about my information not being safe." (P02)

The sense of security was also enhanced through the website requiring users to set a complicated password:

"I personally like the symbols in the password, as most of websites do not use symbols, this unique function makes me feel safer." (P01)

Despite the group highlighting the importance of security and confidentiality, interestingly, one participant acted as a disconfirming case, suggesting this increased security should not be at the expense of accessibility. When passwords are too complicated, users can be locked out of their own account:

"Instead of increasing security, I think it should lower the difficulty of accessing to the website. Since the password must include the symbols like <>?!"£$%^&, I am often trapped and failed to access to the website." (P06)

4.4.4 Theme 4: Improvements to design and delivery to increase usability and personalisation

As well as positive features of the platform design and delivery, participants identified some areas to improve the usability of the platform. This theme comprises two subthemes relating to the length and clarity of individual Web pages and to the navigation, both within the platform (between sessions) and increasing flexibility in the order of the modules.

4.4.4.1 Subtheme 1: Shorter, clearer sections

While each module was broken into 3 to 5 separate Web pages, participants suggested the content should be broken down into more pages as the amount of reading required on a single page could discourage engagement with the content:

"…some of the pages are extremely long, when I notice it, it makes me want to skim reading. If break it into 2 or 3 pages, I psychologically will feel that it is much easier to read." (P01)

"Ya I think keeping each page short and make it easy to use are necessary to let me motivate." (P04)

In addition to the text heavy content, some users felt the exercises were also too lengthy and could have a negative impact on motivation or concentration:

"It was a bit tedious to fill in about 20 boxes on one page…" (P07)

"8 minutes of a relaxation exercise is just not always feasible, and it left me struggling to concentrate sometimes." (P02).

Taken together, these comments suggest students would find it easier to engage with an intervention that can be accessed in smaller, more manageable chunks. One way to increase the perceived manageability may be to clarify the language used, as some questions were perceived as too repetitive or difficult to discriminate from one another, which could cause frustration:

"Sometimes I felt that some questions were asking analogous things, and I can use same answers for them." (P01)

"On the whole the language was appropriate and understandable, but the difference between most of the multiple question's answers were so subtle it irked me." (P09).

Such clarifications may help to personalise the intervention as some options may be perceived as too generic:

"And sometimes I felt that the options did not cover my actual feelings, like how I would have said that depending on context rumination can either motivate or demotivate me, and it is not consistently one or the other." (P02)

4.4.4.2 Subtheme 2: Simpler, more flexible navigation

This subtheme captures suggestions for improvements to the navigation to improve both the usability and personalisation of the platform. With specific reference to usability, the navigation between modules was viewed as overly complicated as users had to review previous pages before being able to move on. This was seen as unnecessary and confusing:

“I was initially perplexed by why I couldn't go onto the next section, before I realised that I had to go back to the treatment to read my results - it would be a lot easier to just have a next button after you finish the questionnaires!” (P02).

“Agreeing with P02 - why do you have to do all the questionnaires, and THEN click back through everything you've done to see your results? Maybe to be reminded of your answers? Seems unnecessary though.” (P07)

In addition to a more streamlined progression through the site, several participants suggested a clearer menu page would help them to keep track of which session they had reached and motivate them to engage with new content:

“I have to go back to the front page then pick up the next one by myself, but sometimes it is very hard to remember the title that I was reading. Maybe a 'Next' button or number the treatments on the front page is helpful?” (P01)

“having more detailed information on the title…If i can know exactly what it is on the front page, it would motivate me” (P04)

As well as a simpler navigation within modules, greater flexibility in the order of modules was suggested to personalise the intervention:

“I think that it is a bit clumsy when I am told to do the treatments step by step. For example, if I want to know more about "compassionate self-talk", I must complete all other treatments beforehand so that I can see

that page. But sometimes I do not have so much time to finish all these treatments." (P06).

"…think that the tasks should all be available to do in any order, without having to unlock them, but with the structure that they are currently in as the recommended order. I think this would help personalise the therapy and may improve motivation as people can skip tasks they don't feel are as useful or relevant without having to answer questions about completing them." (P08).

4.4.5 Theme 5: Positive aspects of i-RFCBT content

This theme encompasses views on the specific content of i-RFCBT covering both the techniques included to target rumination as well as the overall tone of the intervention.

4.4.5.1 Subtheme 1: Range of helpful techniques

This subtheme concerns the therapeutic content of the intervention. Participants' comments suggest conceptualising rumination as a habitual behaviour was helpful in terms of providing greater insight into their difficulties and how to replace rumination with more functional behaviours. Becoming more aware of the rumination is a necessary first step towards change. Self-monitoring helped users to understand the negative consequences of rumination and its automatic, habitual nature:

"…I used to blame myself in a very mean way but I usually couldn't notice it, and it made things worse. Now I know it is a bad habit…" (P01)

Participants liked using functional analysis to distinguish between different situations where responses have been either unhelpful or helpful and begin to shift them towards more helpful approaches:

> *"Also, evaluating whether the rumination was helpful or not was great, as you could make it situation specific and work out what is a helpful response in different situations."* (P03).

Without such awareness, users would be unable to make contingency plans to practise in response to a specific cue. As acknowledged by P01, these longstanding habits are difficult to change, but repeatedly practising an alternative, more helpful behaviour such as compassionate self-talk can be helpful:

> *"…although sometimes talk to myself in a kind way is still very hard, especially when I am really pissed off by the really stupid things I made, but at least I can stop it when I notice it."* (P01)

These alternative behaviours, in the form of If-Then plans were helpful in reducing the unconscious, automatic rumination:

> *"I thought the IF-THEN techniques were useful, as practising them can make those responses autonomous rather than the rumination."* (P03)

Other helpful alternative responses identified by participants included experiential exercises such as relaxation and absorption:

> *"I really reluctantly listened to the relaxation exercise...but was very pleasantly surprised! I must admit I wasn't even taking it seriously, but the voice was still incredibly relaxing! I think this is a good idea if participants really do it properly."* (P07)

"I found the relaxation and absorption exercises helpful, especially as you could do them anywhere really." (P02)

Participants also highlighted the idiosyncratic nature of these techniques, valuing the variety provided:

"I think all of the different techniques given would be useful to different people." (P02)

"the website provides many useful tips of dealing with stress." (P06)

4.4.5.2 Subtheme 2: A reassuring tone

This subtheme refers to how participants interpreted the overall tone of the content. The tone of both the written language and audio exercises seemed to provide a sense of connection with the intervention, allowing users to feel supported and reassured:

"I did find the tone supportive, gentle and reassuring…" (P02)

"The tone is gentle and the accent is clear and accurate. This makes me feel comfortable to listen." (P06)

Responses from two participants highlighted the challenge of ensuring the tone is appropriate for a wide range of users, as some individuals may find it patronising. However, while these individuals reported feeling patronised to begin with, they both continued to engage with the content, suggesting that users may be able to adapt to or overlook the tone, as long as the content is engaging:

"I found it a bit patronising to begin with but it became less so as you went on and seemed generally friendly and reassuring." (P08)

"I totally agree with P08, at the beginning I was a bit peeved at the tone but maybe it's the fact I got used to it, or I just decided to concentrate on what was being said rather than the how, which made the whole experience more tolerable." (P09)

4.5 Discussion

The aim of the study was to investigate students' perceived benefits and barriers to using iCBT as well as to seek opinions on a specific internet intervention (i-RFCBT) as a preventive intervention, prior to testing the efficacy of i-RFCBT in a randomised controlled trial (Cook, Mostazir, & Watkins, 2019; Cook & Watkins, 2016). Trials often fail to report the acceptability of an intervention and levels of engagement by participants so it is unclear if dropouts or poor outcomes are due problems with the specific intervention, or with the internet approach more broadly (Newman, Szkodny, Llera, & Przeworski, 2011). Findings from the focus group suggested that, overall, the presentation, design and content of i-RFCBT was acceptable to high-ruminating students. However, there were both benefits and barriers identified to accessing this intervention via the internet, with individual differences on the need for support and preference for face-to-face therapy.

With regard to the design participants described the aesthetics in positive terms as 'clean and clear'; 'spartan'; 'neat' and 'simple'; the use of images served to break up the text and make the content more user-friendly and the overall impression of the design provided a professional and clinical feel to the site, suggesting i-RFCBT displays the three key elements (aesthetics, user-friendliness, overall tone) of a well-designed platform (Kerr et al., 2006).

The suggested improvements to the design and delivery are consistent with previous studies (Fleischmann et al., 2017; Mitchell & Gordon, 2007;

Richards & Timulak, 2012). The first suggestion concerned breaking the content up into shorter, clearer sections. Previous studies have found that students have reported the amount of work required in each session could be off-putting (Fleischmann et al., 2017; Mitchell & Gordon, 2007; Richards & Timulak, 2012). Johansson et al. (2015) suggest non-adherence to interventions occurs when there is a mismatch between the features of the intervention and personal characteristics. For example, where there is a large amount of text this can be perceived as burdensome to fit into one's daily routine and lead to non-adherence. Even if participants persevere with the intervention, finding the amount of reading or exercises burdensome could lead to participants skim-reading or skipping sections that could otherwise be beneficial.

As well as time pressures, symptom severity may also impact on students' ability to engage with large sections of text (Doherty, Coyle & Sharry, 2012). While some students find it helpful to access such interventions when feeling distressed, others report that the content is more helpful when feeling less anxious or depressed as they are able to process more information (Palacios, 2018). Although the current sample is subclinical for depression, rumination and worry can still have a negative impact on concentration (Watkins, 2016), so shorter sections may help high ruminating students to absorb the information in more manageable chunks.

The video case studies helped to engender a sense of not being alone in one's difficulties, described by Knowles et al. (2014) as 'felt identification'. However, some further tailoring may help to further personalise the examples used. Case studies perceived as irrelevant could prevent the user from developing a sense of 'felt identification' with the intervention and may lead to disengagement. These differing views were also found in a content analysis of

patients' perspective of therapist-assisted iCBT (Hadjistavropoulos et al., 2018). While the majority liked the case studies as these helped them to apply the techniques, those who did not like case studies found them difficult to relate to, boring, or an unrealistic representation of their experience of depression and anxiety.

Providing information about data security, access and confidentiality is an important consideration in implementing online therapies. Kerr et al. (2006) found participants suspicious of sites that required providing personal details or a log-in as they were unsure about who had access to this personal information. In Higher Education as Walsh and Richards (2016) found some participants were reluctant to share their responses with their online coach due to concerns about who else may be able to access their data. Reassuringly, participants expressed trust in the i-RFCBT platform and in the research staff to keep their data secure and confidential, in particular highlighting the benefits of a complicated log-in password for keeping their data secure.

Another recommended improvement to increase engagement was a simpler, more flexible navigation, both at the session level (moving from one session to the next) and the module level (ability to choose modules rather than a fixed, linear order). While students are largely highly computer literate, there is still a need to ensure the navigation through the intervention is intuitive in order to avoid unnecessary frustration as this may lead to early dropout (Richards & Timulak, 2012).

Users would prefer to access the modules in any order rather than following a predetermined linear structure. When RFCBT is delivered face-to-face, the therapist conducts a detailed assessment of the patient's rumination and uses this to select which techniques are most likely to be relevant (Watkins,

2016). However, in i-RFCBT users are encouraged to try all the techniques before deciding for themselves which are most helpful. The lack of flexibility could be off-putting as users had to complete irrelevant sections in order to access later modules that they thought would be more personally relevant. Lillevoll et al. (2013) found users were able to overlook some irrelevant content as long as there was other content they felt they were learning from. However, where users found little of relevance, this led to frustration and disengagement (Lillevoll et al., 2013), highlighting the need for more individualised interventions (Fleischmann et al., 2017).

Such individualisation can now be achieved using algorithms. For example, in a large-scale trial of an intervention for students experiencing insomnia (Freeman et al., 2017), participants completed an initial assessment and algorithms then tailored the overall goals of the intervention to their specific needs. While the aim of the current research is to assess the acceptability and effectiveness of i-RFCBT as a complete package, future developments could assess more individualised content, such as incorporating an assessment module and building algorithms into the platform to provide recommendations on which modules to focus on.

With specific reference to the content of i-RFCBT, participants identified a range of helpful techniques and liked the variety as different techniques are likely to benefit different users. This suggests that the key techniques of RFCBT can be successfully delivered as an unguided internet-based intervention for high risk students. As well as individual preferences for specific techniques, there was some suggestion of techniques being helpful in certain situations and less helpful in others. This variability has also been discussed in previous studies of iCBT for students, where emotion-focused techniques may be more

helpful during periods of acute stress such as exams, whereas problem-solving techniques may be more relevant during the regular attendance phase Fleischmann et al. (2017).

In terms of tone, previous studies have acknowledged the need for interventions to be more sensitive to 'Who I am' and 'How I feel' (Knowles et al., 2014). In the current study, participants generally found the tone to be supportive and reassuring, although some found it patronising. Striking the wrong tone, such as appearing patronising (Kerr, 2006), or not acknowledging individual capabilities to implement techniques (Hind et al., 2010) can put users off. Fleischmann et al. (2017) found students wanted a more scientific approach. Including more detail about previous research and the rationale for i-RFCBT may ensure students find the content more age and intellect appropriate.

Overall, students found the design and presentation of i-RFCBT acceptable, making recommendations for further tailoring and individualisation in future iterations. This suggests the potential for i-RFCBT to be successfully implemented as a preventive intervention in students.

Although opinions of i-RFCBT were generally positive, participants identified different potential benefits and barriers of providing interventions via the Internet. Convenience was identified as an important benefit, as the intervention could be accessed at a time and place of one's choosing and fit into daily routines more easily (Richards et al., 2016). Students have irregular working hours, including periods of acute pressure such as exams (Fleischmann et al., 2017) so may find it difficult to commit to a regular appointment time. Previous studies have found students like being able to

access therapies outside normal working hours, particularly during the night (Chan et al., 2016).

Although students felt such an intervention would be convenient, some concerns were raised about not having fixed appointment times, as finding the time to complete the modules would then require considerable self-management. This difficulty with making time to use iCBT has also been reported in work environments (Carolan & de Visser, 2018). Employees were actively encouraged by management to access the intervention during work hours. Despite this endorsement, and ample opportunities to log in, without set appointment times some users still found it difficult to incorporate into the workday schedule (Carolan & de Visser, 2018).

One way of encouraging users to engage with the intervention would be to provide an online coach. The least resource-heavy approach is a coach who simply monitors usage and encourages the user to log on and complete tasks, termed ‘supportive accountability’ with the aim of increasing goal setting, accountability and motivation (Mohr, Cuijpers, & Lehman, 2011). Similar benefits of such minimal support have been found for written book materials delivering CBT for a range of mental health conditions. Farrand and Woodford (2013) found that overall effect sizes did not differ significantly by support type: guided, minimal contact or self-administered). For the interventions targeting depression, minimal contact produced greater effect sizes than either guided or self-administered, indicating that simply increasing the amount of support does not necessarily lead to better outcomes.

One advantage to using supportive accountability is that, as such support does not involve therapeutic input, it could potentially be provided by a paraprofessional, rather than a qualified clinician (Conley et al., 2016), peer

support via an online community (Coulson et al., 2016), or even inbuilt by using auto-messages triggered by specific client behaviours (Titov et al., 2013). It may be that providing a clear rationale for the self-help materials and brief check-ins to monitor progress is sufficient and considerably less resource-heavy than fully guided interventions. Indeed, in a trial of an internet intervention for stress in students (Harrer et al., 2018), participants were provided with minimal contact, but could request more in-depth feedback for each module, that addressed specific problems and provided encouragement. Very few students (5%) actively requested this detailed feedback (Harrer et al., 2018), suggesting that adherence-focused guidance (monitoring usage and sending reminders to non-engagers) may be sufficient for the majority of students.

The responses from the focus group suggested that, for some students, supportive accountability would be sufficient, whereas other individuals would prefer more in-depth therapeutic support. In studies where such therapeutic support is provided to all users, students generally appreciated having a supporter (Palacios et al., 2018), but expressed some reservations about the format of the support (written feedback on completed exercises, received at the end of each module). Students have described these feedbacks as too generic and not sufficiently focused on their personal difficulties (Fleischmann et al., 2017; Palacios et al., 2018). Some students felt unable to form a meaningful connection with their supporter in writing, suggesting this is easier to achieve with face-to-face, or at least telephone, contact (Palacios et al., 2018).

However, Cavanagh et al. (2018) argue that the patient-professional alliance may be less important in iCBT than in face-to-face therapy, as if the intervention is sufficiently engaging and interactive, there is potential to form a patient-programme alliance that could improve adherence and outcomes

(Berger, 2016). They found patient-professional alliance, patient-programme alliance and overall treatment satisfaction were all associated with symptom improvements (depression, anxiety, quality of life) at 6-month follow-up, with no interactions between predictors, suggesting the two different forms of alliance contribute independently and additively to clinical outcomes. This suggests that clinical benefit can be achieved through unguided interventions, provided the user forms a patient programme-alliance.

One factor that may be important in developing a patient-programme alliance is how comfortable the user feels expressing themselves online. The focus group reported differences in the ease with which they could express themselves in writing compared to face-to-face interaction, consistent with reports in previous studies (Gerhards et al., 2011; Knowles et al., 2014). For some of the focus group, the ability to express their feelings in writing provided a strong disinhibiting effect, consistent with previous findings that being alone allowed individuals to reveal their true self (Gerhards et al., 2011), to be more honest and to engage in deeper self-reflection (Donkin & Glozier, 2012) and removed the perceived social pressures and fear of judgment associated with face-to-face conversation (Cook & Doyle, 2002).

In contrast, other focus group members reported that the one-sided nature of unguided internet therapy may have an inhibiting effect as the intervention does not respond to them as a therapist would. Previous research suggests some common factors such as empathy, warmth and genuineness are relatively easy to convey in the written materials, whereas more complex therapeutic skills such as flexibility and responsiveness to the client, which are important to keep clients engaged, may be more difficult to achieve through written materials (Richardson, Richards, & Barkham, 2010a). This lack of

interaction may explain why some individuals find it difficult to express themselves in iCBT and may not get sufficient benefit from the online materials to persevere with the intervention. Indeed, some participants expressed a strong preference for face-to-face contact, saying that, for them personally, iCBT could never replace talking to a therapist. Reasons for seeking face-to-face support were consistent with the previously identified functions of support: personal contact; providing feedback, clarification or prompting to go into further detail; tailoring content to the individual (Gerhards et al. 2011).

Walsh and Richards (2016) suggest personality and approach to work play an important role in successful engagement with internet interventions. Students who are particularly conscientious, goal driven and self-motivated may be particularly well suited to internet therapy (Walsh & Richards, 2016). Recent studies have suggested support may be an individual preference rather than a necessity (Hadjistavropoulos et al., 2017; Harrer et al., 2018).

Dear, Gandy et al. (2015a, p.1921) hypothesised the support may not be necessary when iCBT programmes are 'sufficiently credible, engaging, of a high quality and involve some level of screening for suitability'. The findings from the focus group suggest that, despite some students strongly favouring support, i-RFCBT was seen to be credible, engaging and of a high enough quality to allow some students to complete the exercises without additional support. In addition, the screening ensured only high ruminating students were selected for the intervention and the intervention's explicit focus on worry and rumination may have helped to make it more personally relevant for this high-risk subgroup than more general iCBT interventions.

The range of views demonstrate that students identify both advantages and disadvantages to both guided and unguided versions of online therapies. In

terms of implementation it may therefore be beneficial to offer both the unguided and guided version of the intervention in order to balance the benefits of convenience and ease of expression with the benefits of support. Students would then have a choice over whether to complete the modules unguided, or whether guided i-RFCBT (e.g. an option to access the intervention via the university's Wellbeing services) would help them to get the full benefit of the intervention.

4.5.1 Strengths and limitations

This study adds to the currently limited literature on the acceptability of preventive internet interventions for undergraduates. Previous qualitative studies of students' opinions of internet interventions have mostly focused on treatment samples, or have not assessed clinical caseness during recruitment, making it unclear whether the participants were viewing iCBT as a treatment or preventive intervention (Fleischmann et al., 2017; Mitchell & Gordon, 2007). The inclusion of the diagnostic interview in the current study ensured the sample matched the same inclusion criteria as those for the RESPOND trial (i.e. a targeted prevention).

The sample is limited in terms of gender and ethnicity, with only one male and two different ethnicities. Male gender is a significant predictor of dropout from self-guided interventions, possibly because females are generally more conscientious about health problems so may be better able to self-motivate in the absence of a supporter. (Karyotaki et al., 2015). Qualitatively assessing more males' opinions of i-RFCBT would therefore allow for better tailoring to males' help-seeking needs. International students are a subgroup that are particularly at risk of mental health difficulties due to cultural and

financial barriers (Bradley, 2000). While the current sample included four East Asian students, further research could investigate whether i-RFCBT is culturally appropriate for a wider range of students.

No coach was providing written support to focus group participants so, while the majority of the group expressed a preference for some form of support, these comments should be considered hypothetical. Specifically, previous studies have reported criticisms of the written support as being too generic or scripted (Earley et al., 2017; Fleischmann et al., 2017) so responses from users who have received guided i-RFCBT may be less positive about the added benefits of support. It would therefore be informative to conduct a similar qualitative study of guided i-RFCBT, with the addition of questions relating to the feedback and the therapeutic alliance.

Despite the anonymity of the online focus group potentially encouraging more disclosure of sensitive information than face-to-face focus groups (Williams et al., 2012), it is notable that only 9 of the 13 participants contributed to the forum, with the number of comments ranging from 5-25 per participant, which may have limited the richness of the data. The timing of the online focus group may have hindered a more active and in-depth discussion as it was conducted across the Christmas break and early January exams. Additionally, a more active moderation, for example posting prompts and follow-up questions on the forum (Williams et al., 2012) may have improved the number of responses. Reminder emails were sent to encourage participants to comment, but messages from the moderator posted directly on the forum may have encouraged participants to post more regularly or to elaborate further, thereby increasing the richness of the data.

Investigations of acceptability are vital in the development of new interventions, as any negative attitudes will impact on uptake (Knowles et al., 2014). Despite the limitations identified, the current study provides some initial evidence that internet interventions in general and i-RFCBT in particular may be acceptable forms of preventive intervention for at-risk students. A greater focus on prevention and the development of more widely accessible interventions have been identified as strategic priorities for universities (Universities UK, 2017). Given the growing prevalence of mental health difficulties and increased demand for services (Universities UK, 2018), the implementation of i-RFCBT within Higher Education Institutions may provide a viable alternative for individuals who are reluctant to access current services. This has particular promise in terms of enhancing the general wellbeing of university students as this is a subgroup shown to be reluctant to seek help for common mental health disorders (Davies, Morriss, & Glazebrook, 2014).

CHAPTER 5: Trial protocol for i-RFCBT to prevent depression in students

5.1 Preface

The qualitative study (Chapter 4) indicated that i-RFCBT may be an acceptable preventive intervention for high-ruminating undergraduates. Having established that i-RFCBT was sufficiently engaging, the next step was to design a randomised-controlled trial to test whether i-RFCBT can prevent depression in high-risk students. The protocol for this RCT is reported in:

Cook, L., & Watkins, E. (2016). Guided, internet-based, rumination-focused cognitive behavioural therapy (i-RFCBT) versus a no-intervention control to prevent depression in high-ruminating young adults, along with an adjunct assessment of the feasibility of unguided i-RFCBT, in the REducing Stress and Preventing Depression trial (RESPOND): study protocol for a phase III randomised controlled trial. *Trials, 17*, 1. doi:10.1186/s13063-015-1128-9

This paper forms the majority of this chapter.

The original aim of the thesis was focused on high ruminating young adults (aged 18-24). However, despite employing several recruitment strategies (contacting university departments, social media, charities), the only successful approach was through universities. Only seven (3%) of the participants in the RESPOND trial were not registered at a UK university. As a result, the focus of the thesis shifted from young adults in general to students as a distinct at-risk population. The protocol paper included in this chapter was published during the recruitment phase. For this reason, Chapter 5 refers to recruiting young adults, and student status was not an inclusion criterion.

The RESPOND trial sought to contribute to the literature by replicating and extending the Topper et al. (2017), using a fully powered phase III RCT, including diagnostic outcome measures, to test whether guided i-RFCBT would prevent depression in UK university students. In addition, as unguided interventions have greater scope for widespread implementation, RESPOND also included an adjunct quasi phase II pilot arm was included within the overall RCT design as an initial test of the feasibility of unguided i-RFCBT.

Due to the shift from focusing on young adults, to focusing specifically on university students, following publication of the protocol paper a further hypothesis was developed regarding the role of stressful life events. As outlined in Chapter 1 (Section 1.8), it is the combination of both rumination and stressors that appear to have particularly detrimental effects in student populations. As high rumination was an inclusion criterion for the RESPOND trial, we hypothesised that i-RFCBT would be most beneficial for students who were also experiencing high stress levels.

RESPOND (REducing Stress and Preventing Depression): comparing guided internet-based rumination focused cognitive behavioural therapy (i-RFCBT) versus a no-intervention control to prevent depression in high ruminating young adults, with adjunct assessment of the feasibility of unguided i-RFBCT: Study protocol for a phase III randomised-controlled trial

Lorna Cook*, Edward Watkins

* Corresponding author: lzc204@exeter.ac.uk; E.R.Watkins@exeter.ac.uk

Mood Disorders Centre, School of Psychology, University of Exeter, EX4 4QG, UK

Trial status

Recruitment began in November 2013 and was ongoing at time of submission.

Abbreviations

CONSORT: Consolidated standards of reporting trials; EPQ-R: Eysenck Personality Questionnaire-Revised Neuroticism sub-scale; GAD-7: Generalized anxiety disorder 7-item scale; GP: General practitioner; ITT: Intention-To-Treat; MI: multiple imputation; MRC: Medical research council; PHQ-8/PHQ-9: Patient health questionnaire-8 item or 9 item; PSQ: Psychosis Screening Questionnaire; PSWQ: Penn State Worry Questionnaire; RCT: Randomised controlled trial; RFCBT: rumination-focused cognitive-behavioural therapy; RNT: repetitive negative thought; RRS: Ruminative Response Scale of the Response Styles Questionnaire; RT: repetitive thought; SCID-I: Structured Clinical Interview for DSM-IV; TAU: Treatment-as-usual

Competing interests

The authors declare they have no competing interests.

Authors' contributions

LC: conception, design, manuscript writing and final approval of the manuscript. EW: conception, design, manuscript writing and final approval of the manuscript.

Acknowledgements

This work is supported by University of Exeter, UK, through a matched funded PhD studentship to a successful Wellcome Trust Capital Bid. We are grateful to Jenny Cadman and Dr Yusuke Umegaki (therapists for guided therapy and assisting with randomisation), Rosario Melero (assisting with recruitment and therapist for guided therapy) and Mohammod Mostazir (assistance with power calculation).

5.2 Abstract

Background: Depression is a global health challenge. Prevention is highlighted as a priority to reduce its prevalence. Although there are effective preventive interventions, efficacy and coverage can be improved. One proposed means to increase efficacy is by targeting interventions at specific risk factors, such as rumination. Rumination-focused CBT (RFCBT) was developed to specifically target depressive rumination, and reduces acute depressive symptoms and relapse for patients with residual depression in a randomised-controlled trial. Preliminary findings from a Dutch randomised prevention trial in 251 high-risk 15-22-year-olds selected with elevated worry and rumination found that both supported internet-RFBCT and group-delivered RFCBT equally reduced depressive symptoms and onset of depressive cases over 1 year, relative to no-intervention control.

Methods/design: A Phase III randomised controlled trial following the MRC Complex Interventions Framework, to extend the Dutch trial in the UK, with the addition of diagnostic interviews, primarily testing whether guided internet-RFCBT reduces onset of depression relative to no-intervention control. High risk young adults (aged 18-24), selected with elevated worry/rumination, recruited through universities and internet advertisement, will be randomised to receive either guided internet-RFCBT, supported by clinical psychologists or mental health paraprofessionals, or no-intervention control. As an adjunct arm, participants are also randomised to unguided internet-RFCBT self-help, in order to provide an initial test of the feasibility and effect size of this intervention. While participants are also randomised to unguided internet-RFCBT, the trial was designed and powered as a Phase III trial comparing guided internet-RFCBT versus no-intervention control. In the comparison between these two

arms, the primary outcomes are: a) onset of major depressive episode over a 12-month period, assessed with Structured Clinical Interview for Diagnosis 3 months (post-intervention), 6 months and 15 months after randomisation. Secondary outcomes will be collected on: incidence of generalized anxiety disorder, symptoms of depression and anxiety; levels of worry and rumination, measured at baseline and the same follow-up intervals. In relation to the pilot investigation of unguided internet-RFCBT (adjunct intervention arm), we will assess the feasibility and acceptability of data collection procedures, levels of attrition, effect size and acceptability of the unguided internet-RFCBT intervention.

Discussion: Widespread implementation is necessary for effective prevention, suggesting that the internet may be a valuable mode of delivery. Previous research suggests guided internet-RFCBT reduces incidence rates relative to controls. We are also interested in developing and evaluating an unguided version to potentially increase availability and reduce costs.

Trial Registration: Current Controlled Trials ISRCTN12683436. Date of registration: 27/10/2014

Key Words: Randomised Controlled Trial; Cognitive Behavioural Therapy (CBT); Rumination; Depression; Prevention; Internet-Delivery

5.3 Background

Depression is one of the leading causes of disease burden worldwide, with substantial individual, societal and economic impact [1]. Current treatments have only a limited impact on this disease burden because of: lack of treatment availability, high proportion of patients failing to respond (40%+ partial or non-response) and high levels of relapse or recurrence (50-80%) [2]. Additionally, treatments provided in the acute phase of disorder do not reduce incidence rates. Effective preventive interventions are therefore needed to reduce the disease burden of depression.

Preventive interventions for depression have mainly focused on children and adolescents, and have predominantly used CBT strategies. Meta-analyses [3-5] have found that universal interventions (aimed at entire populations, regardless of risk factors) had only small-to-insignificant effect sizes post-intervention and longer-term effects were mixed. Greater effect sizes were found for targeted interventions (selective: aimed at a subgroup presenting with known risk factors; indicated: aimed at individuals with subclinical symptoms) and these effects were sustained for longer than universal interventions [5]. Critiques of prevention research trials include: a focus on treatment effects (change in symptoms relative to controls [3]) rather than on a reduction in incidence rates [6]; insufficient statistical power due to low base-rates (particularly in universal samples) and short follow-up periods such that longer-term effects remain unclear [5].

While there are some early positive findings from prevention research, there is scope for improvement in terms of efficacy, cost-effectiveness, and acceptability [7]. Firstly, interventions should be targeted at higher risk individuals rather than universal populations [7]. Such individuals have the most

to gain from an intervention, and the base rate of new cases will be higher in high risk groups, meaning that smaller sample sizes are needed to obtain adequate statistical power to detect an effect [6]. Such individuals could be identified on the basis of personal and familial history, cognitive, or biological vulnerabilities to depression and/or subsyndromal symptoms. Risk factors can be used not only to identify individuals but also as a direct target for intervention [7]. Additionally, although current interventions are largely aimed at specific disorders, there is increasing evidence for transdiagnostic processes, which are risk factors for multiple disorders [8, 9]. Targeting such processes has the potential to impact on several disorders with a single intervention [10].

Repetitive negative thought (RNT), incorporating worry and rumination, has been proposed as a potential target for selective prevention programmes [7]. There is strong evidence that RNT contributes to the onset and maintenance of a range of disorders, including depression, anxiety and physical health issues [11]. Prospective longitudinal studies have found that rumination predicted a) future depressive symptoms, even after controlling for baseline depressive and anxious symptoms, across a range of follow-up periods [12-15]; b) onset and duration of episodes of major depression [16-19] and c) mediated the effects of other risk factors on the onset of depression [20]. Rumination and worry have also been found to predict future levels of other disorders, including anxiety, eating disorders and substance abuse [18]. Furthermore, experimental studies provide evidence that rumination causally influences negative mood and a range of cognitive processes [11], including increased negative thinking [21], impaired concentration [22] and impaired problem-solving [23]. This relationship between RNT and emotional disorders is also found in children and adolescents [12, 18, 24-26]. Moreover, Hankin [27] demonstrated that rumination is a

specific risk factor for depression in adolescence, with rumination prospectively predicting fluctuations in depressive symptoms and internalising problems, but not anxious arousal or externalising problems. There is gender bias in depression rates (approximately 2:1 female: male [28]). Differences in rumination levels can partially explain this gender bias, with 27% of the association between gender and depression explained by rumination [27]. Critically, recent experimental and clinical studies have shown that with brief interventions, levels of rumination and worry can be reduced (e.g. [29-33]). This suggests that rumination/worry could be a particularly promising target in improving the efficacy of preventive interventions.

Widespread dissemination and coverage of interventions is important for effective prevention. Traditional face-to-face therapy is not well-suited for such widespread implementation. Alternative modes of delivery, such as Internet-based treatments, have potential advantages including: reaching large numbers at relatively low cost; greater ease of access and convenience for the user; available at any time and place; greater autonomy for the client, anonymity, and greater time to reflect [6, 34, 35]. There is emergent evidence that internet-based CBT is an effective, feasible, and acceptable treatment for acute depression and anxiety [36, 37]. Acceptability ratings for Internet-based therapies are generally high [35]. However, difficulties with motivation and adherence are a potentially important issue for Internet-based therapies for depression. Although purely self-guided internet interventions for depression are available, they are generally less effective and have greater drop-out than guided interventions for depression with therapist input [36, 38, 39]. Andersson [34] therefore argued for some form of guidance in order to achieve similar effectiveness to face-to-face therapies.

The feasibility, acceptability, and efficacy of internet-based rumination-focused CBT (i-RFCBT) to prevent depression in adolescents and young adults has recently been investigated in the Netherlands ([40]; ZonMw funded project). The intervention is based on rumination-focused cognitive behavioural therapy (RFCBT) developed by Watkins et al.[30, 32]. Watkins et al. [32] conducted a randomised-controlled trial comparing treatment-as-usual (TAU, antidepressant medication) versus TAU plus RFCBT in patients with medication-refractory residual depression. The addition of RFCBT reduced depressive symptoms more than medication alone, with improvements in remission rates (62% vs. 21%) and reduction in 5-month relapse rates (9.5% vs. 53%) Moreover, changes in rumination scores were found to be a significant mediator of these treatment effects. These positive treatment and relapse prevention results led Topper et al. [40] to adapt this intervention for prevention.

In a prevention trial of RFCBT, 251 students aged 15-22 with elevated worry and/or rumination (scoring on top quartiles of respective measures: ≥ 50 on Penn State Worry Questionnaire (PSWQ; [41]; ≥ 40 on Ruminative Response Scale of the Response Styles Questionnaire (RRS; [15])) but who did not currently meet diagnostic criteria for depression or generalized anxiety disorder were recruited, and randomised into face-to-face group RFCBT, internet-delivered RFCBT (i-RFCBT), or a no-intervention control group. Participants were assessed for symptoms and ‘caseness’ of depression and anxiety on standardised self-report measures (Patient Health Questionnaire, PHQ-9; [42]; Generalized Anxiety Disorder Screener, GAD-7; [43]) at baseline, post-intervention, 3 month and 12 month follow-ups. This study indicated the feasibility of recruiting and retaining participants for such a prevention study and indicated the acceptability of these interventions. Further, group RFCBT and

internet RFCBT reduced worry, rumination, depression, and anxiety symptoms significantly more than waiting list control. At 12 month follow-up, cumulative incidence rates for depression (estimated from “caseness” on PHQ-9) are reduced in the two RFCBT intervention groups (13.1%) relative to controls (32.2%). Moreover, reductions in rumination and worry were found to mediate the effects of RFCBT on symptom severity.

These findings are encouraging. However, there are several key limitations of the Dutch study: (a) there is not a diagnostic interview to determine incidence of major depression, with the study instead using self-report and only able to assess point prevalence rather than retrospective incidence; (b) similarly, it is not known whether the participants had previous episodes of depression, i.e., whether the intervention prevents first onset or relapse/recurrence of depression.

5.3.1 Study aims and objectives

The primary aim of this phase III efficacy trial is to replicate and extend the Dutch study [40] to compare guided i-RFCBT with a no-intervention control. If the target sample size based on the comparison of guided i-RFCBT to controls in the Dutch trial is achieved, the aim is to assess whether the findings from this previous trial can be replicated in a different population of undergraduates in the UK.

The RESPOND study will address the limitations of the Dutch trial by including a well-validated diagnostic interview (Structured Clinical Interview for DSM-IV (SCID-I [44]) to increase accuracy in determining current and past diagnostic status, and to allow for stratification on history of depression. Although including previously depressed participants is not consistent with strict definitions of initial onset prevention studies, there is a strong argument for

preventing further relapses and recurrences, especially as a major risk factor for a depressive episode is a history of depressive episodes [6].

One key change from the design of the Dutch trial is the selection of a young adult population aged 18-24-years, principally undergraduates, rather than 15-22 years-old, in order to recruit participants able to provide their own informed consent. This age group was chosen for a number of reasons: (a) for pragmatic reasons to improve feasibility and logistics of recruitment, since parental consent can be a barrier to recruitment for an internet-based prevention study [45]; (b) larger effect sizes are found for older adolescents in preventive studies, perhaps because older adolescents are better able to understand the intervention compared to younger adolescents or children [4] and c) life transitions such as moving out of the family home have been shown to increase the incidence of depression [46]. Additionally depression is prevalent in this population [47] and the number of students experiencing high levels of worry, stress and symptoms of depression and anxiety is also high [48], indicating that there is a significant group of at-risk students who could be targeted with a preventive intervention.

While previous research suggests guided interventions are more efficacious than unguided interventions, making the study of guided i-RFCBT our primary goal, clinically relevant benefits could still be obtained with unguided interventions as these have the potential to be accessed by larger numbers at a lower cost, and are essential for making highly scalable interventions. As a quasi-phase II pilot arm, we will therefore also include an unguided version of i-RFCBT to pilot its feasibility. This inclusion aims to assess the feasibility of retention and acceptability of the unguided intervention, as well as to estimate its effect sizes and variability to aid planning for a fully powered

definitive trial of the unguided version, with respect to rates of incidence and levels of symptoms (descriptives and confidence intervals), as a separate analysis from the primary Phase III design.

5.4 Methods/Design

5.4.1 Study Design

Phase III efficacy study: The phase III study will consist of a single (researcher) blind parallel-group randomised-controlled trial (RCT), comparing guided i-RFCBT versus a no-intervention control group, with this our primary research question.

Quasi-Phase II pilot arm: A separate adjunct arm of unguided i-RFBCT will be included as a quasi-phase II pilot arm to enable a feasibility study of this intervention. This will be a separate question, and there will be no direct comparison between unguided i-RFCBT and the guided i-RFCBT or control arms in the phase III efficacy study.

5.4.2 Setting

The study will be conducted over the internet and by telephone so we will recruit from around the UK. The intervention will be delivered on the Internet, with the guided version being supported by trained staff at the University of Exeter.

5.4.3 Participant inclusion criteria

Participants will be young adults resident in the UK aged 18-24 with elevated RNT, defined as scoring above the 75th percentile on at least one measure of worry/rumination (≥ 50 on the PSWQ [41] and/or ≥ 40 on the RRS [15]). Additionally, participants must be able to understand written English to engage with the intervention, and have private internet access to ensure confidentiality. In line with standard practice, participants currently receiving antidepressant

medication will be eligible, provided the dosage has been stable for at least the previous month.

5.4.3 Participant exclusion criteria

Because this is a prevention study, participants will be excluded if they meet diagnostic criteria for a current (within past month) major depressive episode. Additionally, potential participants will be excluded if they report: current and significant substance abuse or dependence; current symptoms of psychosis or bipolar disorder; current psychological therapy or active suicide risk.

5.4.4 Recruitment procedure

The main recruitment pathway involves contacting university departments around the UK by email and asking them to circulate an advert to their undergraduate students (as successfully used by Kingston et al. [49]). Generic discipline email addresses, or named individuals within the departmental administration team where possible, will be obtained using internet searches. Departments will be asked to circulate an included advert in the form of an attached pdf, containing a hyperlink to an online trial website that provides information and the initial online screening measures, to undergraduates within their department. The pdf format ensures departments can display the advert as a poster if they are not permitted to circulate by email. The number of emails sent out each week will be modulated depending on response rates.

A Facebook and Twitter account will be set up to help circulate the advert, particularly to non-students. Relevant organisations working with young people and/or mental health issues will also be asked to advertise a link to the study on their website.

5.4.5 Screening, baseline and consent procedure

Initial Online screening: An online screening website will be used to identify potentially eligible participants. A brief introduction to the study is included on the introductory page. Consent to online screening is obtained by informing potential participants that by clicking continue on this introductory page they are consenting for their responses to be stored by the researchers and that this data is subject to the Data Protection Act 1998.

A series of short questionnaires is then presented to identify potentially eligible participants, by collecting basic demographic information (age, sex, ethnicity, location, how they found out about the study) and screening on shortened versions of the PSWQ (4 items, range 4-20, cut-off ≥12) and RRS (5 items, range 5-20, cut-off ≥ 10) as used by the Dutch trial to identify individuals with elevated RNT (i.e., > 75th percentile) and the PHQ-8 [50] (PHQ-9 minus the suicidal thought question) to exclude participants who are likely to meet a diagnosis for current depression (cut-off ≥15).

Automated feedback informs participants whether they are eligible for further screening. Those excluded on low worry/rumination are informed that worry and rumination do not appear to be a significant problem for them and thanked for their interest. Those excluded on high PHQ score are given a message explaining that their scores indicate low mood which is affecting their quality of life and that they may be experiencing an episode of clinical depression. This message advises them to see their GP and provides contact details of organisations offering support and advice. Eligible participants are invited to leave their contact details (name, telephone number and email address) as consent to be contacted. The full information sheet and consent

form are then sent by email to the participant with an invitation to participate in a telephone interview with the researcher.

Telephone screening and baseline assessment: The researcher will provide the interviewee with an overview of the trial, the clinical interview, and ask for verbal consent. Interviews will be audio-recorded, with the participant's consent, so that diagnostic status can be independently rated. The screening interview consists of brief screening questions for alcohol and drug use, symptoms of bipolar disorder and psychosis (Psychosis Screening Questionnaire, PSQ [51]), assessment of any relevant past or current treatments, and the Structured Clinical Interview for DSM-IV (SCID-I; [44]) sections on current and past depressive episodes, dysthymia, and any relevant anxiety disorders and eating disorders. As the primary objective of this study is to investigate the prevention of depression, anxiety and eating disorders will be measured but participants meeting criteria for a disorder will not be excluded from this study.

Excluded participants are given feedback including advice to visit their GP and contact details of organisations for further support. Additionally, any risk reported during the interview is assessed using a well-established protocol to ensure appropriate clinical support is obtained. Eligible participants are then asked to complete baseline measures, assessing episodic stress (the Episodic Life Event Interview, part of the UCLA Life Stress Interview [52]); levels of worry and rumination (PSWQ and RRS); symptom severity of depression and generalized anxiety (PHQ-9 and GAD-7); neuroticism (Eysenck Personality Questionnaire-Revised Neuroticism sub-scale (EPQ-R; [53]) and history (family history of depression, experience of abuse in childhood). Excepting the episodic stress interview, which is always completed during the interview, baseline

measures can be completed during the telephone interview, or returned by email/post.

Consent to trial: All eligible participants will then be invited to enter the trial and asked to return written consent to participate. Once consent is received, participants will be randomised (see Figure1).

5.4.6 Randomisation and allocation concealment

Independent computer-generated block randomisation to the guided i-RFCBT, unguided i-RFCBT or the no-intervention control group will be used. Randomisation will be stratified by sex and by past history of depression (presence or absence of past depressive episodes) to assess the effect of sex on outcomes and to examine potential differences between prevention of first onset and relapse prevention. The randomisation uses blocks of 3 in order to ensure close parity of randomisation across the intervention arms across time. Because of the 2 levels of stratification by sex and by level of depression, with blocks of 3, the researcher would not be able to anticipate or determine allocation easily, and it was deemed not necessary to use varying block sizes. In order to preserve blinding of the study researcher, randomisation will be conducted by a third party not involved in assessing or treating the participants, who will also inform the therapist, who will be responsible for informing participants of their allocation.

5.4.7 Sample size calculation for Phase III efficacy trial

Power and sample size calculations were based on testing the primary question of the efficacy of guided internet-RFCBT in terms of reducing onset of major depression relative to no-intervention control. For our primary comparison of guided i-RFCBT versus no-intervention control, the Topper et al study [40] using

the binary outcome of number of individuals meeting caseness for depression at 12 months, reported 13.1% incidence of depression in guided i-RFCBT and 32.2% incidence in no-intervention control (hazard ratio = 0.41). Assuming similar effect sizes to the Topper et al study [40] for our intended time-to-outcome survival analysis over 12 months, then to detect this hazard ratio of 0.41 between these arms at two-tailed 5% alpha level, 75 participants recruited to each arm would provide 86% power.

Estimates for change in depressive symptoms pre-to-post intervention for guided i-RFCBT relative to waiting list control indicate that 78 participants per arm has power of 80% to detect observed effect size of *d* = 0.51 from the Dutch trial [40] at two-tailed 5% alpha level, allowing for the 20% follow-up drop-out attrition observed in the Dutch study.

5.4.8 Sample for quasi-phase II pilot arm

In the absence of any data on the unguided i-RFCBT, no power and sample size calculation was conducted for this arm. We will therefore aim to recruit the same number of participants for this arm as the other arms (*n* = 78), giving a total sample size of 234. The inclusion of this intervention arm is to explore feasibility of this unguided intervention with respect to attrition, acceptability, and estimates of incident rate and effect size.

5.4.9 Interventions

5.4.9.1 Guided i-RFCBT

The guided intervention is an English version of i-RFCBT (called MindReSolve). RFCBT is derived from theoretical models [11] and experimental findings, which propose that there are distinct types of repetitive thought (RT) with distinct consequences: constructive RT is characterized by a concrete, specific, and

action-oriented mode of processing, focusing on how events happen, whereas unconstructive RT is characterised by an abstract and evaluative processing mode, focusing on the meaning and implications of events and difficulties [11]. In experimental studies, relative to the abstract mode, the concrete mode improved problem-solving [54, 55] and reduced emotional reactivity in response to failure [56]. Underpinning RFCBT is the idea that shifting individuals into the concrete mode will reduce unconstructive rumination: consistent with this, repeated training of dysphoric and depressed participants to become more concrete reduces depression and rumination in both a proof-of-principle study and a randomised controlled trial [31, 33]. RFCBT therefore involves experiential and imagery exercises to adaptively shift processing mode (including concreteness, absorption, compassion), as well as functional analysis to help patients spot when rumination starts, distinguish between helpful versus unhelpful RT, and learn more functional responses. RFCBT seeks to change the process of thinking as opposed to the content of thoughts as in standard CBT [30]. In addition, rumination is conceptualised as a form of avoidance [11, 57], which is targeted on behavioural activation principles [58] with avoidance behaviour replaced with more appropriate approach behaviours.

I-RFCBT consists of six modules, each taking around an hour to complete in session and 1-to-2 weeks to practise. It includes psycho-education, mood diaries, on-line experiential exercises using audio-recordings, pictures, and video vignettes of students' experiences of the therapy. The modules each follow the same basic structure: reflection on previous session; introduction of new technique; practical exercises and planning how to practise or implement the technique in daily life. The specific behaviour change techniques are drawn from the following groups in the BCT Taxonomy (v1)[59]: goals and planning

(goal setting, action planning, review behaviour and behavioural contract); feedback and monitoring (self-monitoring of behaviour and outcomes); shaping knowledge (information about antecedents); natural consequences (information about social and environmental consequences and monitoring of emotional consequences); associations (prompts/cues, associative learning); repetition and substitution (behavioural practice/rehearsal, behaviour substitution, habit formation); antecedents (restructuring physical and social environment, avoiding/reducing cues for the behaviour); self-belief (mental rehearsal of successful performance, focus on past success, self-talk). The key strategies include coaching participants to spot warning signs for rumination and worry, and then to make IF-THEN plans in which an alternative strategy is repeatedly practised to the warning signs. These strategies include: being more active, slowing things down, breaking tasks down, opposite action, relaxation, concrete thinking, becoming absorbed, self-compassion, and assertiveness.

The intervention is accessed through a secure website, with each participant having a password protected account. Participants' log-ins are automatically recorded by the programme, allowing for an automated measure of treatment compliance. Reminder emails will be sent to participants after two weeks if they have not completed the module.

The participant can work through each module at his own pace but can only move from one module to the next once the coach has provided feedback. The coach will provide feedback on these responses within 2 working days, in particular highlighting any positive steps made and encouraging participants to sustain these as well as pointing out areas to focus on over the next module. Participants will also be able to send questions to their assigned therapist throughout the programme if they are having difficulty with a specific exercise.

The intervention will be supported by qualified clinicians who have received specific training in the rumination-focused CBT approach. Treatment fidelity is ensured through the use of fixed modules in the platform, ensuring all participants receive identical content. Detailed template responses for each module provide the coach with constrained feedback faithful with the treatment model, which they can then tailor to individual clients' responses. All responses from both client and coach are automatically saved by the online platform and a random sample will be checked against the templates to ensure they are faithful to the treatment. Furthermore, coaches will be provided with ongoing supervision with the developer of RFCBT to encourage fidelity. Supervision meetings will involve a brief overview of all clients and a more in-depth discussion of cases deemed to be more complex or where there is risk or non-response to the intervention.

5.4.9.2 Unguided i-RFCBT

The unguided version of the therapy contains the same six modules as the guided version, with almost identical content, adapted for self-help, including some conditional feedback on common difficulties with exercises. Participants are able to move freely from one module to the next, but are advised to spend 1-2 weeks on each to allow time for practice. Participants in the unguided version will be made aware that there is no coach monitoring their responses. However, they will be told that their questionnaire scores will be monitored on a weekly basis to check for any risk reported.

5.4.9.3 Control condition

Participants in the control condition will be informed that they have been allocated to carry on as usual. In order to ensure participants' welfare,

participants are permitted to access any other treatments throughout the course of the study, as necessary. They will also be able to access the unguided i-RFCBT at the end of the study if they so wish.

5.4.10 Blinding

This is a single blind study, with the researcher conducting outcome measures blind to allocation. Participants will be asked at the end of the screening interview not to disclose their allocation to the researcher in any of their future correspondence with the researcher and reminded of the importance of this prior to and during each follow-up interview. Due to the intervention, participants and therapists cannot be blinded.

5.4.11 Follow-up assessments and outcome measures

The primary outcome of interest of this study is the onset of a major depressive episode over a 12-month period, which we will assess with the SCID-I at 3 (post-intervention), 6, and 15 months after randomisation. The use of the SCID-I will allow for the ascertainment of depressive episodes that may have occurred between assessments (continuous time-to-onset and occurrence), and will also enable us to assess clinically significant symptoms of anxiety (particularly generalized anxiety disorder) that may have arisen in isolation or comorbid with depression. Severity of depressive symptoms is measured using the PHQ-9 and anxiety symptoms using the GAD-7. The effect of the intervention on levels of worry and rumination will be assessed using the PSWQ and RRS. A number of potential confounding variables are also measured: stressful life events, using the Episodic Life Event Interview and any treatments received outside the trial (medication, therapy, use of self-help materials). Each assessment will take place via a telephone interview, with the option of the questionnaire measures

being returned by email or post. To increase participant retention and completion of follow-ups, multiple attempts and multiple means (email, telephone, post) will be used to contact participants. Additionally, to increase motivation to complete the follow-up measures, lottery draws for £50 in vouchers will be held, with each participant receiving one ticket per completed follow-up.

5.4.12 Feasibility and acceptability outcome measures (Quasi-Phase II pilot arm)

With respect to the unguided intervention, feasibility and acceptability of data collection procedures, levels of attrition, effect size and acceptability of the unguided internet RFCBT intervention will be measured, to aid planning for a fully powered, definitive, Phase III trial. Feasibility of data collection procedures will be assessed by measuring missing items on clinical outcome measures, number and timing of drop-outs and whether these vary across arms. The acceptability of the intervention will be assessed using a behavioural index, measuring number of modules completed, time spent logged into the site and which modules are completed more easily or frequently than others.

5.4.13 Statistical analysis plan for phase III efficacy trial

Data cleaning will follow the protocol set out by Tabachnick and Fidell [60]. Statistical analysis will follow CONSORT standards [61]. Unplanned missing data will be handled via Multiple Imputation (MI). Sensitivity analysis, assuming a variety of MI models (Missing at Random; Missing Not at Random), will verify the likely impact of missing data. Auxiliary variables will be used to improve the estimation of missing data. Primary analyses will be conducted on the Intention-To-Treat (ITT) sample.

Subsequent analyses will use the Complier Average Causal Effect (CACE) analysis [62, 63]. CACE assumes that randomisation has no direct effect on outcome variable, and rather that the effect of treatment depends on compliance to treatment (operationalized in terms of completing four out of six modules), which in turn is dependent on randomisation. It therefore provides estimates of a treatment effect taking into account adherence and compliance with the treatment, whilst retaining the benefits of randomisation. This model is thus an exemplar of using an Instrumental Variable (IV) where randomisation is the instrument, which is correlated with compliance to the treatment, and directly unrelated to the outcome. In simple terms, CACE finds the difference in the outcome variable between the compliers in the treatment arm and the compliers in the control arm had they been offered the treatment, assuming the rates of compliance are similar in both arms as a consequence of randomisation.

As a prevention study, the main outcome of interest is the occurrence and time to onset of any depressive episode. Cox regression survival analyses will be performed to examine the effect of the preventive intervention on episode onsets of major depression. Participants will be censored upon measurement dropout or end of study. Although condition will be the main independent variable included in the model, we will also consider sex and history of past depression (the stratification variables).

The secondary outcome of occurrence/time to onset of generalized anxiety disorder will also be assessed using Cox regression survival analyses. Symptom severity and levels of rumination/worry will be examined using mixed model ANCOVAs: between group (ITT/CACE) and repeated measures (3-15

month follow-ups), with baseline symptom levels and stratification variables as covariates.

5.4.14 Mediation and moderation analysis

Mediational analyses will be used to test the hypothesis that rumination acts as mediator of the treatment effects of condition on onset of major depression using the approach outlined by Kraemer et al. [64]. Potential moderators (e.g. stratification variables and baseline characteristics) will also be investigated using this approach.

5.4.15 Ethical approval

Ethical and professional guidelines will be followed at all times, in line with Good Clinical Practice guidelines. Ethical approval has been obtained from the Ethics Committee of the School of Psychology, University of Exeter (Ref: 2012/554). Any possible adverse events witnessed by the researcher or the therapist will be discussed as soon as possible with the supervisor. If this is deemed to be an adverse event, an adverse event report will be completed. In the case of serious adverse events, the University of Exeter, as sponsor, will also be notified using the same report and a follow-up phone call.

5.5 Discussion

The current trial has been designed to build on the findings from the ZonMw trial, assessing the efficacy of guided i-RFCBT in a UK-based young adult population relative to a no-intervention control, in the prevention of depression. Critically, to overcome the limitations of this study, diagnostic interviews at each assessment point will allow for more accurate measures of incidence rates across the course of the follow-up period.

I-RFCBT may provide an effective and acceptable intervention for the prevention of depression in young adults. Widespread implementation is a key factor in prevention and the internet may provide a valuable tool in increasing access. Furthermore, while previous evidence suggests guided therapy will be more efficacious, the assessment of an unguided version allows a preliminary investigation of the potential benefits of increased availability and reduced cost that this may provide.

5.6 References

1. WHO: *The Global Burden of Disease 2004 Update.* Switzerland: WHO Press; 2008.

2. Andrews G, Issakidis C, Sanderson K, Corry J, Lapsley H: **Using survey data to inform public policy: comparison of the cost-effectiveness of treatment of ten mental disorders.** *The Journal of British Psychiatry* 2004, **184:**526-533.

3. Horowitz JL, Garber J: **The prevention of depressive symptoms in children and adolescents: A meta-analytic review.** *Journal of Consulting and Clinical Psychology* 2006, **74:**401–415.

4. Stice E, Shaw H, Bohon C, Marti NC, Rohde P: **A meta-analytic review of depression prevention programs for children and adolescents: Factors that predict magnitude of intervention effects.** *Journal of Consulting and Clinical Psychology* 2009, **77:**486–503.

5. Merry SN, Hetrick SE, Cox GR, Brudevold-Iversen T, Bir JJ, McDowell H: **Psychological and educational interventions for preventing depression in children and adolescents (Review).** *Cochrane Database of Systematic Reviews* 2011, **12**.

6. Muñoz RF, Cuijpers P, Smit F, Barrera AZ, Leykin Y: **Prevention of Major Depression.** *Annual Review of Clinical Psychology* 2010, **6:**181-212.

7. Topper M, Emmelkamp PMG, Ehring T: **Improving prevention of depression and anxiety disorders: Repetitive negative thinking as a promising target** *Applied and Preventive Psychology* 2010, **14:**57-71.

8. Harvey AG, Watkins E, Mansell W, Shafran R: *Cognitive behavioural processes across psychological disorders.* Oxford, UK: Oxford University Press; 2004.

9. Nolen-Hoeksema S, Watkins ER: **A heuristic for developing transdiagnostic models of psychopathology.** *Perspectives on Psychological Science* 2011, **6:**589–609.

10. Nehmy TJ: **School-based prevention of depression and anxiety in Australia: Current state and future directions.** *Clinical Psychologist* 2010, **14:**74–83.

11. Watkins ER: **Constructive and Unconstructive Repetitive Thought.** *Psychological Bulletin* 2008, **134:**163-206.

12. Abela JRZ, Brozina K, Haigh EP: **An examination of the response styles theory of depression in third- and seventh-grade children: A short-term longitudinal study** *Journal of Abnormal Child Psychology* 2002, **30:**515–527.

13. Broderick PC, Korteland C: **A prospective study of rumination and depression in early adolescence.** *Clinical Child Psychology and Psychiatry* 2004, **9:**383–394.

14. Butler LD, Nolen-Hoeksema S: **Gender differences in responses to depressed mood in a college sample.** *Sex Roles* 1994, **30:**331–346.

15. Nolen-Hoeksema S, Morrow J: **A prospective-study of depression and posttraumatic stress symptoms after a natural disaster—the 1989 Loma-Prieta Earthquake.** *Journal of Personality and Social Psychology* 1991, **61:**115–121.

16. Just N, Alloy LB: **The response styles theory of depression tests and an extension of the theory.** *Journal of Abnormal Psychology* 1997, **106:**221–229.

17. Nolen-Hoeksema S: **The role of rumination in depressive disorders and mixed anxiety/depressive symptoms.** *Journal of Abnormal Psychology* 2000, **109:**504–511.

18. Nolen-Hoeksema S, Stice E, Wade E, Bohon C: **Reciprocal relations between rumination and bulimic, substance abuse, and depressive symptoms in female adolescents.** *Journal of Abnormal Psychology* 2007, **116:**198-207.

19. Robinson MS, Alloy LB: **Negative cognitive styles and stress-reactive rumination interact to predict depression: A prospective study.** *Cognitive Therapy and Research* 2003, **27:**275–292.

20. Spasojevic J, Alloy LB: **Rumination as a common mechanism relating depressive risk factors to depression.** *Emotion* 2001, **1**.

21. Lyubomirsky S, Nolen-Hoeksema S: **Effects of self-focused rumination on negative thinking and interpersonal problem-solving.** *Journal of Personality and Social Psychology* 1995, **69:**176–190.

22. Lyubomirsky S, Kasri F, Zehm K: **Dysphoric rumination impairs concentration on academic tasks.** *Cognitive Therapy and Research* 2003, **27:**309–330.

23. Donaldson C, Lam D: **Rumination, mood and social problem solving in major depression.** *Psychological Medicine* 2004, **34:**1309–1318.

24. McLaughlin KA, Hatzenbuehler MS: **Mechanisms linking stressful life events and mental health problems in a prospective, community-based sample of adolescents.** *Journal of Adolescent Health* 2009, **44:**153-160.

25. Muris P, Roelofs J, Meesters C, Boomsma P: **Rumination and worry in nonclinical adolescents.** *Cognitive Therapy and Research* 2004, **28:**539-554.

26. Schwartz JA, Koenig LJ: **Response styles and negative affect among adolescents.** *Cognitive Therapy and Research* 1996, **20:**13-36.

27. Hankin B: **Rumination and Depression in Adolescence: Investigating Symptom Specificity in a Multiwave Prospective Study.** *Journal of Clinical Child & Adolescent Psychology* 2008, **7:**701-713.

28. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE: **Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication.** *Archives of General Psychiatry* 2005, **62:**593-602.

29. Watkins ER, Moberly NJ: **Concreteness training reduces dysphoria: A pilot proof-of-principle study.** *Behaviour Research and Therapy* 2009, **47:**48-53.

30. Watkins ER, Scott J, Wingrove J, Rimes KA, Bathurst N, Steiner H, Kennell-Webb S, Moulds M, Malliaris Y: **Rumination-focused cognitive behaviour therapy for residual depression: a case series.** *Behaviour Research and Therapy* 2007, **45:**2144-2154.

31. Watkins ER, Baeyens CB, Read R: **Concreteness training reduces dysphoria: proof-of-principle for repeated cognitive bias modification in depression.** *J Abnorm Psychol* 2009, **118:**55-64.

32. Watkins ER, Mullan E, Wingrove J, Rimes K, Steiner H, Bathurst N, Eastman R, Scott J: **Rumination-focused cognitive-behavioural therapy for residual depression: phase II randomised controlled trial.** *The British Journal of Psychiatry* 2011, **199:**1-6.

33. Watkins ER, Taylor RS, Byng R, Baeyens C, Read R, Pearson K, Watson L: **Guided self-help concreteness training as an intervention for**

major depression in primary care: a Phase II randomized controlled trial *Psychological Medicine* 2012, **42:**1359-1371.

34. Andersson G: **The promise and pitfalls of the internet for cognitive behavioral therapy.** *BMC Medicine* 2010, **8:**82.

35. Richardson T, Stallard P, Velleman S: **Computerised cognitive behavioural therapy for the prevention and treatment of depression and anxiety in children and adolescents: a systematic review** *Clinical Child and Family Psychology Review* 2010**:**275-290.

36. Spek V, Cuijpers P, Nyklicek I, Riper H, Keyzer J, Pop V: **Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis.** *Psychological Medicine* 2007, **37:**319-328.

37. Andrews G, Cuijpers P, Craske MG, McEvoy P, Titov N: **Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis.** *PloS one* 2010, **5:**e13196.

38. Christensen H, Griffiths KM, Mackinnon AJ, Brittliffe K: **Online randomized trial of brief and full cognitive behaviour therapy for depression.** *Psychological Medicine* 2006, **36:**1737-1746.

39. Andersson G, Cuijpers P: **Internet-based and other computerized psychological treatments for adult depression: a meta-analysis.** *Cognitive Behavioral Therapy* 2009, **38:**196-205.

40. Topper M, Emmelkamp PMG, Watkins E, Ehring T: **Prevention of anxiety disorders and depression by targeting excessive worry and rumination in adolescents and young adults: A randomized controlled trial.** In submission.

41. Meyer TJ, Miller ML, Metzger RL, Borkovec TD: **Development and validation of the Penn State Worry Questionnaire.** *Behaviour Research and Therapy* 1990, **28:**487-495.

42. Kroenke K, Spitzer RL, Williams JBW: **The PHQ-9: Validity of a brief depression severity measure.** *Journal of General Internal Medicine* 2001, **16:**606-613.

43. Spitzer RL, Kroenke K, Williams JBW, Löwe B: **A brief measure for assessing generalized anxiety disorder: The GAD-7.** *Archives of Internal Medicine* 2006, **166:**1092-1097.

44. First MB, Spitzer RL, M. G, Williams JBW: *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition With Psychotic Screen (SCID-I/P W/ PSY SCREEN).* New York: Biometrics Research, New York State Psychiatric Institute; 2002.

45. Hoek W, Schuurmans J, Koot HM, Cuijpers P: **Effects of internet-based guided self-help problem-solving therapy for adolescents with depression and anxiety: A randomized controlled trial.** *PLoS ONE* 2012, **7**.

46. Reinherz HZ, Paradis AD, Giaconia RM, Stashwick CK, Fitzmaurice G: **Childhood and adolescent predictors of major depression in the transition to adulthood** *American Journal of Psychiatry* 2003, **160:**2141-2147.

47. Eisenberg D, Gollust SE, Golberstein E, Hefner JL: **Prevalence and Correlates of Depression, Anxiety and Suicidality Among University Students.** *American Journal of Orthopsychiatry* 2007, **77:**534–542.

48. **Mental Distress Survey Overview** [http://www.nus.org.uk/Global/Campaigns/20130517%20Mental%20Distress%20Survey%20%20Overview.pdf]

49. Kingston REF, Watkins ER, O'Mahen HA: **An Integrated Examination of Risk Factors for Repetitive Negative Thought.** *Journal of Experimental Psychopathology* 2013, **4:**161-181.

50. Kroenke K, Strine TW, Spitzer RL, Williams JBW, Berry JT, Mokdad AH: **The PHQ-8 as a measure of current depression in the general population.** *Journal of Affective Disorders* 2008, **114:**163-173.

51. Bebbington PE, Nyani T: **The Psychosis Screening Questionnaire.** *International Journal of Methods in Psychiatric Research* 1995, **5:**11-19.

52. Hammen C: *Episodic Life Event Interview: UCLA Stress Interview.* Los Angeles, CA: UCLA Department of Psychology; 2004.

53. Eysenck SBG, Eysenck HJ, Barrett P: **A revised version of the psychoticism scale.** *Personality and Individual Differences* 1985, **6:**21-29.

54. Watkins ER, Baracaia S: **Rumination and social problem solving in depression.** *Behaviour Research and Therapy* 2002, **40:**1179–1189.

55. Watkins ER, Moulds M: **Distinct modes of ruminative self-focus: Impact of abstract versus concrete rumination on problem solving in depression.** *Emotion* 2005, **5:**319-328.

56. Watkins ER, Moberly NJ, Moulds ML: **Processing mode causally influences emotional reactivity: Distinct effects of abstract versus concrete construal on emotional response.** *Emotion* 2008, **8:**364-378.

57. Borkovec TD, Alcaine OM, Behar E: **Avoidance theory of worry and generalized anxiety disorder.** In *Generalized anxiety disorder: Advances in research and practice.* Edited by R. G. Heimberg CLT, & D. S. Mennin New York, NY: Guilford; 2004: 77–108

58. Martell CR, Addis ME, Jacobson NS: *Depression in context: Strategies for guided action.* New York: Norton; 2001.

59. Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, Eccles MP, Cane J, Wood CE: **The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions.** *Annals of behavioral medicine* 2013, **46:**81-95.

60. Tabachnick BG, Fidell LS: *Using multivariate statistics.* 4th edn. Needham Heights, MA: Allyn & Bacon; 2001.

61. Schulz KF, Altman DG, Moher D: **CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials.** *BMC Medicine* 2010, **8:**18.

62. Angrist JD, Imbens GW, Rubin DB: **Identification of Causal Effects Using Instrumental Variables.** *Journal of the American Statistical Association* 1996, **91:**444-455.

63. Dunn G, Maracy M, Tomenson B: **Estimating treatment effects from randomized clinical trials with noncompliance and loss to follow-up: the role of instrumental variable methods.** *Statistical methods in medical research* 2005, **14:**369-395.

64. Kraemer HC, Wilson GT, Fairburn CG, Agras WS: **Mediators and moderators of treatment effects in randomized clinical trials.** *Archives of General Psychiatry* 2002, **59:**877-883.

CHAPTER 6: Outcomes of the RESPOND trial

This chapter reports the outcomes of the RESPOND trial, as published in:

Cook, L., Mostazir, M., & Watkins, E. (2019). Reducing Stress and Preventing Depression (RESPOND): Randomized Controlled Trial of Web-Based Rumination-Focused Cognitive Behavioral Therapy for High-Ruminating University Students. *Journal of Medical Internet Research, 21*(5), e11349. doi:10.2196/11349

The original paper is included as published, with footnotes added to provide further details on the included analyses. The term ‘usual care control’ is used to describe the control condition, as this was the terminology requested by the journal. This condition is the same as the ‘control condition’ as described in the protocol paper (Section 5.4.9.3).

The published paper is then followed by seven Appendices which provide additional analyses and clarifications: Mediation analyses (Appendix A), Discussion of Recruitment Approach (Appendix B), Overview of stressful events (Appendix C), Decomposing the Stress Interaction (Appendix D), ANCOVA tables including multiple imputation and effect sizes (Appendix E), Data management and cleaning (Appendix F) and Comorbid anxiety disorders (Appendix G). The measures used for the baseline and follow-up interviews are included in Appendix 3.

REducing Stress and Preventing Depression (RESPOND): a randomised controlled trial of web-based rumination-focused cognitive behavioural therapy (i-RFCBT) for high ruminating university students

Lorna Cook[1], Mohammod Mostazir[2], Edward Watkins*[1]

* Corresponding author: E.R.Watkins@exeter.ac.uk

[1]SMART Lab, Mood Disorders Centre, School of Psychology, University of Exeter, EX4 4QG, UK

[2]College of Life and Environmental Sciences (CLES), School of Psychology, University of Exeter, EX4 4QG, UK

Acknowledgements

This work was supported by University of Exeter, UK, through a matched funded PhD studentship to a successful Wellcome Trust Capital Bid. The funders had no involvement in the research or the submission of this manuscript for publication.

We are grateful to Jenny Cadman, Dr Yusuke Umegaki (therapists for guided therapy and assisting with randomisation) and Rosario Melero (assisting with recruitment and therapist for guided therapy).

Conflicts of Interest

Edward Watkins developed the original RFCBT intervention. The other authors declare they have no competing interests.

Abbreviations

CACE: Complier average causal effect; CBT: Cognitive-behavioural therapy; CMD: Common mental health disorder; CONSORT: Consolidated standards of reporting trials; GAD: Generalised anxiety disorder; GAD-7: Generalised anxiety disorder 7-item scale; GP: General practitioner; HR; Hazard ratio; (i-)RFCBT: (Web-based) Rumination-focused cognitive-behavioural therapy IRR: Incidence rate ratio; ITT: Intention-To-Treat; MDE: Major depressive episode; MI: multiple imputation; PHQ-8/PHQ-9: Patient health questionnaire-8 item or 9 item; PSQ: Psychosis Screening Questionnaire; PSWQ: Penn State Worry Questionnaire; RCT: Randomised controlled trial; RNT: repetitive negative thought; RRS: Ruminative Response Scale of the Response Styles Questionnaire; RT: repetitive thought; SCID-I: Structured Clinical Interview for DSM-IV

6.1 Abstract

Background: Prevention of depression is a priority to reduce its global disease burden. Targeting specific risk factors, such as rumination, may improve prevention. Rumination-focused CBT (RFCBT) was developed to specifically target depressive rumination.

Objective: The primary objective was to test whether guided i-RFCBT would prevent the incidence of major depression relative to usual care in UK university students. The secondary objective was to test the feasibility and estimated effect sizes of unguided i-RFCBT.

Methods: To address the primary objective, a Phase III RCT was designed and powered to compare high risk university students (*N* = 235), selected with elevated worry/rumination, recruited via an open access website in response to circulars within universities and internet advertisement, randomised to receive either guided i-RFCBT (interactive web-based RFCBT, supported by asynchronous written web-based support from qualified therapists), or usual care control. To address the secondary objective, participants were also randomised to an adjunct arm of unguided (self-administered) i-RFCBT. Primary outcome was onset of a major depressive episode over 15 months, assessed with structured diagnostic interviews at 3 (post-intervention), 6 and 15 months post-randomisation, conducted by telephone, blind to condition. Secondary outcomes of symptoms of depression and anxiety and levels of worry and rumination were self-assessed through questionnaires at baseline and the same follow-up intervals.

Results: Participants were randomised to guided i-RFCBT (*N* = 82), unguided i-RFCBT (*N* = 76) or usual care (*N* = 77). Guided i-RFCBT reduced risk of depression by 34% relative to usual care (HR = 0.66, 95% CI [0.35, 1.25], *P* =

.20). Participants with higher levels of baseline stress benefited most from the intervention (HR: 0.43, 95% CI [0.21, 0.87], *P* = .02). Significant improvements in rumination, worry and depressive symptoms were found in the short to medium term. Of six modules, guided participants completed a mean of 3.46 modules (SD = 2.25), with 46.34% (38/82) compliant (completing ≥4 modules). Similar effect sizes and compliance rates were found for unguided i-RFCBT.

Conclusions: Guided i-RFCBT can reduce the onset of depression in high-risk young people reporting high levels of worry/rumination and stress. The feasibility study argues for formally testing unguided i-RFCBT for prevention: if the observed effect sizes are robustly replicated in a Phase III trial, it has potential as a scalable prevention intervention.

Trial registration: Current Controlled Trials ISRCTN12683436. Date of registration: 27/10/2014

Keywords: Randomised Controlled Trial; Cognitive Behavioural Therapy (CBT); Rumination; Depression; Prevention; Internet-Delivery

6.2 Introduction

Depression is the leading cause of disease burden worldwide, accounting for 7.5% of all years lived with disability in 2015 [1], with considerable individual, societal and economic consequences. Although there are effective evidence-based acute treatments, their impact is limited because of poor access to treatments [2], high rates of non-response [3] and the recurrent nature of depression, with 50-80% of patients experiencing two or more episodes [4]. It is estimated that even with optimal acute treatment at full coverage, only 34% of the disease burden would be averted [5]. As a consequence, a strong case has been made that prevention is needed to reduce the global burden of depression [6].

Preventive interventions, mainly using cognitive-behavioural therapy (CBT) approaches, can reduce symptoms of depression and prevent the incidence of depression (see meta-analyses [7-9]), with an average reduction in incidence rates of 21% [10]. These meta-analyses suggest that targeted interventions (selective interventions aimed at subgroups with known risk factors; indicated interventions aimed at those with subclinical symptoms) produce larger and longer-lasting effects than universal interventions aimed at entire populations. A meta-analysis [11] of 21 preventive interventions (15 using CBT approaches) found that selective interventions and indicated interventions had lower incidence rate ratios (IRR) (0.72 and 0.76 respectively) relative to controls than universal interventions (IRR = 0.90). Merry et al. [8] also found both universal and targeted interventions reduced incidence relative to no intervention in the short to medium term (3-9 months post-intervention) but only targeted interventions reduced incidence at 12 months. Thus, targeting at-risk groups may improve the efficacy of preventive interventions for depression [6],

in part because the base rate is higher in targeted samples so it is easier to detect a significant effect with smaller sample sizes [12].

The incidence of depression rises steeply from the age of 14 through into young adulthood, with increased rates in females (2:1 female: male) emerging at around 12 years old and continuing into young adulthood [13]. The UK Adult Psychiatric Morbidity Survey found increasing rates of common mental health disorders (CMDs: incorporating depression and anxiety disorders) among young women (16-24-year-olds), rising from 22.2% in 2007 to 28.2% in 2014 [14], with rates in young women almost three times those of young men (10.0%) in 2014. Because early onset is linked to greater chronicity [15] and other negative long-term outcomes, such as poorer academic and occupational performance [1, 16], prevention may be particularly effective and impactful for this age group.

Within this age range, university students are a particularly high-risk group, with a weighted mean prevalence for depression of 30.6% (range 10-85%) across 24 studies [17] relative to estimates of 10.8%-22% in non-students of the same age range [18, 19]. This increased prevalence may be due to the specific pressures of university and associated lifestyle changes, such as leaving the family home for the first time, forming new friendships, more self-directed learning and irregular sleep patterns [20]. Students who experience mental health difficulties during their studies are at greater risk of poor academic outcomes [16] and dropout [21].

Despite these challenges, students often do not seek help from relevant services [22, 23]. Alternative delivery modes, such as web-based interventions, offer advantages that may be attractive to students, including: availability at any time and place, anonymity which may reduce the stigma of seeking help and

more time to reflect on the treatment material [12, 24, 25]. A recent systematic review and meta-analysis of 17 web-based and computer-delivered interventions for higher education students found reductions in depression, anxiety and stress when compared to inactive controls [26]. However, sample sizes were generally small and the authors recommend further larger scale trials to assess the effectiveness of web-based interventions in university students.

One such relatively large-scale trial by Topper et al. [27] tested a guided web-based targeted preventive intervention for 251 high school and university students aged 15-22 with high levels of self-reported worry and/or rumination. Participants were randomised to face-to-face group rumination-focused cognitive-behavioural therapy (RFCBT), guided web-based RFCBT (i-RFCBT), or a no-intervention control group. This preventive intervention is based on rumination-focused cognitive-behavioural therapy (RFCBT), previously shown to be effective in treating residual depression [28]. There is considerable evidence that rumination plays a causal role in the onset and duration of major depressive episodes [29, 30]. Within a student population, rumination predicts change in depression over 6 months [31]. Rumination interacts with other risk factors to both maintain depression (the combination of rumination, low self-esteem and stressful life events predicts maintenance of depressive symptoms over 6 weeks [32]) and predict the onset of depressive symptoms (engaging in rumination in response to stress prospectively predicted an increase in subsequent depressive symptoms [33]). These studies suggest that specifically targeting ruminative responses to stressful events could reduce depression.

RFCBT specifically targets repetitive negative thought (RNT), incorporating both rumination and worry, defined as a thinking style that is

repetitive, intrusive, difficult to disengage from, perceived as unproductive and that captures mental capacity [34]. RNT is a transdiagnostic process, involved in the onset and maintenance of a range of emotional disorders including depression and, anxiety as well as physical health issues [29, 35], including in children and adolescents [36-39]. Targeting transdiagnostic risk factors has the potential to improve the efficacy of prevention by impacting on multiple disorders with a single intervention [27].

In the Topper et al [27] trial, both web-based and group-delivered RFCBT reduced symptoms of depression and anxiety (*d* = 0.36 to 0.72) relative to controls. Cumulative incidence rates at the final 12-month follow-up were significantly lower in both RFCBT intervention conditions for depression (14.7% web-based; 15.3% group) relative to the usual care control condition (32.4% depression), with no difference between i-RFCBT versus group RFCBT. In support of the hypothesised mechanism of change, reductions in worry and rumination were found to mediate the effects of the interventions on prevalence of depression and GAD. These findings suggest that targeting rumination may have preventive effects for depression and are consistent with evidence that targeted prevention can be effective in adolescents and young adults. Topper et al. [27] included both secondary and university students to form a heterogeneous sample. Given the evidence that undergraduates may form a distinct at-risk subgroup for depression, the primary aim of the current phase III efficacy trial was to test whether these beneficial effects of guided i-RFCBT on onset of depression relative to usual care [27] could be extended to a selective UK high-risk undergraduate population.

We also aimed to address several key limitations of the Topper et al. [27] trial: (a) there was no diagnostic interview to assess depression and self-report

measures were only able to estimate point prevalence caseness; (b) because history of depression was not assessed, participants' prior history of depression was not known and therefore it was not possible to discriminate whether the intervention prevented first onset or relapse/recurrence of depression. To address these methodological limitations, we included a well-validated diagnostic interview (Structured Clinical Interview for DSM-IV; SCID-I [40]) to increase accuracy of current diagnostic status and measure retrospective incidence.

We hypothesized that in high-ruminating undergraduates, guided i-RFCBT, relative to usual care, would significantly reduce the onset of major depressive episodes over the course of the 15 months post-randomization follow-up (primary outcome). Rumination has also been found to increase the negative effect of stressful life events on depressive symptoms in young people and students [32, 33]. This observed interaction is consistent with the evidence that rumination contributes to depression by exacerbating existing negative mood and negative cognitions and by repetitively dwelling on difficulties [29, 30], such as result from stressful events. As such, a tendency to ruminate would be expected to have less impact when things are going well and there is less to dwell on, relative to when things are difficult. We therefore hypothesised that i-RFCBT would be particularly beneficial for high ruminating undergraduates who were also experiencing stressful life events, as this would be the group for whom rumination would be most detrimental.

As a secondary aim, we explored the feasibility and acceptability of an unguided version of i-RFCBT to prevent depression. Topper et al., [27] used i-RFCBT that was guided and supported by a therapist because prior evidence suggested that, at least for acute treatment for depression, guided i-CBT is

significantly more effective than unguided (i.e., self-help) i-CBT [41-43], and only guided i-CBT produces similar treatment effects to face-to-face therapy in patients with acute depressive symptoms [24]. A key rationale for web-based therapy is to increase the coverage, availability, and accessibility of treatment, by potentially reaching large numbers of people through the internet and by overcoming hurdles such as geographical distance, poor mobility, and scheduling appointments in the working day. However, any form of guided i-CBT (including i-RFCBT) is necessarily limited in its scalability because coverage is determined by the number and availability of therapists. In contrast, an unguided form of web-based therapy has nearly limitless scalability as there are no such constraints, and, thus, even with smaller effect sizes than guided interventions, has significant potential to reduce the disease burden of depression [44]. Such an intervention would be particularly beneficial for preventing depression because effective prevention requires an intervention to be highly scalable and able to reach very high numbers of people. As a secondary question, we therefore explored the feasibility and acceptability of an unguided version of i-RFCBT in a quasi-phase II pilot arm, and estimated its effect sizes to inform a fully powered trial, with respect to incidence rates and symptom levels (descriptives and confidence intervals).

6.3 Methods

6.3.1 Trial Design

6.3.1.1 Phase III efficacy study

The phase III study consisted of a single (researcher) blind parallel-group RCT, comparing guided i-RFCBT versus a usual care control group. For full details,

see the trial protocol paper [45] and Current Controlled Trials ISRCTN12683436.

6.3.1.2 Quasi-Phase II pilot arm

To assess the feasibility of unguided i-RFCBT, a separate adjunct arm of unguided i-RFBCT was included as a quasi-phase II pilot arm. For efficiency, participants were randomised to this arm within the overall trial design, but there was no direct comparison between the unguided and guided arms. The unguided arm was compared to the control group in order to estimate effect sizes of an unguided version of i-RFCBT for the planning of future efficacy trials.

6.3.2 Participants

Participants were university students resident in the UK aged 18-24 with elevated repetitive negative thought (RNT), defined as scoring above the 75th percentile on at least one measure of worry/rumination: ≥ 50 on Penn State Worry Questionnaire (PSWQ; [46]); and/or ≥ 40 on the Ruminative Response Scale (RRS; [47]), using the same criteria as Topper et al., [27]. As a prevention study, participants were excluded if they met diagnostic criteria for a current (within past month) major depressive episode (MDE). Additionally, potential participants were excluded if they reported any of the following: current and significant substance abuse or dependence; current symptoms/diagnosis of psychosis or bipolar disorder; current psychological therapy or active suicide risk. In line with standard practice, receipt of antidepressant medication was not an exclusion criterion, providing the dose had been stable for at least one month.

6.3.3 Sample size calculation and recruitment

For the primary question comparing guided i-RFCBT to usual care control, assuming a similar hazard ratio of 0.41 for the guided i-RFCBT vs. usual care control [27], 75 participants per arm would provide 0.86 power (two-tailed 5% alpha level) to detect this effect. For change in depressive symptoms, the observed effect size was *d* = 0.51 [27]. Seventy-eight participants per arm would be needed for 80% power to detect a similar effect at two-tailed 5% alpha level, allowing for 20% follow-up drop-out attrition. With no previous evidence for unguided i-RFCBT, the comparison of unguided i-RFCBT to usual care was conducted as a feasibility study as a first step to conducting a fully powered trial of unguided i-RFCBT. As such, no power or sample size calculations were conducted for the unguided arm. We aimed to recruit the same number (*N* = 78) as the other two arms.

The full recruitment procedure is outlined in Cook and Watkins [45]. Briefly, 1834 university departments in the UK were contacted between 14/11/2013 and 10/12/2014 (1527 contacted twice) and asked to advertise the study. Three hundred and thirty-six departments confirmed the study was advertised either by email or as a poster. This advert contained a link to an open access screening website. Twitter and Facebook were also used to circulate the advert to young people who expressed an interest in the following terms: stress; worry; rumination; mental health; self-esteem; wellbeing; research; psychology; cognitive-behavioural therapy; online therapy. Additionally, three organisations working with young people and/or in the field of mental health agreed to advertise the study.

A two-step procedure identified eligible participants. In the first step, an open access screening website with conditional automated feedback identified

potential participants for further screening by screening in those with elevated RNT (> 75th percentile) using shortened versions of the PSWQ (4 items, range 4-20, cut-off ≥12) and RRS (5 items, range 5-20, cut-off ≥ 10), as developed by Topper et al. [48]. A conservative cut-off of 15 on PHQ-8 [49] excluded individuals likely to be experiencing a current MDE. Eligible participants provided contact details as consent to be contacted for further telephone screening.

In the second step, a telephone interview consisted of brief screening questions for alcohol and drug use, symptoms of bipolar disorder and psychosis (Psychosis Screening Questionnaire, PSQ; [50]), assessment of any relevant past or current treatments, and the SCID-I [40] sections on current and past depressive episodes, dysthymia, and any relevant anxiety disorders and eating disorders. As the primary objective was to investigate the prevention of depression, diagnoses of anxiety disorders and eating disorders were recorded but participants meeting criteria for any of these disorders were not excluded from the study. Consent to interview was obtained verbally and included providing their general practitioner's (GP) contact details so that appropriate clinical support could be obtained in the event of disclosure of suicidal risk. The interview was audio-recorded, with consent, so that diagnostic status could be independently checked. The same researcher conducted the baseline and follow-up telephone interview assessments ensuring continuity of contact between research team and participants. Two hundred and fifty-four participants were eligible, of whom 235 returned written informed consent and were randomised to guided i-RFCBT (*N* = 82), unguided i-RFCBT (*N* = 76) or usual care control (*N* = 77). The CONSORT diagram (Figure 6.1) indicates the numbers excluded at baseline for each of the exclusion criteria.

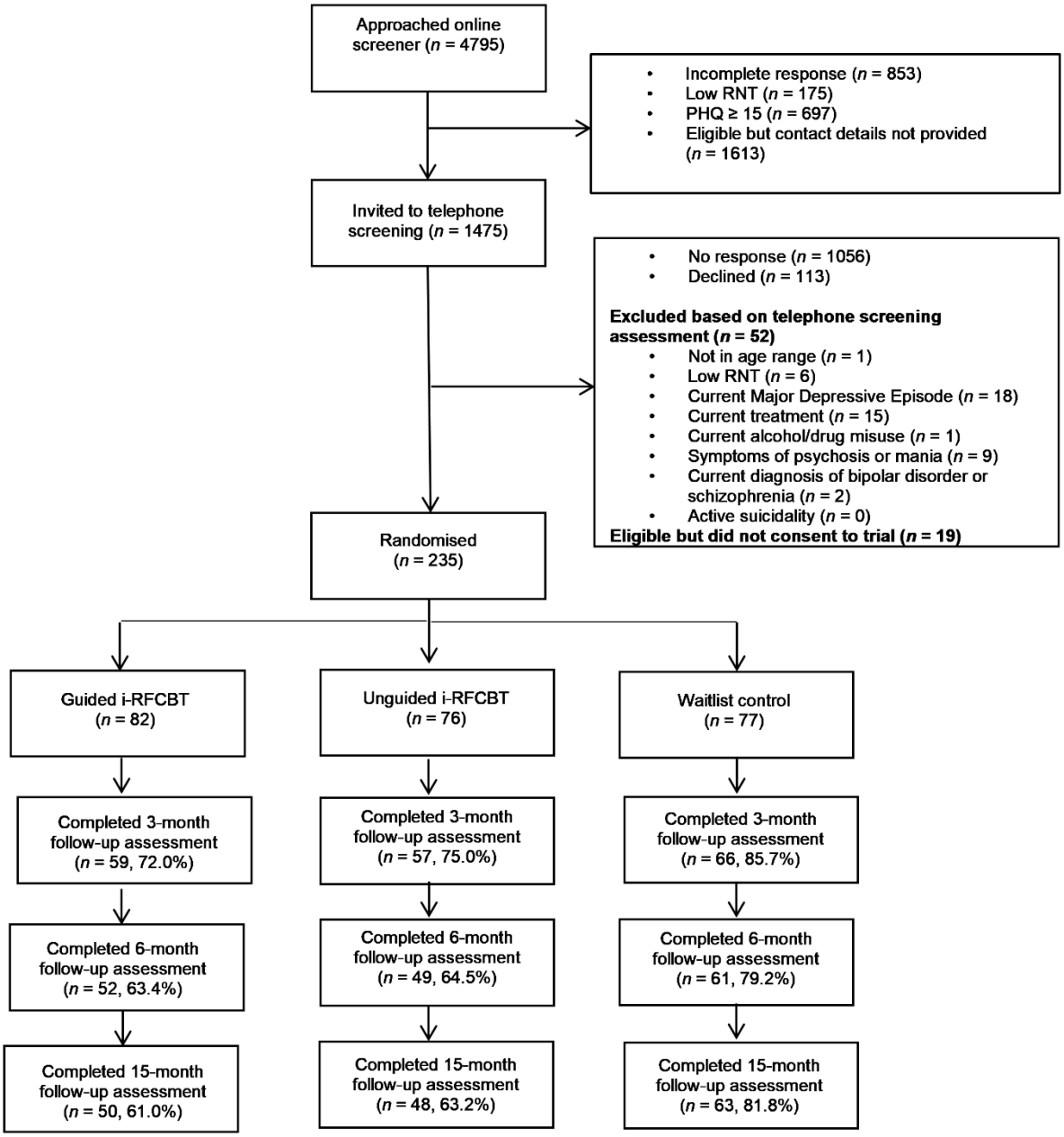


Figure 6.1. CONSORT Trial flowchart.

6.3.4 Interventions

6.3.4.1 Guided i-RFCBT

The guided intervention was an English version of i-RFCBT (called MindReSolve), translated and adapted from the version used by Topper et al. [27] to include case examples relevant to university students (see Multimedia

Appendix 1). RFCBT differs from standard CBT by seeking to change the process of thinking rather than the content of individual thoughts [51]. RFCBT [52] was developed from theoretical models and experimental findings indicating distinct types of repetitive thought (RT) with different consequences [29]: unconstructive RT involves an abstract, evaluative processing mode focused on the meaning and evaluation of events and difficulties, leading to a range of negative consequences such as poorer problem-solving and greater emotional reactivity, relative to constructive RT, which involves concrete, specific and action-oriented processing [53]. RFCBT therefore aims to shift participants from an abstract and evaluative style to a concrete, specific and action-oriented style [29], consistent with evidence that concreteness training reduces depression [54].

RNT is also theoretically conceptualised as a mental habit acting as a form of avoidance and maintained by negative reinforcement [55]. RFCBT therefore involves counterconditioning the avoidant ruminative response with more helpful coping strategies and approach behaviours [52]. In practice, this involves functional analysis of rumination to help users spot triggers for rumination, to distinguish between helpful and unhelpful RT and to countercondition unhelpful RT with more functional responses through the formulation of contingency 'If-Then' plans [52].

The internet treatment was delivered on the internet platform and software owned, programmed, and hosted by Minddistrict [56], accessed by a research licence purchased from Minddistrict by the research team. The specific content of the i-RFCBT intervention was developed and entered into the platform using its Content Management System (CMS) by the research team led by Edward Watkins, using the same key intervention principles and

techniques as face-to-face RFCBT as described in Watkins [52], adapted for the internet. I-RFCBT contains the same key components as face-to-face RFCBT [52], split into six one-hour modules, each in turn split into 3 or 4 sessions consisting of a single webpage, with one to two weeks recommended per module for practice of the techniques. The content includes psycho-education, mood diaries, experiential audio exercises, pictures, and video vignettes of university students talking about their own experiences of the intervention. Modules follow the same basic structure: reflection on previous module; introduction of new technique; experiential in-session exercises; plans for implementation. The specific behaviour-change techniques are drawn from the following groups in the BCT Taxonomy (v1) [57]: goals and planning (goal setting, action planning, review behavior and behavioural contract), feedback and monitoring (self-monitoring of behaviour and outcomes), shaping knowledge (information about antecedents), natural consequences (information about social and environmental consequences and monitoring of emotional consequences), associations (prompts/cues and associative learning), repetition and substitution (behavioural practice/rehearsal, behaviour substitution, and habit formation), antecedents (restructuring physical and social environment, avoiding/reducing cues for the behaviour), and self-belief (mental rehearsal of successful performance, focus on past success, and self-talk). The key strategies include coaching participants to spot warning signs for rumination and worry, and then to make IF THEN plans in which an alternative strategy is repeatedly practised in response to the warning signs. These strategies include being more active, slowing things down, breaking tasks down, opposite action, relaxation, concrete thinking, becoming absorbed, self-compassion and assertiveness.

The intervention was accessed individually, for free, on a secure, password-protected website. Access was granted by email link, inviting the participant to set up a personal account and password. The intervention was supported by qualified clinicians who had received additional specific training in RFCBT. This support consisted of asynchronous written feedback provided by the clinician at the end of each module. Feedback served to highlight positive steps and identified areas to focus on in the following module. Feedback was constrained by template responses for each module, faithful to the RFCBT model, which could be adapted to individual participants' responses. All content and module order was identical across participants, ensuring treatment fidelity. Each module was self-paced but the participants were advised to spend one to two weeks on each and could only access the next module once feedback from the clinician was received, typically within 2 working days. Clinicians monitored log-ons and sent personalised reminder emails if there was no log-on for over a week. The platform also sent an automatic weekly reminder if the platform had not been accessed for a week. Suicidal risk was also monitored using a well-established departmental protocol to determine level of risk and seek clinical support as appropriate.

Therapists were provided with regular supervision with the developer of RFCBT (EW) to further encourage treatment fidelity. All (100%) feedbacks reviewed by EW were faithful to the intervention model (over 10% of therapist feedbacks sampled – a minimum of the three initial feedbacks for each therapist, plus a random sub-set of later feedbacks).

6.3.4.2 Unguided i-RFCBT

The content of unguided i-RFCBT was almost identical to guided i-RFCBT with minor adaptations for self-help to include some automatic online conditional feedback addressing common challenges with the exercises. Access was granted via email link to set up a personal account and password. Participants could then access all modules without restriction but were advised to spend one to two weeks on each to allow time for practice. Responses were not monitored except for weekly checks of questionnaires to identify and follow up suicidal risk as necessary.

6.3.4.3 Usual care control condition

Participants in the usual care control condition were permitted to access any other treatments during the study, as necessary. They were also offered access to unguided i-RFCBT at the end of the follow-up period.

6.3.5 Measures

All measures were completed at baseline, 3 months, 6 months and 15 months unless otherwise stated. Diagnostic interviews for the primary outcome were conducted by telephone, with the option to complete self-report questionnaire measures for secondary outcomes during the telephone interview or request for them to be returned by email/post.

The Structured Clinical Interview for DSM-IV (SCID-I; [40]) is a semi-structured diagnostic interview for Axis I DSM-IV Diagnoses. The SCID-I was used to assess MDE (current and/or past), anxiety disorders and eating disorders. Inter-rater reliability for Axis I diagnoses is fair to excellent, with a mean Kappa of 0.71 [58]. In the event of disclosure of suicidal risk during the diagnostic

interview, the researcher followed a well-established departmental protocol to assess risk and obtain clinical support as needed.

The Episodic Life Event Interview, part of the UCLA Life Stress Interview [59], assessed the number and impact of stressful events since the previous assessment (for previous 3 months at baseline). Participants provided a list of events experienced and a subjective rating of stress experienced as a result of the worst event. The original scale ranges from 1 'none' to 5 'severe'. Participants scored 0 if no events were experienced. To aid analysis and interpretation, stress was recoded to collapse 0 'no event' and 1 'event experienced but no stress' into a single 'no stress' category. The recoded stress scale therefore ranges from 0 'no stress' to 4 'severe stress'.

The Penn State Worry Questionnaire (PSWQ; [46]) is a 16-item self-report questionnaire assessing frequency, intensity and automaticity of worry (e.g. 'My worries overwhelm me'; 'I know I shouldn't worry about things, but I just can't help it'). It is scored from '1' (not at all typical of me) to '5' (very typical of me), with higher scores indicating higher levels of worry. Internal consistency is high with good test-retest reliability [46]. The PSWQ has also been shown to have good predictive validity for symptoms of anxiety and depression [60].

The Ruminative Response Scale (RRS; [47]) is a self-report measure of frequency of ruminative responses to depressed mood, with items relating to the self (e.g. 'Think about all your shortcomings, failings, faults and mistakes'), one's symptoms (e.g. 'Think about how hard it is to concentrate') and possible causes and consequences of one's mood (e.g. 'Go away by yourself and think about why you feel this way'). Items are scored from 1 (almost never) to 4 (almost always). Higher scores indicate higher levels of rumination. The RRS

has good internal consistency, moderate test-retest reliability, acceptable convergent validity and good predictive validity [47, 61, 62].

The Patient Health Questionnaire (PHQ-9; [63]) is a nine-symptom measure of depressive symptoms. Scores range from 0-27, with higher scores indicating greater severity. The PHQ-9 is a reliable and valid measure of severity of depressive symptoms [63].

The Generalised Anxiety Disorder Screener (GAD-7; [64]) is a standardised self-report measure of symptoms of anxiety. Scores range from 0-21 and higher scores indicate more severe symptoms. Spitzer, Kroenke, Williams and Löwe [64] demonstrated good validity and reliability of the GAD-7.

Demographics and Treatment At baseline, participants were asked if they had any family history of depression (including whom and how recently) and whether they had experienced any physical, sexual or emotional abuse before the age of 16 (yes/no questions with no further details requested). Participants were asked to report whether they had received any mental health treatments (medication, therapies, use of self-help materials) prior to or during the trial. Timing, duration and (for medication) dosage was recorded.

6.3.6 Randomisation, allocation concealment and blinding

Independent computer-generated block randomisation (block size of 3), stratified by sex (male vs. female) and history of depression (presence or absence of past depressive episodes) was used to allocate participants to the guided i-RFCBT, unguided i-RFCBT or usual care control in a 1:1:1 ratio. Varying block sizes were not used as the 2 levels of stratification ensured it would be difficult for the researcher to anticipate or determine allocation. A third party not involved in assessing or treating the participants implemented the

random allocation sequence and informed the therapist of the condition for each participant. The researcher responsible for recruitment and screening was blind to allocation and unable to influence the order of consents. As a single blind trial, the researcher conducting outcome assessments was blind to allocation. The researcher was not involved with any element of treatment delivery. To preserve researcher blinding, participants were notified of their treatment allocation by a trial therapist. Due to the nature of the intervention, participants and therapists could not be blinded.

6.3.7 Statistical analysis for phase III efficacy trial

Data cleaning followed the protocol set out by Tabachnick and Fidell [65]. Unplanned missing data was handled via Multiple Imputation (MI). Sensitivity analysis, assuming a variety of MI models (Missing at Random; Missing Not at Random), verified the likely impact of missing data. Auxiliary variables were used to improve the estimation of missing data[2]. Primary analyses were conducted on the Intention-To-Treat (ITT) sample. Additional analyses assessed the effect of compliance using the Complier Average Causal Effect (CACE) analysis [66]. CACE provides an unbiased estimate of the benefits of compliance by comparing the compliers in the intervention group to a comparable subgroup of the control group who would have complied had they been offered the intervention. Compliance was defined in the protocol as fully completing at least 4 of 6 modules, i.e., accessing all of the sections in each of

[2] For the ANCOVA models, multiple imputation was used for missing data on the outcome symptom variables (PHQ, GAD, PSWQ, RRS). The MI was conducted using Stata's MI command switch, using a multivariate normality assumption. Baseline scores on each of the outcome variables were used to impute missing values, with baseline characteristics used as auxiliary variables (age, gender, ethnicity, past MDE, past treatment, randomisation arm). These variables were used because any baseline variables that might be associated with the outcome of interest are a good candidate to be included in the MI-model and all these variables are believed to be associated with the missing outcomes of interest.

those modules [45]. Analyses were carried out using statistical software Stata (version-15.1 [67]).

As a prevention study, the primary outcome was the occurrence and time to onset of any depressive episode by 15-month follow-up. In order to investigate this, Cox-proportional hazard models were fitted to the depression event data, with diagnosis of an episode of major depression at any point during the follow-up period as the outcome and time to onset measured in weeks from randomisation date. Participants were censored upon measurement dropout or end of study. The Cox proportional hazard model was initially adjusted for both stratification variables: past depression and gender, as they have previously been found to influence likelihood of depression. Additionally, as baseline stress was expected to increase risk of depression and Topper et al. [27] controlled for stressful life events, severity of baseline stress was included in the model. To examine the hypothesis that i-RFCBT would be especially beneficial in high ruminators experiencing high stress, we further tested the potential interactions between intervention condition and baseline stress, and intervention condition and history of depression within the Cox-proportional hazard analysis.

Secondary outcomes of symptom severity and levels of rumination/worry were examined using mixed model ANCOVAs: between group (ITT/CACE) and repeated measures (3-15-month follow-ups), controlling for baseline symptom levels.

6.3.8 Feasibility and acceptability (Quasi-Phase II pilot arm)

Feasibility of data collection procedures were assessed by measuring missing items on clinical outcome measures, number and timing of drop-outs and whether these varied across arms. The acceptability of the intervention was

assessed using a behavioural index, measuring the number of online modules completed.

6.3.9 Ethical approval and informed consent

Ethical and professional guidelines were followed at all times, in line with Good Clinical Practice guidelines. Ethical approval was obtained from the Ethics Committee of the School of Psychology, University of Exeter (Ref: 2012/554). Participants returned written informed consent including permission to contact their general practitioner (GP) if significant risk was disclosed (see Multimedia Appendix 2).

6.4 Results

6.4.1 Demographics

For brevity, baseline demographics for the three arms are included in Table 6.1. As noted earlier, the primary comparison is guided i-RFCBT versus usual care control, with a separate analysis of the feasibility and acceptability of the adjunct unguided i-RFCBT arm.

6.4.2 Survival analysis: guided i-RFCBT vs. usual care control

Twenty-seven participants in the primary comparison of guided i-RFCBT vs. control completed no follow-ups and no minimum survival time could be estimated[3], so the ITT survival analyses were conducted on $N = 132$ (guided $N = 63$, control $N = 69$). Participants with a family history of depression were more likely to be lost to follow-up than those without: $\chi^2(1) = 3.89$, $P = .049$. No other

[3] In the case of time to event analysis using a survival analysis, the analysis accounts for missing data as anyone dropping out early still contributes data to the point of drop-out i.e. a censored observation. The outcome (i.e. time-to-event) is not imputed in survival analysis. Participants who did not complete any follow-up measures were not included as no outcome event was recorded. Missing data in the covariates may be imputed, but this was not necessary as the baseline variables included in the Cox model did not include missing data (Allison, P. D., 2010).

baseline variables were linked to loss to follow-up: all *t*s on continuous measures < 1.70; all χ^2 on categorical variables < 1.74; all *P*s > .09.

Table 6.1. Baseline characteristics of usual care, guided i-RFCBT and unguided i-RFCBT ITT samples.

	Usual Care (n=77)	Guided i-RFCBT (n=82)	Unguided i-RFCBT (n=76)
Sex: N Female (%)	64 (83)	68 (83)	64 (84)
Age in years: M (SD)	20.27 (1.55)	20.43 (1.65)	20.53 (1.30)
Ethnicity: N White (%)	70 (91)	77 (94)	67 (88)
English mother tongue: N (%)	71 (92)	75 (91)	64 (84)
Previous major depressive episode: N Yes (%)	29 (38)	34 (41)	29 (38)
Received previous mental health treatment: N Yes (%)	38 (49)	38 (46)	31 (41)
Family history of depression: N Yes (%)	39 (51)	42 (51)	33 (43)
Parent with history of depression: N Yes (%)	34 (44)	34 (41)	29 (38)
Reported history of sexual abuse: N Yes (%)	7 (9)	5 (6)	5 (7)
Reported history of physical abuse: N Yes (%)	7 (9)	1 (1)	7 (9)
Reported history of emotional abuse: N Yes (%)	17 (22)	10 (12)	11 (14)
PHQ-9: M (SD)	5.6 (4.1)	5.6 (3.2)	5.4 (3.6)
GAD-7: M (SD)	6.6 (4.3)	7.3 (4.2)	7.1(4.0)
PSWQ: M (SD)	61.9 (9.0)	62.0 (9.5)	60.3 (10.5)
RRS: M (SD)	47.9 (11.1)	49.8 (10.6)	47.2 (10.7)
Number of stressful events in past 3 months: M (SD)	3.6 (2.3)	3.8 (2.4)	3.4 (1.8)
Subjective rating of worst event	2.20 (1.11)	2.57 (0.96)	2.53 (0.92)

Note. ITT=intention-to-treat; PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalised Anxiety Disorder Screener; PSWQ = Penn State Worry Questionnaire; RRS = Ruminative Response Scale.

There was no overall difference in incidence of depression (*P* = .64): 29% (*N* = 18) of participants receiving guided i-RFCBT and 33% (*N* = 23) of participants receiving usual care experienced MDE during the follow-up period. A Cox proportional hazard model was conducted, including past depression, gender

and baseline stress as potential predictors of incidence of depression[4]. Because the majority (83%) of participants were female and there was no significant effect of gender in predicting depression, this variable was removed from the model, such that the final model controlled for past depression and baseline stress. As expected, history of depression significantly increased risk, with participants with a history of depression over two and a half times more likely to experience an MDE than participants without: HR = 2.62, 95% CI [1.37, 5.01], *P* = .004. Baseline stress marginally increased risk of MDE: HR = 1.40, 95% CI [0.99, 1.99], *P* = .06. When controlling for both past depression and baseline stress, there was a 34% reduced risk of depression in the guided i-RFCBT condition relative to usual care, although this difference was not significant: HR = 0.66, 95% CI [0.35, 1.25], *P* = .20 (see Figure 6.2).

[4] This model was reported as it included the stratification variables and controlled for baseline stress, which was significantly different between the two groups. Without controlling for these covariates, the HR = 0.89, 95% CI [0.48, 1.64), *p* = 0.70 for guided vs. control and HR = 0.76, 95% CI [0.40, 1.46], *p* = 0.41 for unguided vs. control.

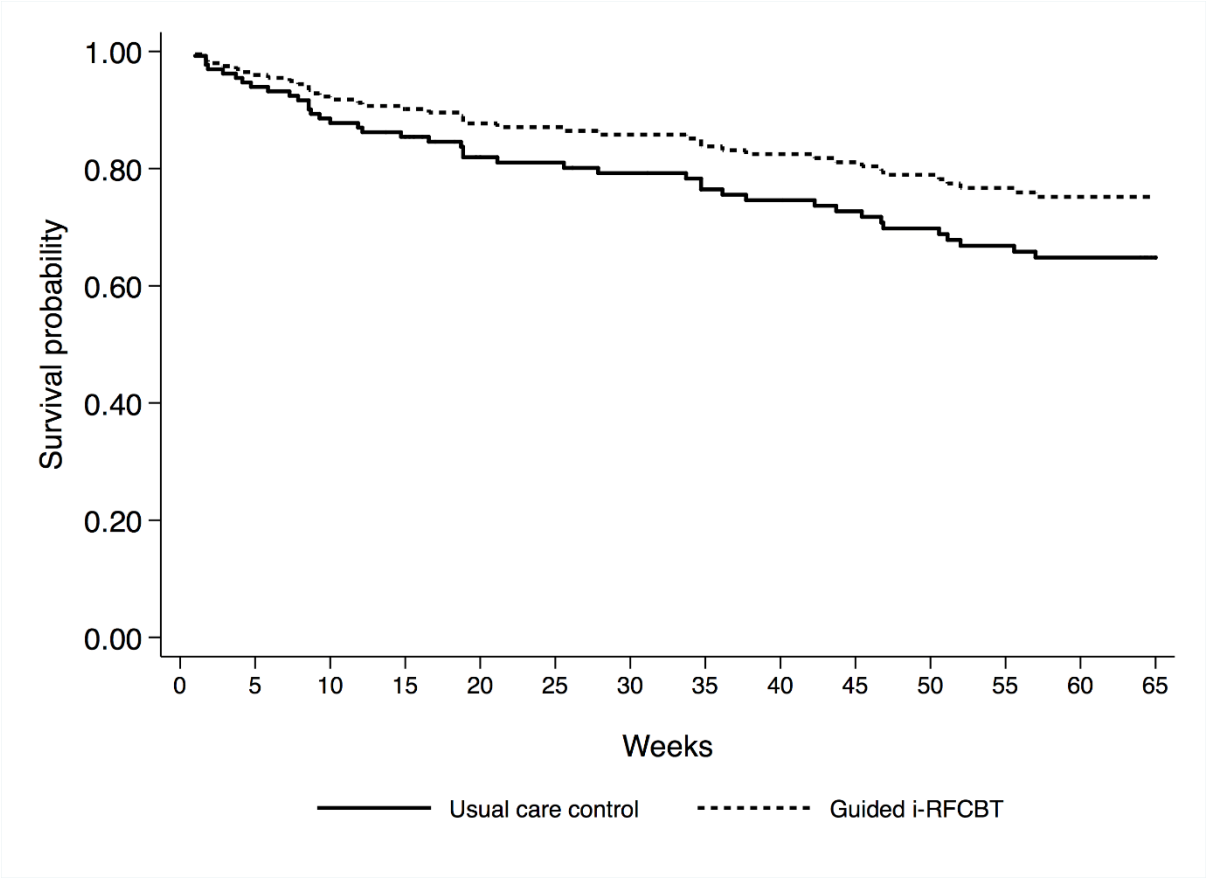


Figure 6.2. Survival curves for guided i-RFCBT and usual care controls, adjusted for past depression and baseline stress.

For Cox-proportional hazard models including the interactions between intervention condition and baseline stress, and intervention condition and history of depression, there was no differential effect of intervention between first onset (i.e., no history of depression) or relapse/recurrence (i.e., prior history of depression) for incidence of major depression and this interaction was removed from the final model (HR: 0.54, 95% CI [0.15, 1.94], *P* = .34; guided i-RFCBT: 38.9% first onset; 61.1% relapse vs. usual care: 36.4% first onset; 63.6% relapse). Both the effects of past depression (HR: 2.52, 95% CI [1.32, 4.81, *P* = .005) and baseline stress (HR: 1.99, 95% CI [1.22, 3.24], *P* = .006)

remained significant[5]. As hypothesised, there was a significant interaction of intervention condition by baseline stress (HR: 0.43, 95% CI [0.21, 0.87], *P* = .02), indicating a greater benefit of guided i-RFCBT relative to usual care (risk of MDE decreased by 57%) for undergraduates with higher baseline stress. Plotting the interaction between intervention group and baseline stress (see Figure 6.3) suggests that at higher levels of stress, guided i-RFCBT markedly reduces the risk of a depressive episode relative to usual care, with this effect reversing at low levels of stress (albeit in a small number of participants, only 13.1% scoring either 0 or 1).

[5] Note that because the interaction effect is now included in the model, the effects of the intervention group and baseline stress cannot be interpreted on their own. Rather these Hazard ratios indicate that, when stress is zero, those who were in the guided intervention condition had a higher risk of experiencing MDE, but the interaction indicates that, as stress level increases, the risk of depression reduces, relative to usual care.

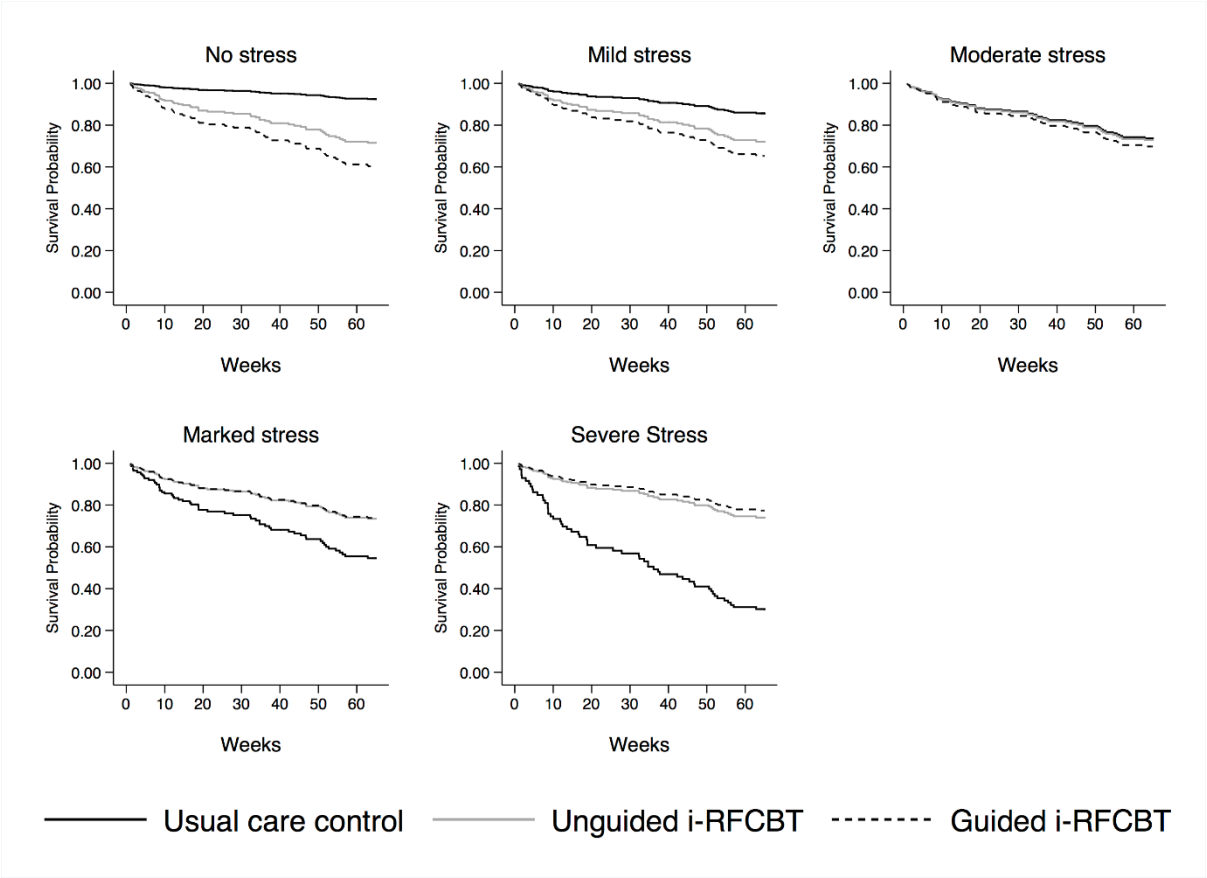


Figure 6.3. Survival curves for guided i-RFCBT, unguided i-RFCBT and usual care controls at each level of baseline stress.

As further sensitivity analyses, to investigate the effect of compliance on outcomes, we conducted a complier average causal effect (CACE) analysis, using the Loeys and Goetghebur [66] method, which only allows for inclusion of the randomisation variable in the model, and using regression based adjustments to include past depression and baseline stress, which compares compliers in the intervention group to all other participants [68]. The mean completion for guided i-RFCBT was 3.46 (*SD* = 2.25) for the full ITT sample (*N* = 159), with 46.34% (38/82) compliant by completing at least 4 of the 6 modules. Rates of compliance were higher among those with follow-up outcome data (*N* = 132) as used for the CACE analysis, at 60.32% (38/63). The results of

the CACE analyses (see Supplement 1) were equivalent to the ITT analysis. We therefore only report the primary ITT analysis.

6.4.3 Secondary analyses on PHQ, GAD, RRS and PSWQ

Baseline adjusted ANCOVAs were conducted for each of the symptom measures, at each of the three follow-ups. Estimated means, between-group differences and confidence intervals are displayed in Table 6.2 for the case completers and following multiple imputations (50 imputations). For the complete cases, at 3 months, rumination scores were significantly lower for guided i-RFCBT relative to usual care; at 6 months, both worry and depression scores were significantly lower for guided i-RFCBT relative to usual care, and there was no evidence of significant between-group differences at 15 months. Similar patterns were found when using multiple imputation to account for differing levels of missing data across the follow-ups.

6.4.4 Retention, acceptability and effect sizes of unguided i-RFCBT

Nineteen (25%) unguided participants did not complete any follow-up assessments. Participants were significantly more likely to be lost to follow-up in unguided i-RFCBT than in usual care: $\chi^2(1) = 4.53$, $P = .03$.

Due to the exploratory nature of the unguided version of i-RFCBT, no formal CACE analysis of compliance was undertaken for the unguided intervention. In the full ITT sample, unguided participants completed an average of 2.66 modules ($SD = 2.35$). Rates of compliance (38.16% unguided) were not significantly different from guided i-RFCBT ($\chi^2(1) = 1.08$, $P = .30$). For the unguided intervention, participants logged in an average of 6.25 times ($SD = 5.21$) and accessed the intervention over an average period of 114.92 days ($SD = 105.51$). The median (interquartile range) was 87 days (22-173). Guided

participants logged in an average of 7.97 times (*SD* = 5.65), and accessed the intervention over an average period of 110.13 days (*SD* = 108.44). The median (interquartile range) was 67 days (38-15).

Table 6.2. Baseline adjusted symptom measures at 3, 6 and 15 months: guided i-RFCBT vs. usual care controls.

Time-point	Measure	Guided i-RFCBT	Usual care		
		Mean [95% CI]	Mean [95% CI]	Difference [95% CI]	MI-Difference [95% CI]
Follow-up 1 (3 months) *N* = 114	PHQ9	4.75 [3.74, 5.76]	5.40 [4.48, 6.33]	-0.65[b] [-2.02; 0.72]	-0.55[b] [-2.05-0.96]
	GAD7	5.58 [4.51, 6.66]	6.27 [5.28, 7.25]	-0.69[b] [-2.15; 0.78]	-0.53[b] [-2.14, 1.09]
	PSWQ	57.27 [54.85, 59.69]	58.45 [56.23, 60.67]	-1.18[b] [-4.46, 2.11]	-0.75[b] [-4.35, 2.86]
	RRS[a]	44.34 [41.66; 47.02]	48.21 [45.73, 50.68]	-3.87[c] [-7.53, -0.21]	-3.69[b] [-8.01, 0.63]
Follow-up 2 (6 months) *N* = 105	PHQ9	3.70 [2.48, 4.92]	5.52 [4.42, 6.62]	-1.82[c] [-3.46, -0.18]	-1.97[c] [-3.87, -.063]
	GAD7	4.72 [3.44, 5.99]	6.06 [4.91, 7.20]	-1.34[b] [-3.05, 0.38]	-1.15[b] [-3.16, 0.85]
	PSWQ	54.83 [52.19, 57.48]	58.41 [56.03, 60.79]	-3.58[c] [-7.14, -0.02]	-2.71[b] [-6.68, 1.25]
	RRS	41.74 [38.15, 45.34]	46.35 [43.12, 49.58]	-4.60[b] [-9.47, 0.26]	-3.98[b] [-9.48, 1.52]
Follow-up 3 (15 months) *N* = 108	PHQ9	4.47 [3.23, 5.71]	4.82 [3.73, 5.91]	-0.35[b] [-2.00, 1.30]	-0.38[b] [-2.30, 1.55]
	GAD7	4.42 [3.16, 5.68]	5.73 [4.62, 6.83]	-1.31[b] [-2.99, 0.38]	-1.10[b] [-2.10, 0.80]
	PSWQ	54.81 [51.71, 57.91]	58.11 [55.39, 60.84]	-3.30[b] [-7.43, 0.82]	-1.74[b] [-6.53, 3.06]
	RRS	46.15 [42.59, 49.72]	44.65 [41.53, 47.78]	1.50[b] [-3.28, 6.28]	1.16[b] [-3.99, 6.31]

Note. PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalised Anxiety Disorder Screener; PSWQ = Penn State Worry Questionnaire; RRS = Ruminative Response Scale.
[a]*N* = 115 for RRS at 3 months due to one partially completed questionnaire set; [b]not significant; [c]*P <.05*.

6.4.5 Estimates of hazard ratios for unguided i-RFCBT vs. usual care

No formal significance analyses were undertaken, but hazard ratios and confidence intervals were estimated relative to usual care. Using a Cox-proportional hazard model including past depression and baseline stress, unguided i-RFCBT showed a 36% reduced risk of developing a depressive

episode relative to controls: HR: 0.64; 95% CI [0.33, 1.24]. A similar interaction between intervention and baseline stress was found as for guided i-RFCBT (HR: 0.48, 95% CI [0.23, 1.00], such that unguided i-RFCBT had larger effect sizes for undergraduates with moderate to severe levels of baseline stress (see Figure 3).

Between group differences for unguided i-RFCBT vs. usual care were estimated with baseline adjusted ANCOVAs for both case completers and using multiple imputations (50 imputations). Estimated means and confidence intervals are displayed in Table 6.3. Due to the exploratory nature of this comparison, significance testing was not conducted. Patterns of change and confidence intervals indicate similar symptom changes to those found in the guided i-RFCBT vs. usual care control ANCOVAs.

Table 6.3. Baseline adjusted symptom measures at 3, 6 and 15 months: unguided i-RFCBT vs. usual care controls.

Time-Point	Measure	Unguided i-RFCBT	Usual care		
		Mean [95% CI]	Mean [95% CI]	Difference [95% CI]	MI-Difference [95% CI]
Follow-up 1 (3 months) *N* = 116	PHQ9	4.02 [3.07, 4.96]	5.21 [4.33, 6.10]	-1.20 [-2.49, 0.10]	-1.18 [-2.65, 0.28]
	GAD7	4.94 [3.90, 5.99]	5.98 [5.01, 6.96]	-1.04 [-2.47, 0.39]	-1.06 [-2.60, 0.49]
	PSWQ	55.77 [53.26, 58.28]	57.60 [55.26, 59.95]	-1.84 [-5.28, 1.61]	-1.35 [-4.87, 2.17]
	RRS	44.47 [41.89, 47.06]	47.01 [44.60, 49.42]	-2.54 [-6.08, 1.01]	-2.42 [-6.19, 1.34]
Follow-up 2 (6 months) *N* = 104	PHQ9	4.38 [3.20, 5.56]	5.35 [4.30, 6.40]	-0.97 [-2.56, 0.61]	-1.04 [-2.89, -0.81]
	GAD7	4.20 [2.96, 5.44]	5.93 [4.83, 7.03]	-1.73 [-3.38, -0.07]	-2.09 [-3.92, -0.28]
	PSWQ	54.51 [51.60, 57.42]	58.06 [55.47, 60.65]	-3.55 [-7.46, 0.36]	-3.35 [-7.36, 0.67]
	RRS	41.27 [38.07, 44.47]	45.20 [42.35, 48.04]	-3.93 [-8.22, 0.37]	-4.12 [-8.94, 0.69]
Follow-up 3 (15 months) *N* = 107	PHQ9	4.20 [3.00, 5.40]	4.69 [3.64, 5.73]	-0.49 [-2.08, 1.11]	-0.92 [-2.61, 0.77]
	GAD7	4.49 [3.28, 5.70]	5.52 [4.46, 6.57]	-1.03 [-2.63, 0.58]	-1.36 [-3.23, 0.52]
	PSWQ	53.78 [50.75, 56.81]	57.56 [54.93, 60.19]	-3.78 [-7.79, 0.24]	-4.34 [-8.57, -0.09]
	RRS	42.07 [38.59, 45.54]	43.85 [40.84, 46.86]	-1.78 [-6.40, 2.83]	-2.61 [-7.93, 2.71]

Note. PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalised Anxiety Disorder Screener; PSWQ = Penn State Worry Questionnaire; RRS = Ruminative Response Scale.

6.5 Discussion

6.5.1 Principal Results and Comparison with Prior Work

The main aim was to test if guided i-RFCBT could be effective in preventing depression in undergraduate students in the UK over one-year follow-up. When controlling for both past depression and baseline stress,

guided i-RFCBT reduced the risk of experiencing an MDE by 34% relative to usual care. Whilst this effect size was not significant and smaller than that found by Topper et al. [27], it is consistent with the wider prevention literature, which reports an average reduction in incidence of 21% [10] and a 28% (IRR = .72) reduction in incidence relative to controls for selective, predominantly CBT, interventions [11]. It may be that the current study was underpowered to detect a main preventive effect of i-RFCBT as it used a larger effect size estimate derived from Topper et al. [27].

As hypothesized, guided i-RFCBT was significant at preventing the onset of MDE in high-risk undergraduates relative to usual care when they experienced moderate or above levels of baseline stress, with a hazard ratio of 0.43 when moderated by baseline stress. This is consistent with theoretical models of rumination and the RFCBT treatment approach. The tendency to ruminate about difficulties or low mood is more likely to increase risk for depression in the context of stressful events, which activates that habitual tendency and provides subject matter to ruminate about. Even someone with a habitual tendency to ruminate is less likely to have frequent rumination in the absence of any difficulties. Furthermore, one key mechanism by which rumination is proposed to increase vulnerability to depression is by exacerbating and prolonging negative affect and distress [29, 30]: rumination does not have deleterious effects in the absence of negative mood, and it is thus the confluence of stressful events that lower mood and the tendency to ruminate that particularly confers risk for depression [32]. This pattern of results suggests a partial replication of Topper et al. [27], by indicating that guided i-RFCBT may be a helpful preventive intervention for university students with

high levels of rumination and worry, who also experience at least moderate levels of stress.

We note that the observed interaction between i-RFCBT and baseline stress could also be interpreted as indicating RFCBT is unhelpful compared to usual care, for users who are experiencing little to no current stress. However, given the small number of participants reported low levels of baseline stress, this reversal is based on low power, and needs to be treated with caution.

The findings on the symptom measures suggest guided i-RFCBT was effective in the short to medium term, by reducing rumination, worry, and symptoms of depression at 3 and 6 months relative to usual care, but that these improvements were not sustained over the longer term. Watkins and Nolen-Hoeksema [55] hypothesised that rumination could be conceptualised as a learnt habit, triggered by particular cues such as low mood. Within this analysis, successful long-term reduction of the ruminative habit requires extensive repetition and rehearsal of alternative more adaptive responses to the triggers for rumination. It may be that i-RFCBT was too brief or that participants did not practise enough to produce long-term change in the ruminative habit. It may also be that further engagement and booster sessions some months after the initial intervention phase would enhance the longer-term effects of the intervention [69]. These could take the form of explicit reminders to practice techniques (flashcards, text/email reminders; [70]) and/or increasing the generalisability of the new more helpful techniques across a broader range of contexts [70].

One possible reason for the difference in findings between the current study and Topper et al. [27] is the means of assessing onset of depression: RESPOND used structured clinical interview, whereas Topper et al. [27] used

cut-offs on self-report questionnaires, which may overestimate incidence. Another potential explanation is the different samples. Although their sample included university students, the average age was 17.5 years, compared to 20.4 years in RESPOND. Cases of depression begin to rise steeply from the age of 14 [13] so it may be that the developmental risks during mid to late adolescence differ from those in university students and either that i-RFCBT was more efficacious in younger participants or the base-rate was higher in the younger sample, increasing the power of the trial.

Compliance rates and the pattern of findings and preliminary effect sizes and confidence intervals for unguided i-RFCBT were similar to those for guided i-RFBCT[6]. These findings are in contrast to the literature on web-based acute treatment for depression, which generally demonstrates larger effect sizes for guided interventions relative to unguided [41-43]. This benefit of therapist guidance has also previously been found for indicated preventive interventions in university students [71]. As a preliminary finding from a feasibility pilot, further large-scale trials are needed to confirm whether this potential equivalence between unguided and guided i-RFCBT is robust. We speculate that only selecting high-ruminating participants for the trial meant that i-RFCBT was highly relevant and engaging to participants, thus ameliorating the relative benefits of guidance on treatment motivation and completion.

Given the need for widespread dissemination of preventive interventions, an efficacious unguided intervention would be valuable, even if it

[6] Guided participants completed a mean of 3.46 modules (58% of the total content). While this is lower than the amount completed in previous trials of guided iCBT (average of 80.8% of content; van Ballegooijen et al., 2014), it is comparable to the amount completed in the previous trial of i-RFCBT (Topper et al., 2017). Reasons for there being lower levels of compliance for i-RFCBT than other internet interventions could include the sample (students face external academic pressures, high ruminators are prone to avoidance); structural issues with the platform (e.g. the lack of flexiblility); or dropping out because symptoms improve early on.

had somewhat reduced effect sizes relative to the guided version, because it would not be constrained by therapist numbers or availability unlike a guided treatment and could be enormously scaled up to increase accessibility [44]. Additionally, unguided interventions may benefit a previously unreached population as many university students do not seek professional help for mental health difficulties [22, 23] and could therefore be more attracted to self-help interventions. In support of this, an unguided preventive intervention for students with elevated distress ratings reduced depressive symptoms relative to usual care at 2 months follow-up [72], with two thirds of the trial completers reporting unmet need (needing but not seeking help) in the previous year. As i-RFCBT targets worry and rumination, rather than focusing on depression, this may further attract those who prefer self-help to manage their symptoms as worry is a common experience without the perceived stigma of mental illness [27]. These initial findings on the acceptability and effect sizes of the unguided version provide some promise in terms of potential benefits and suggests the value of further studies to formally test unguided i-RFCBT as a preventive intervention.

Despite the need for larger scale trials to test the robustness of these findings, several strengths of RESPOND are identified. Firstly, the RESPOND trial addressed some of the methodological limitations of the Topper et al. [27] trial by including diagnostic interviewing. This allowed for retrospective diagnoses, capturing any episodes occurring between follow-up interviews, as well as baseline history of depression to assess the effect of prior history on risk of a further MDE.

The use of online and telephone-based measures allowed for recruitment throughout the UK, with participants from a wide range of university

departments and geographical locations, increasing the generalisability of the findings within this demographic. The target sample size was achieved through this recruitment strategy and this would therefore be a suitable approach for a larger scale trial of i-RFCBT.

6.5.2 Limitations

There were several limitations to the study. First, the sample was disproportionately female, limiting the generalisability of the findings. However, females consistently report higher levels of rumination [73] and higher levels of depression, so a trial selecting on this basis will necessarily attract more female participants.

Second, despite a successful recruitment strategy, there was a considerable proportion of missing data at follow-up, particularly in the intervention conditions (albeit in the context of planning the sample size for 20% drop-out attrition). Additionally, follow-up assessments were sometimes incomplete as participants did not always return the questionnaires after the follow-up interview, despite reminders being sent. Future trials should therefore further emphasise to participants the importance of follow-up data during the baseline assessment and ensure all measures are completed during the interview. Third, common to many e-Mental health trials, the participants were not blind to the treatment condition, and, as such, results could have been influenced by response bias and expectancy effects.

6.5.3 Conclusions

Despite these limitations, taken together, the findings from the Topper et al. [27] trial and from the current RESPOND trial, suggest that i-RFCBT is an effective and acceptable intervention for preventing depression in adolescents

and undergraduates experiencing high levels of rumination and worry. This demonstrates the value in targeting a preventive intervention at identified risk factors. This intervention may be particularly effective in individuals experiencing high levels of stress. The initial findings relating to unguided i-RFCBT suggest this may be efficacious in preventing depression, which, if shown to be robust in a fully powered trial, would have significant implications for the scalability of i-RFCBT.

6.6 References

1. World Health Organization. Depression and other common mental disorders: global health estimates. Geneva, Switzerland: WHO; 2017. Accessed: 23/04/2018. Webcitation: http://www.webcitation.org/6ytV1RIIN

2. Eisenberg D, Hunt J, Speer N, Zivin K. Mental health service utilization among college students in the United States. J Nerv Ment Dis 2011;199(5):301-8 PMID: 21543948.

3. Griffiths CA, Griffiths LJ. Recovery and reliable change rates for patients scoring severe on depression, anxiety or impaired functioning in a psychological therapies service: IAPT. Mental Health Review Journal 2015;20(1):28-35.

4. Judd LL. The clinical course of unipolar major depressive disorders. Arch Gen Psychiatry 1997;54(11):989-91 PMID: 9366654.

5. Andrews G, Issakidis C, Sanderson K, Corry J, Lapsley H. Utilising survey data to inform public policy: comparison of the cost-effectiveness of treatment of ten mental disorders. Br J Psychiatry 2004;184:526-33 PMID: 15172947.

6. Topper M, Emmelkamp PMG, Ehring T. Improving prevention of depression and anxiety disorders: Repetitive negative thinking as a promising target. Applied and Preventive Psychology 2010;14(1-4):57-71.

7. Horowitz JL, Garber J. The prevention of depressive symptoms in children and adolescents: A meta-analytic review. J Consult Clin Psychol 2006;74(3):401-15 PMID: 16822098.

8. Merry SN, Hetrick SE, Cox GR, Brudevold-Iversen T, Bir JJ, McDowell H. Psychological and educational interventions for preventing depression in children and adolescents. The Cochrane database of systematic reviews 2011(12):CD003380 PMID: 22161377.

9. Stice E, Shaw H, Bohon C, Marti CN, Rohde P. A meta-analytic review of depression prevention programs for children and adolescents: factors that predict magnitude of intervention effects. J Consult Clin Psychol 2009;77(3):486-503 PMID: 19485590.

10. van Zoonen K, Buntrock C, Ebert DD, Smit F, Reynolds CF, 3rd, Beekman AT, et al. Preventing the onset of major depressive disorder: a meta-analytic review of psychological interventions. Int J Epidemiol 2014;43(2):318-29 PMID: 24760873.

11. Cuijpers P, van Straten A, Smit F, Mihalopoulos C, Beekman A. Preventing the onset of depressive disorders: a meta-analytic review of psychological interventions. Am J Psychiatry 2008;165(10):1272-80 PMID: 18765483.

12. Muñoz RF, Cuijpers P, Smit F, Barrera AZ, Leykin Y. Prevention of major depression. Annu Rev Clin Psychol 2010;6:181-212 PMID: 20192789.

13. Hankin BL, Young JF, Abela JR, Smolen A, Jenness JL, Gulley LD, et al. Depression from childhood into late adolescence: Influence of gender, development, genetic susceptibility, and peer stress. J Abnorm Psychol 2015;124(4):803-16 PMID: 26595469.

14. McManus S, Bebbington P, Jenkins R, Brugha T. Mental health and wellbeing in England: Adult Psychiatric Morbidity Survey 2014. Leeds, UK: NHS Digital; 2016. Accessed 23/04/2018. Webcitation: http://www.webcitation.org/6ytaQR4yA

15. Pine DS, Cohen P, Gurley D, Brook J, Ma Y. The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. Arch Gen Psychiatry 1998;55(1):56-64 PMID: 9435761.

16. Hysenbegasi A, Hass SL, Rowland CR. The impact of depression on the academic productivity of university students. J Ment Health Policy Econ 2005;8(3):145-51 PMID: 16278502.

17. Ibrahim AK, Kelly SJ, Adams CE, Glazebrook C. A systematic review of studies of depression prevalence in university students. J Psychiatr Res 2013;47(3):391-400 PMID: 23260171.

18. Aalto-Setälä T, Marttunen M, Tuulio-Henriksson A, Poikolainen K, Lönnqvist J. One-month prevalence of depression and other DSM-IV disorders among young adults. Psychol Med 2001;31(5):791-801 PMID: 11459377.

19. Newman DL, Moffitt TE, Caspi A, Magdol L, Silva PA, Stanton WR. Psychiatric disorder in a birth cohort of young adults: prevalence, comorbidity, clinical significance, and new case incidence from ages 11 to 21. J Consult Clin Psychol 1996;64(3):552-62 PMID: 8698949.

20. National Institute of Mental Health. Depression and college students. Bethesda, MD: NIMH; 2003. Accessed: 23/04/2018. Webcitation: http://www.webcitation.org/6ytaW7SOz

21. Eisenberg D, Golberstein E, Hunt JB. Mental Health and Academic Success in College. The BE Journal of Economic Analysis & Policy 2009;9(1).

22. Eisenberg D, Gollust SE, Golberstein E, Hefner JL. Prevalence and correlates of depression, anxiety, and suicidality among university students. Am J Orthopsychiatry 2007;77(4):534-42 PMID: 18194033.

23. National Union of Students, editor Lost in transition? – provision of mental health support for year olds moving to further and higher education. All Party Parliamentary Group on Students; 2015; London, UK. Accessed: 23/04/2018. Webcitation: http://www.webcitation.org/6ytahrOtN

24. Andersson G. The promise and pitfalls of the internet for cognitive behavioral therapy. BMC Med 2010;8:82 PMID: 21138574.

25. Richardson T, Stallard P, Velleman S. Computerised cognitive behavioural therapy for the prevention and treatment of depression and anxiety in children and adolescents: a systematic review. Clin Child Fam Psychol Rev 2010;13(3):275-90 PMID: 20532980.

26. Davies EB, Morriss R, Glazebrook C. Computer-delivered and web-based interventions to improve depression, anxiety, and psychological well-being of university students: a systematic review and meta-analysis. J Med Internet Res 2014;16(5):e130 PMID: 24836465.

27. Topper M, Emmelkamp PM, Watkins E, Ehring T. Prevention of anxiety disorders and depression by targeting excessive worry and rumination in adolescents and young adults: A randomized controlled trial. Behav Res Ther 2017;90:123-36 PMID: 28049069.

28. Watkins ER, Mullan E, Wingrove J, Rimes K, Steiner H, Bathurst N, et al. Rumination-focused cognitive-behavioural therapy for residual depression: phase II randomised controlled trial. Br J Psychiatry 2011;199(4):317-22 PMID: 21778171.

29. Watkins ER. Constructive and unconstructive repetitive thought. Psychol Bull 2008;134(2):163-206 PMID: 18298268.

30. Nolen-Hoeksema S, Wisco BE, Lyubomirsky S. Rethinking Rumination. Perspect Psychol Sci 2008;3(5):400-24 PMID: 26158958.

31. Morrison R, O'Connor RC. Predicting psychological distress in college students: the role of rumination and stress. J Clin Psychol 2005;61(4):447-60 PMID: 15468342.

32. Ciesla JA, Felton JW, Roberts JE. Testing the cognitive catalyst model of depression: does rumination amplify the impact of cognitive diatheses in response to stress? Cogn Emot 2011;25(8):1349-57 PMID: 21432645.

33. Connolly SL, Alloy LB. Rumination interacts with life stress to predict depressive symptoms: An ecological momentary assessment study. Behav Res Ther 2017;97:86-95 PMID: 28734979

34. Ehring T, Zetsche U, Weidacker K, Wahl K, Schonfeld S, Ehlers A. The Perseverative Thinking Questionnaire (PTQ): validation of a content-independent measure of repetitive negative thinking. J Behav Ther Exp Psychiatry 2011;42(2):225-32 PMID: 21315886.

35. Nolen-Hoeksema S, Watkins ER. A Heuristic for Developing Transdiagnostic Models of Psychopathology: Explaining Multifinality and Divergent Trajectories. Perspect Psychol Sci 2011;6(6):589-609 PMID: 26168379.

36. Abela JR, Brozina K, Haigh EP. An examination of the response styles theory of depression in third- and seventh-grade children: a short-term longitudinal study. J Abnorm Child Psychol 2002;30(5):515-27 PMID: 12403154.

37. McLaughlin KA, Hatzenbuehler ML. Mechanisms linking stressful life events and mental health problems in a prospective, community-based sample of adolescents. J Adolesc Health 2009;44(2):153-60 PMID: 19167664.

38. Nolen-Hoeksema S, Stice E, Wade E, Bohon C. Reciprocal relations between rumination and bulimic, substance abuse, and depressive symptoms in female adolescents. J Abnorm Psychol 2007;116(1):198-207 PMID: 17324030.

39. Schwartz JAJ, Koenig LJ. Response styles and negative affect among adolescents. Cognitive Therapy and Research 1996;20(1):13-36.

40. First MB, Spitzer RL, Gibbon M, Williams JBW. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition With Psychotic Screen (SCID-I/P W/ PSY SCREEN). New York: Biometrics Research, New York State Psychiatric Institute; 2002.

41. Andersson G, Cuijpers P. Internet-based and other computerized psychological treatments for adult depression: a meta-analysis. Cogn Behav Ther 2009;38(4):196-205 PMID: 20183695.

42. Gellatly J, Bower P, Hennessy S, Richards D, Gilbody S, Lovell K. What makes self-help interventions effective in the management of depressive symptoms? Meta-analysis and meta-regression. Psychol Med 2007;37(9):1217-28 PMID: 17306044.

43. Spek V, Cuijpers P, Nyklicek I, Riper H, Keyzer J, Pop V. Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. Psychol Med 2007;37(3):319-28 PMID: 17112400.

44. Cuijpers P, Riper H, Andersson G. Internet-based treatment of depression. Current Opinion in Psychology 2015;4:131-5.

45. Cook L, Watkins E. Guided, internet-based, rumination-focused cognitive behavioural therapy (i-RFCBT) versus a no-intervention control to prevent depression in high-ruminating young adults, along with an adjunct assessment of the feasibility of unguided i-RFCBT, in the REducing Stress and Preventing Depression trial (RESPOND): study protocol for a phase III randomised controlled trial. Trials 2016;17:1 PMID: 26725476.

46. Meyer TJ, Miller ML, Metzger RL, Borkovec TD. Development and validation of the Penn State Worry Questionnaire. Behav Res Ther 1990;28(6):487-95 PMID: 2076086.

47. Nolen-Hoeksema S, Morrow J. A prospective study of depression and posttraumatic stress symptoms after a natural disaster: the 1989 Loma Prieta Earthquake. J Pers Soc Psychol 1991;61(1):115-21 PMID: 1890582.

48. Topper M, Emmelkamp PM, Watkins E, Ehring T. Development and assessment of brief versions of the Penn State Worry Questionnaire and the Ruminative Response Scale. The British journal of clinical psychology 2014;53(4):402-21 PMID: 24799256.

49. Kroenke K, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. J Affect Disord 2009;114(1-3):163-73 PMID: 18752852.

50. Bebbington PE, Nyani T. The Psychosis Screening Questionnaire. International Journal of Methods in Psychiatric Research 1995;5:11-9.

51. Watkins ER, Scott J, Wingrove J, Rimes K, Bathurst N, Steiner H, et al. Rumination-focused cognitive behaviour therapy for residual depression: a case series. Behav Res Ther 2007;45(9):2144-54 PMID: 17367751.

52. Watkins ER. Rumination-focused Cognitive Behavioural Therapy for Depression. New York: Guilford Press; 2016. ISBN: 9781462525102.

53. Watkins ER, Moberly NJ, Moulds ML. Processing mode causally influences emotional reactivity: distinct effects of abstract versus concrete construal on emotional response. Emotion 2008;8(3):364-78 PMID: 18540752.

54. Watkins ER, Taylor RS, Byng R, Baeyens C, Read R, Pearson K, et al. Guided self-help concreteness training as an intervention for major depression in primary care: a Phase II randomized controlled trial. Psychol Med 2012;42(7):1359-71 PMID: 22085757.

55. Watkins ER, Nolen-Hoeksema S. A habit-goal framework of depressive rumination. J Abnorm Psychol 2014;123(1):24-34 PMID: 24661156.

56. Minddistrict. URL: https://www.minddistrict.com. Accessed: 19/06/2018. Webcitation: http://www.webcitation.org/70IFG4ZML

57. Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. Ann Behav Med 2013;46(1):81-95 PMID: 23512568.

58. Lobbestael J, Leurgans M, Arntz A. Inter-rater reliability of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I) and Axis II Disorders (SCID II). Clin Psychol Psychother 2011;18(1):75-9 PMID: 20309842.

59. Hammen C. Episodic Life Event Interview: UCLA Stress Interview. Los Angeles, CA: UCLA Department of Psychology; 2004.

60. Hong RY. Worry and rumination: differential associations with anxious and depressive symptoms and coping behavior. Behav Res Ther 2007;45(2):277-90 PMID: 16635479.

61. Butler LD, Nolen-hoeksema S. Gender differences in responses to depressed mood in a college sample. Sex Roles 1994;30(5-6):331-46.

62. Nolen-Hoeksema S. The role of rumination in depressive disorders and mixed anxiety/depressive symptoms. J Abnorm Psychol 2000;109(3):504-11 PMID: 11016119.

63. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;16(9):606-13 PMID: 11556941.

64. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006;166(10):1092-7 PMID: 16717171.

65. Tabachnick BG, Fidell LS. Using multivariate statistics 4th edn. Needham Heights, MA: Allyn & Bacon; 2001. ISBN: 9780321056771.

66. Loeys T, Goetghebeur E. A causal proportional hazards estimator for the effect of treatment actually received in a randomized trial with all-or-nothing compliance. Biometrics 2003;59(1):100-5 PMID: 12762446.

67. StataCorp. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC; 2017.

68. Odondi L, McNamee R. Performance of statistical methods for analysing survival data in the presence of non-random compliance. Stat Med 2010;29(29):2994-3003 PMID: 20963732.

69. Van Voorhees BW, Mahoney N, Mazo R, Barrera AZ, Siemer CP, Gladstone TR, et al. Internet-based depression prevention over the life course: a call for behavioral vaccines. Psychiatr Clin North Am 2011;34(1):167-83 PMID: 21333846.

70. Hertel PT, Mathews A. Cognitive Bias Modification: Past Perspectives, Current Findings, and Future Applications. Perspect Psychol Sci 2011;6(6):521-36 PMID: 26168375.

71. Conley CS, Durlak JA, Shapiro JB, Kirsch AC, Zahniser E. A Meta-Analysis of the Impact of Universal and Indicated Preventive Technology-Delivered Interventions for Higher Education Students. Prevention science : the official journal of the Society for Prevention Research 2016;17(6):659-78 PMID: 27225631.

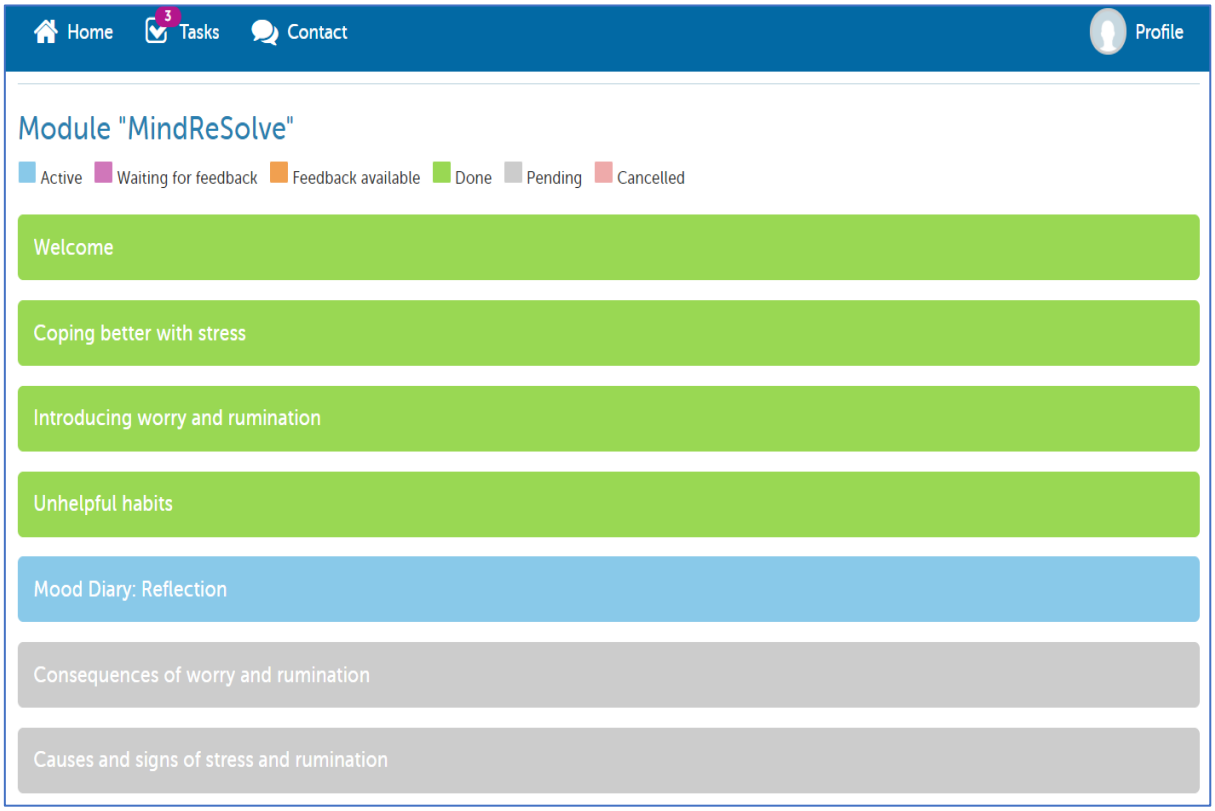
72. Lintvedt OK, Griffiths KM, Sorensen K, Ostvik AR, Wang CE, Eisemann M, et al. Evaluating the effectiveness and efficacy of unguided internet-based self-help intervention for the prevention of depression: a randomized controlled trial. Clin Psychol Psychother 2013;20(1):10-27 PMID: 21887811.

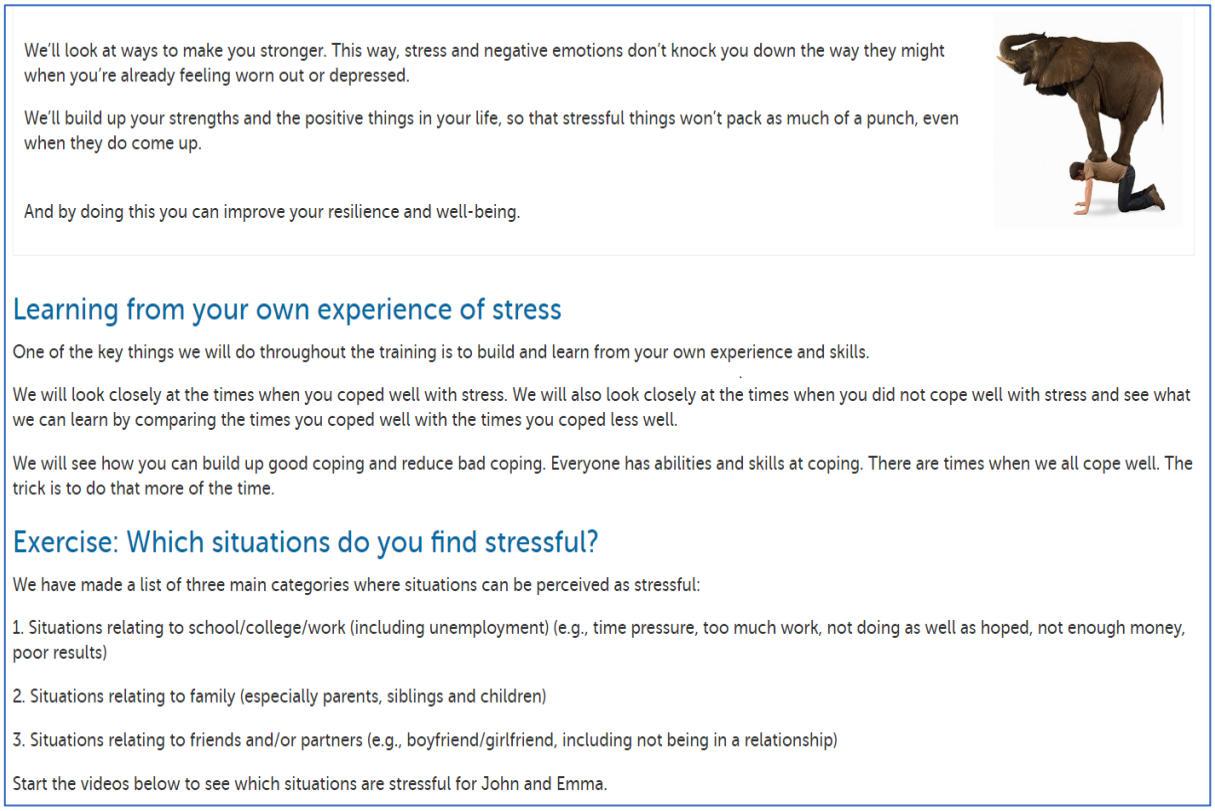
73. Robichaud M, Dugas MJ, Conway M. Gender differences in worry and associated cognitive-behavioral variables. J Anxiety Disord 2003;17(5):501-16 PMID: 12941362.

Supplementary file 1: Complier analyses for guided i-RFCBT vs. controls

By the Loeys and Goethghebur (2003) method, compliers in guided i-RFCBT did not have reduced incidence of depression relative to estimated compliers in usual care (HR: 0.81, 95% CI [0.33, 2.53], *P* = .69). Similarly, when regression-based adjustments for past depression and baseline stress were included, compliers in guided i-RFCBT did not have significantly reduced incidence of depression relative to non-compliers (HR: 0.58, 95% CI [0.22, 1.50], *P* = .26). However, compliance interacted with baseline stress, so that compliers for guided i-RFBCT had reduced incidence relative to non-compliers at higher levels of stress (HR: 0.35, 95% CI [0.16, 0.75], *P* = .01).

Multimedia Appendix 1 i-RFCBT Screenshots





Now, practise using the Mood Diary, by completing one for today and yesterday combined.

- Across today and yesterday, think of a time during either day when you felt particularly **bad.** For example you could have been upset, depressed, nervous, or angry. Write down when this was and what the situation was. Describe which emotion you felt (in one or two words, and give a rating out of 10), how you responded (including whether you ruminated) and what the consequence of the way you responded was.
- Do the same for another time over the last 2 days when you felt **good, or a time when you felt a bit better**. Fill in when this was, what the situation was. Describe which emotion you felt (and give a rating out of 10), how you responded and what the consequence was.

	Time Felt Worse	Time Felt Better
Write down what was going on when you felt that way. When was this? Where were you, what were you doing, who was around?		
Write down the emotion(s) you felt and rate on sliding scale from 0-10. You need to move the slider for the computer to register your response, so if you want to indicate 0, move the slider along a bit and then back to 0.		

Learning to respond differently (and better) to stress

We can also start to make plans to do something different in response to the warning signs in order to stop the stress getting worse and to have a more effective response. These plans are a way to "*nip problems in the bud*" and to stop stress building up.

These plans only need to be simple plans of the following form - if I notice this sign of stress/ warning sign/ trigger, then I can do this more effective alternative. We call these plans **"If – Then" plans.**

For example, if feeling tense is a warning sign that you are about to worry, which it is for many people, then you could have a plan like "If I notice that I am getting tense, then I can do something relaxing to stop myself getting more wound up".

Emma

Emma knows that she will feel bad when she is alone at home and doesn't have anything to do. Now, watch the next video in which Emma tells you how she could respond to this situation in order to feel better.

Listening exercise

During the next listening exercise you are going to make a mental link between being faced with this problem and thinking it through in a concrete way. As best you can, try to keep the following plan in mind:

When I

notice my warning signs and stress signals,

I will

focus on being in the Present, so that I can come up with helpful HOW questions.

0:00

What was the effect of this exercise on your feelings, thoughts and bodily sensations?

Welcome to the fourth modu Conversations line training! You've already finished half of the training. We've gone through a lot of information over the last few weeks. Hopefully you feel like you've learned something from it and it has helped you to start to feel more in control of your stress. This week you will be taught some new strategies and tools to use in stressful situations.

Before we move on, let's have a quick look at what you learned last week.

Looking back at last week's module

Last week you practiced two new strategies.

First, you learned to **relax and focus on the present** when you notice stress and tension, so that you can calm down, reduce the tension, and make a clearer decision about what to do next.

Second, you learned to think about your problems in a concrete and specific way by **asking yourself How-questions**. This concrete thinking helps to get problems into perspective and reduce overgeneralization, leads to better problem-solving and moves you toward action.

How did it go with...?

Over the last week hopefully you practised being concrete and relaxing by repeatedly listening to the audio-recordings. You also continued to practise your IF-THEN plans in daily life.

Were you able to try out one or more of your IF-THEN plans? If so, which one(s)?

Over the last two weeks, how often have you been bothered by any of the following problems? Tick each relevant box.

	Not at all	Several days	More than half the days	Nearly every day
Little interest or pleasure in doing things	○	○	◉	○
Feeling down, depressed, or hopeless	○	○	◉	○
Trouble falling or staying asleep or sleeping too much	○	○	◉	○
Feeling tired or having little energy	○	○	◉	○
Poor appetite or overeating	○	○	◉	○
Feeling bad about yourself –or that you are a failure or have let yourself or your family down	○	○	◉	○
Trouble concentrating on things, such as reading the newspaper or watching television	○	○	◉	○
Moving or speaking so slowly that other people could have noticed. Or the opposite –being so fidgety of restless that you have been moving around a lot more than usual	○	○	◉	○
Thoughts that you would be better off dead, or of hurting yourself in some way	○	○	◉	○

Your responses on this questionnaire suggest you have been thinking about death or harming yourself. If you have had thoughts of suicide, we strongly recommend you contact your family doctor or general practitioner RIGHT AWAY for advice and tell them how you are feeling. If you don't think you can stay safe, please go to the nearest hospital accident and emergency room. If none of these options are available, please contact a family member or a trusted friend, so that you won't be alone right now. If your concerns are less urgent and you would find it helpful to talk confidentially about your feelings you can contact the Samaritans www.samaritans.org or www.befrienders.org.

Multimedia Appendix 2 RESPOND information sheet and consent form

Participant information sheet

Study Title: Targeting worry and rumination to prevent the onset of depression in young adults: A randomised-controlled trial comparing guided and unguided internet-based rumination focused cognitive behavioural therapy and a no treatment control.

This study is being conducted as a PhD project by Lorna Cook, supervised by Professor Edward Watkins, at the Mood Disorders Centre, University of Exeter. Please take a few minutes to read this information sheet and consent form carefully. Your participation is entirely your choice. Please take your time to think about whether or not you would like to participate. If you have any questions, please contact Lorna lzc204@exeter.ac.uk.

Why is this study being done? The purpose of the study is to investigate whether an internet-based therapy targeting worry and rumination is able to prevent depression in young adults. The therapy aims to help people to find better ways of handling day-to-day stress and reduce their risk of future problems, such as depression and anxiety. There are some positive early findings from the Netherlands to suggest that this therapy might be effective in preventing depression in teenagers and young adults. We are interested to find out if the same therapy might be effective in preventing depression in young adults in the UK.

As the therapy aims to target worry and rumination and prevent depression, it is important that participants have elevated levels of worry and rumination but are not currently depressed. You would still be eligible to take part if you have a history of depression, provided you are currently well.

What will happen if I agree to take part in the study?

- You will participate in a brief telephone interview to assess your eligibility, current and past symptoms of depression.
- If it is confirmed during the interview that you are eligible for the trial, you will be asked whether you consent to take part. You may give verbal consent immediately and return the consent form after the interview, or you can take some time to think about it and return the consent form if you decide to participate.
- The researcher will ask you to complete some baseline measures. You can choose to complete these during your telephone interview or ask for them to be sent to you to complete on paper/electronically. These questionnaires will assess symptoms of depression and anxiety. The baseline measures will also ask some brief questions about some risk factors for depression.
- To participate, you will need to provide us with a current email address, telephone number and your general practitioner's name and contact details.
- Once we have received your written consent, you will be allocated by chance to receive either internet-based rumination-focused CBT (RFCBT) guided by a therapist, a self-help version of internet-based RFCBT or to a no treatment control group. There is a 2/3 chance of

receiving some form of the therapy. However, we don't yet know if this therapy is effective in preventing depression, which is why the control group is so important.

<u>If you are allocated to the guided therapy group:</u>

- You will be allocated to a trained online therapist who will guide you through the internet therapy. They will give you feedback on the exercises and you can also send them messages.
- You will be given a log-in and can work through the modules at a time that suits you.
- The therapy consists of six modules and each module should take one to two weeks to complete.
- You will be asked to complete some questions about your mood and depressive symptoms at the end of each module.
- You will have access to the internet therapy for the whole length of the follow-up period so that you can continue to practise the techniques if you wish.

<u>If you are allocated to the unguided therapy group</u>

- You will have access to a self-help version of the internet therapy, which contains the same content but without the therapist contact.
- This therapy will also consist of six modules and you can choose how quickly or slowly you complete them.
- There will be no-one giving feedback on your responses while you are working through the therapy. However, a member of the team will

monitor responses weekly in order to check for and follow up on any risk reported.

- The programme will save your answers and the research team will view these as part of the data analysis.

If you are allocated to the control group:

- You will be asked to carry on as normal. If you feel the need, you will be allowed to access any other treatments of your choice throughout the study.
- We will ask you at each follow-up to tell us what treatments, if any, you have used so that we can take these into account in our results.

Follow-up measures:

- All participants will be contacted at regular intervals (initially at 3 months from entering the study, and then 3 months and 1 year after that first follow-up) and asked to complete questionnaires about worry, rumination and symptoms of anxiety and depression. The same researcher who conducted your screening interview will also ask you to repeat that interview at each follow-up point. This longer term follow-up data is really valuable in helping us to understand if the internet therapy works or not.
- With your permission, each of the telephone interviews will be audio-recorded to enable us to check the conduct and reliability of the interviews.

What side effects or risks can I expect from being in the study?

The risks of participating in the study are minimal. There are no known side effects of the therapy and controls will simply be asked to carry on as normal. However, given the nature of the topic it is important to consider the following points before deciding whether or not to participate:

- Some of the questions ask about symptoms of depression or anxiety, including suicidal thoughts. You may find answering some of these questions makes you feel uncomfortable. If at any point you do not wish to answer a particular question you can simply refuse and move to the next question without giving any reason for doing so.
- If at any stage you are thinking about suicide, we urge you to speak to your GP or go to the nearest Accident and Emergency or phone one of the suicide hotlines at www.samaritans.org or www.befrienders.org
- If you report any suicidal thoughts on the research measures, the researcher will ask you some more detailed questions about your thoughts and feelings. The researcher is not a clinician and will follow a well-established procedure for assessing and acting on suicide risk to ensure you get appropriate clinical support. It may be necessary for the researcher to contact your GP directly to inform them of your difficulties. Depending on your responses, this would involve either sending a letter to your GP to notify them of your thoughts or phoning your GP to suggest they meet with you. In urgent cases, your GP or an ambulance would be contacted while you were still on the phone, in order to obtain immediate clinical help.
- For those in both the guided and unguided therapy, your responses on the questionnaires at the end of each module will be closely monitored and any suicidal thoughts you report will be followed up using the same

procedure above to obtain appropriate clinical support for you. In the guided group, your therapist will see your responses when you submit a module and will follow up any risk as soon as possible. In the unguided group, as you are free to work through the modules at your own pace and we will not know when you have completed a particular module, a member of the team will log in on a weekly basis to check for any risk reported. Again, they will follow the procedure outlined above.

- In the control group, any suicidal thoughts will only be assessed during the follow-up measures.
- Your symptoms may not improve, or may get worse over the course of the study. We have good reason to believe that the therapy will help but we cannot guarantee that it will work for any one particular person.
- This is a research trial and we cannot provide treatment or support beyond what is included in the internet therapy. Your GP retains responsibility for your clinical care throughout the trial. If you are distressed by any of your symptoms, or the researchers tell you that your symptoms are worsening, you are advised to speak to your GP. They will be able to offer you support and advice about your mood and how to manage your stress better.

What are the benefits of taking part in the study?

The regular follow-ups will allow us to track your mood and notify you if any of your symptoms seem to be worsening. If your responses suggest that your mood requires attention, we may advise you to speak to your GP or a mental health practitioner.

We have evidence to suggest that the therapy may be helpful in reducing stress and risk of later depression or anxiety. You may therefore find that the therapy helps you to manage your problems more effectively.

If you are in the control group, your involvement in the trial will not take up much of your time. It will only involve completing the measures four times over the course of the study. During that time you will be able to access any other therapies you might find useful. Once you have completed the follow-ups you would be allowed to access the unguided version of the therapy if you so wished.

The information you provide may help us to better understand how to prevent depression in young adults. This will hopefully allow us to provide better therapies that help young adults manage their stress and worry and reduce their risk of depression.

Will my information be kept confidential?

Any information you provide will be kept strictly confidential, except where disclosure to third parties is required by law or the professional guidelines for psychologists. You will be asked to provide contact details for your GP so that we can contact them if there is any significant risk of harm to yourself or others.

You will be given a unique anonymity code so any information you provide will only be identifiable by the code, not your name. Any forms that do contain your personal details (such as the consent form) will be stored separately from the other materials. Your data will be stored securely at the University of Exeter

using password protected files and lockable filing cabinets that can only be accessed by the research team.

What will happen with the results?

Results will be written up as part of Lorna's PhD thesis and potentially published in a journal. Your name or any other personally identifiable material will never be included in any written reports or publications. Any information presented at scientific meetings will also be fully anonymised. If you would like a copy of the findings once they are available, please email Lorna, and she will be happy to send you them to you.

Will I be paid for taking part in this study? You will not be paid for taking part. A regular prize draw will be held. At baseline and each time you complete a follow-up you will receive one entry ticket. You may choose to enter multiple tickets into one single draw or use them one at a time.

What will happen if I decide to participate? Can I change my mind?

Your participation in the study is entirely voluntary. You are free to choose whether or not to take part and if you choose not to, there will be no penalty to you in any way. If you decide to take part you will be asked to keep a copy of this information sheet and to sign the consent form. You have the right to withdraw at any point after signing the consent form, without giving a reason for doing so. Just send us an email if you wish to withdraw from the study.

Can I be stopped from participating?

The researchers may ask you to stop being in the study if they believe it is in your best interests, if you do not follow the study's rules or if the whole study is stopped.

Who can I contact if I have questions about the study?

If at any stage you have any questions, concerns or complaints about any aspect of the study, you can speak in confidence to one of the investigators: Lorna Cook or Professor Ed Watkins. Questions or concerns about the study can also be addressed to Cris Burgess, Chair of the Ethics Committee, School of Psychology, University of Exeter.

Contact details

Lorna Cook (PhD student): lzc204@exeter.ac.uk

Professor Ed Watkins (Co-founder and Director of Mood Disorders Centre and Sir Henry Wellcome Building for Mood Disorders Research): E.R.Watkins@exeter.ac.uk

Dr Cris Burgess (Ethics Chair): C.N.W.Burgess@exeter.ac.uk

Thank you for reading this information sheet

Consent Form

Study Title: Targeting worry and rumination to prevent the onset of depression in young adults: A randomised-controlled trial comparing guided and unguided internet-based rumination focused cognitive behavioural therapy and a no treatment control.

Researchers: Lorna Cook, PhD student, supervised by Prof. Ed Watkins

Please write/type your initials in the boxes below if you agree with the following statements:

1. I have read and understood the information sheet provided and have had the opportunity to ask further questions.	
2. I understand that my GP retains clinical responsibility for me throughout the study and will be contacted in the event of any significant risk of harm to myself or others.	
3. I understand that my participation in the study is voluntary and that I may withdraw from the study at any time, without giving any reason for doing so.	
4. I give consent for my telephone interviews to be audio-recorded so that the research team can check the conduct and reliability of these interviews. (Note: You may still participate without consenting to this audio-recording)	
5. I give my informed consent to participate in this study.	

Participant Name (please print):

Participant email address:

Participant telephone number:

Participant signature: Date:

Researcher Name: Date:

Researcher Signature:

If you are willing to be contacted about participating in further research at the Mood Disorders Centre, please write your initials in the box below. If you do not wish to be contacted, simply leave this box blank.

I am willing to be contacted about participating in further research at the Mood Disorders Centre.	

Please return the completed consent form to Lorna Cook by email (lzc204@exeter.ac.uk) or by post: Sir Henry Wellcome Building for Mood Disorders Research, University of Exeter, Perry Road, EX4 4QG

You will receive a copy signed by the researcher for your records.

Appendix A Mediation analyses

The published paper reported short- to-medium term changes in rumination that are consistent with the hypothesised mechanism of change. The aim of the following analyses was therefore to assess whether the change in rumination mediated the effect of guided i-RFCBT on outcome (Depressive symptoms/MDE onset). The simplest mediation model is shown in Figure 6.4.

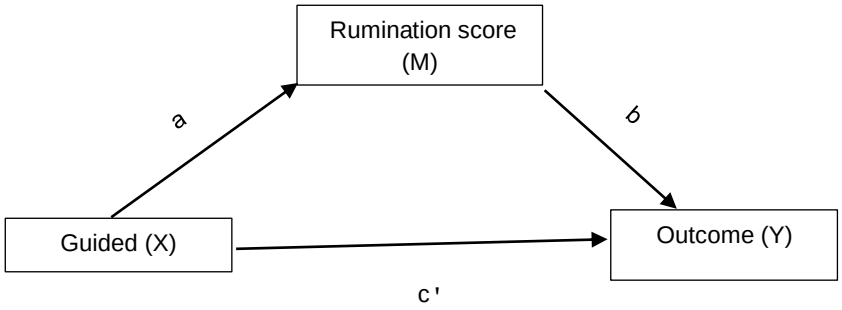


Figure 6.4. Hypothetical mediation model.

In this model, path ‘a’ is the direct effect of the randomisation arm (usual care control vs. guided i-RFCBT) on change in rumination (the mediator) and path ‘b’ is the direct effect of the mediator on the outcome (depression). The indirect effect (the proportion of the treatment effect mediated by change in rumination) is the product a*b. Path ‘c’ is the direct effect of randomisation arm on the outcome, controlling for the effect of mediation. The total intervention effect on outcome is therefore calculated as (a*b) + c.

The criteria outlined by Kraemer et al. (2002) for a mediator specify that: a) the putative mediator is correlated with assigned treatment (i.e. the mediator is a potential result of the treatment); b) change in the mediator has either a main effect or interactive effect on the outcome and c) change in the mediator occurs during the treatment, and before the change in the outcome variable (to

rule out reverse causation). For example, to test for a prospective mediational effect, in the current analysis, the change in rumination during the intervention period (baseline to 3 months) was tested as a putative mediator of onset of depressive episodes up to 15 months follow-up. To test the significance of the mediated effect, standard errors are bootstrapped 1000 times before calculating the 95% confidence intervals (Mackinnon, Lockwood, & Williams, 2004).

Mediation model for depressive symptoms

There was a significant difference in depressive symptoms between guided i-RFCBT and usual care control at the 6-month follow-up (see Figure 6.5 and Table 6.4) so this timepoint was used as the endpoint to test whether change in rumination mediated any effect of the intervention on symptoms of depression. To test a putative mediation effect, the change in rumination over the intervention period (i.e., 3-month follow-up rumination adjusted for baseline rumination) was examined as a potential mediator of the effect of intervention on change in PHQ-9 score from baseline to 6 months follow-up.

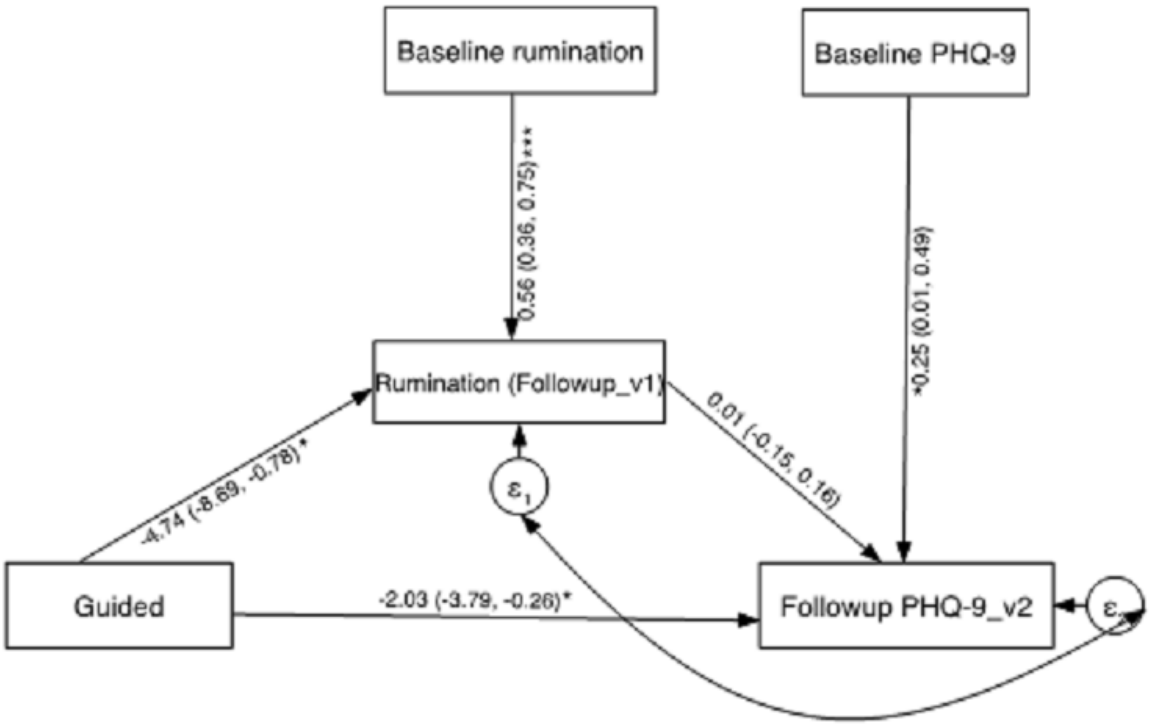


Figure 6.5. Mediation of intervention effect through rumination on PHQ-9 at 6-month follow-up.

Table 6.4. Mediated effect of PHQ-9 score through Rumination (Usual care control vs. Guided i-RFCBT).

Variables	Outcome (3- month follow-up rumination)		Outcome (6- month follow-up PHQ-9)	
Direct effects	Coefficient (95% CI)	p-value	Coefficient (95% CI)	p-value
Baseline rumination	0.56 (0.36 to 0.75)***	<.001	—	—
Follow-up rumination	—	—	0.01 (-0.15 to 0.16)	.947
Baseline PHQ-9			0.25 (0.01 to 0.49)*	.041
Guided	-4.74 (-8.69 to -0.78)*	.019	-2.03 (-3.79 to -0.26)*	.024
Indirect effect (bootstrapped)	—	—	—	—
Guided→ Rumination→PHQ-9	—	—	-0.03 (-1.24 to 1.19)	.967

Note: *p<.05, **p<.01, ***p<.001.

Controlling for the indirect effect and baseline depression, participants who had received guided i-RFCBT had significantly lower PHQ-9 scores than usual care controls at the 6-month follow-up. As expected, baseline rumination is a highly significant predictor of 3-month follow-up rumination. After controlling for baseline rumination, the guided i-RFCBT arm had significantly lower rumination scores at 3 months than the usual care controls. However, change in rumination from baseline to 3-month follow-up rumination did not directly predict change in depressive symptoms from baseline to 6 months, and the indirect effect was not significant. The proportion of the total intervention effect mediated by rumination was -0.03/(-2.03 + -0.03) = 0.015, or 1.45%.

While the intervention has a significant impact on rumination, this analysis suggests this reduction in rumination is not mediating the change in depressive symptoms. However, the analysis may be underpowered to detect a significant mediation effect, as there was dropout attrition at each timepoint, particularly from the guided i-RFCBT arm.

The challenges with fitting mediation models to survival outcomes

The following tests sought to examine whether change in rumination mediated the intervention effects on diagnostic outcomes. There is no consensus on fitting mediation models to Cox models (Lange & Hansen, 2011). One approach is to use a discrete time-to-event model, treating outcome as a latent hazard variable (Pratschke et al., 2016). To treat time as discrete, weeks were rounded up to obtain non-fractional time units, with each of the 65 weeks coded ‘0’ if the participant does not experience MDE, or is censored, and coded ‘1’ when a participant experiences MDE. This discrete-time-to-event model was first tested without mediation to ensure it was estimating the same effects as the Cox model. As the diagnostic outcome is binary, coefficients for the direct paths from covariate to outcome are estimated on a log-scale and Table 6.5 presents the exponentiated coefficients (Odds Ratios) of the three covariates included in the model.

Table 6.5. Logistic model: Odds Ratio for experiencing an MDE (Usual care control vs. Guided i-RFCBT).

Variable	Odds Ratio (95% CI)	p-value
Past-MDE	2.67 (1.38 to5.12)**	.003
Baseline stress	1.40 (0.99 to 1.99)	.060
Randomisation arm (Guided i-RFCBT)	0.66 (0.34 to 1.25)	.201

Note: *p<.05, **p<.01, ***p<.001.

The effects estimated by the logistic model are similar to those in the original Cox model (see Section 6.4.2). We can therefore use simultaneous path equations within this logistic model to test the mediation effect of rumination.

Mediation model (Usual care control vs. Guided i-RFCBT) for incidence of MDE

Using simultaneous equations, the following mediation model (Figure 6.6) for usual care control vs. guided i-RFCBT was used. Proportional hazards discrete time-to-event is specified by creating a latent variable with a variance of 0 and paths from this latent variable to each of the discrete time units (in this case week 1, week 2, week 3 etc.). For the proportional hazard assumption within this model, the latent hazard variable to time-path coefficients were equally constrained (represented by 1). Within this model, the latent hazard is shown to simplify the overall model, but the effect of each variable on survival outcome can be estimated by following their individual pathways. The model therefore estimates the extent to which each variable influences the outcome across the entire time period if each week is weighted equally (Pratschke et al., 2016). Within the current model we are therefore testing whether change in

rumination from baseline to 3-month follow-up mediates the effect of intervention (guided i-RFCBT versus usual care) on risk of MDE across 65 weeks.

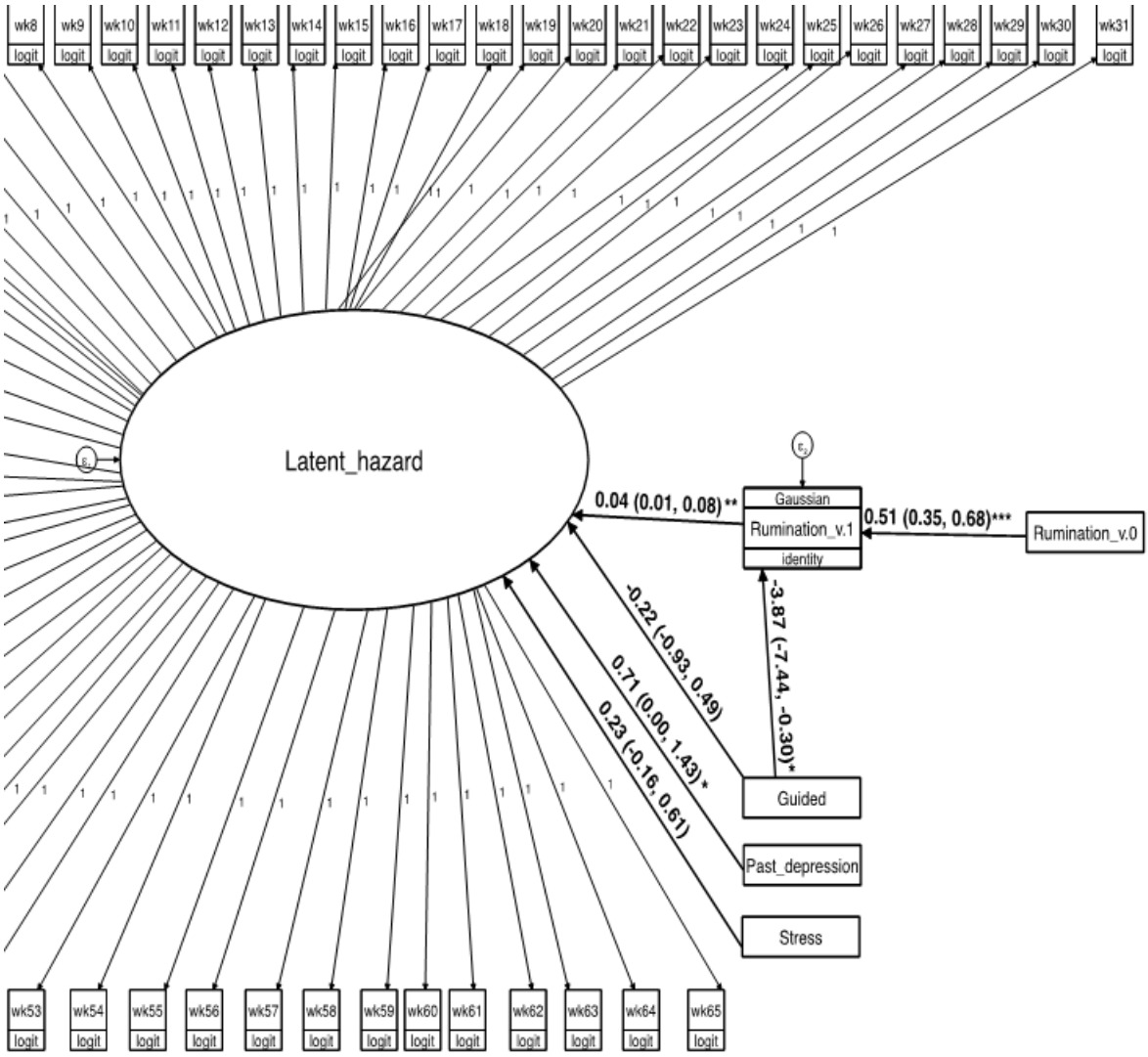


Figure 6.6. Mediation of treatment effect through rumination (Usual care control vs. Guided i-RFCBT).

Note: Image cropped to highlight direct and indirect pathways. All follow-up weeks (1 to 65) are included in the model. *p<.05, **p<.01, ***p<.001.

The results are presented in Table 6.6.

Table 6.6. Mediated effect of onset of MDE through Rumination (Usual care control vs. Guided i-RFCBT).

Variables	Outcome (3-month follow-up rumination)		Outcome (MDE) across 15-month follow-up	
Direct effects	Coefficient (95% CI)	p-value	Coefficient (95% CI)	p-value
'Past-MDE'	—	—	0.71 (0.00 to 1.43)*	.050
Baseline-stress	—	—	0.23 (-0.16 to 0.61)	.252
Baseline rumination	0.51 (0.35 to 0.68)***	<.001	—	—
Follow-up rumination (3 months)	—	—	0.04 (0.01 to 0.08)**	.006
Guided i-RFCBT	-3.87 (-7.44 to -0.30)*	.034	-0.22 (-0.93 to 0.49)	.542
Indirect effect (bootstrapped)	—	—	—	—
Guided i-RFCBT→ Rumination→MDE	—	—	-0.18 (-0.42 to 0.06)	.148

Note: Estimates for MDE outcome are log based. *denotes p<.05, **p<.01, ***p<.001. Standard errors and 95% CIs for indirect effect (a*b) are estimated after correcting for the scaling factor and bootstrapping 1000 times.

The direct effect of the intervention, controlling for the indirect mediation effect and the included covariates (past MDE and stress), suggests there was 20% less risk of experiencing MDE during the 65-week period in the guided i-RFCBT arm compared to usual care. However, this direct effect was not significant. As expected, baseline rumination significantly predicted 3-month follow-up rumination. When controlling for baseline rumination, participants who had received guided i-RFCBT had significantly lower rumination at 3-month follow-up than usual care controls, i.e., a significant change in rumination. The change in rumination was also a significant direct predictor of MDE risk, although the effect was small (0.04). The estimated indirect effect was not significant: (-0.18 (CI: -0.42 to 0.06, *n.s.*). The proportion of the intervention effect on risk of

MDE that was mediated by change in rumination is calculated as the indirect effect over the total effect (-0.18/(-0.22 + -0.18)) = 0.45, or 45%. Change in rumination from baseline to 3-month follow-up did not mediate the effect of the intervention on incidence of MDE. However, it is noteworthy that there was not a direct main effect of the intervention on incidence of MDE. Furthermore, the study was powered to test a main intervention effect and not for a mediational analysis so it may be underpowered to detect a mediator.

Mediation analysis: Subsample with no MDE onset during the intervention period

The previous model includes the full 15-month period (65 weeks) from baseline to the final follow-up. As several participants (*n* = 17) experienced MDE during the intervention phase, these episodes would not meet the temporal precedence criterion (Kraemer et al., 2002). A further analysis therefore excluded participants who experienced MDE, or whose outcome was unknown, before the 3-month follow-up. The sample for this analysis was *N* = 107 (*n* = 50 guided i-RFCBT; *n* = 57 usual care control).

Table 6.7. Mediation model for the subsample with no MDE onset during the intervention period.

Variables	Outcome (3-month follow-up rumination)		Outcome (MDE)	
Direct effects	Coefficient (95% CI)	p-value	Coefficient (95% CI)	p-value
'Past-MDE'	—	—	0.65 (-0.35 to 1.65)	.205
Baseline-stress	—	—	0.88 (0.19 to 1.56)*	.012
Baseline rumination	0.47 (0.30 to 0.63)***	<.001	—	—
Follow-up rumination_v1	—	—	0.02 (-0.03 to 0.07)	.371
Guided	-3.77 (-7.37 to -0.17)*	.040	-1.05 (-2.21 to 0.12)	.078
Indirect effect (bootstrapped)	—	—	—	—
Guided→ Rumination→MDE	—	—	-0.08 (-0.30 to 0.13)	.450

Within this sample, controlling for included covariates, the guided i-RFCBT participants experienced significantly lower rumination at 3-month follow-up than the usual care controls. As in the other models, baseline rumination significantly predicted 3-month follow-up rumination. However, the estimated indirect effect was not significant and the proportion of the intervention effect mediated through rumination was only -0.08 / -1.13 = 0.07 or 7%.

Per protocol mediation analysis: Treatment compliers

A per protocol analysis was conducted to assess whether the intervention effect was mediated by rumination in treatment compliers (those completing ≥ 4 modules): typically a treatment would only be expected to impact on an outcome

when patients receive the treatment at an adequate dose, and by the same logic, the effect of a putative mediator should be stronger in treatment compliers. The mediation analysis was therefore conducted excluding non-compliers from the analysis (*n* = 25). The total per protocol sample was *N* = 107 (*n* = 38 guided i-RFCBT; *n* = 69 usual care control). Results from the per protocol analysis are presented in Table 6.8.

Table 6.8. Per-protocol estimates for the mediation model.

Variables	Outcome (3-month follow-up rumination)		Outcome (MDE)	
Direct effects	Coefficient (95% CI)	p-value	Coefficient (95% CI)	p-value
'Past-MDE'	—	—	0.90 (0.07 to 1.73)*	.033
Baseline-stress	—	—	0.22 (-0.25 to 0.69)	.364
Baseline rumination	0.39 (0.21 to 0.57)***	<.001	—	—
Follow-up rumination (3 months)	—	—	0.05 (0.01 to 0.09)**	.016
Guided i-RFCBT	-4.99 (-9.07 to -0.90)*	.017	-0.32 (-1.22 to 0.59)	.492
Indirect effect (bootstrapped)	—	—	—	—
Guided i-RFCBT→ Rumination→MDE	—	—	-0.25 (-0.65 to 0.16)	.235

Among treatment compliers, the guided i-RFCBT arm experienced significantly lower rumination at 3-month follow-up. Follow-up rumination significantly predicted risk of MDE across 65 weeks. However, the indirect effect of guided i-RFCBT through rumination was not significant. The estimated total effect = (-0.32 + -0.25) = -0.57. The proportion of the effect mediated through rumination is -0.25/-0.57 = 0.44, or 44%. This is equivalent to the proportion of intervention effect mediated through rumination for the full ITT sample.

Taken together, these mediation analyses did not find change in rumination significantly mediated the effect of guided i-RFCBT on depressive symptoms or onset of MDE. However, given the trial was powered to detect a main intervention effect and there was drop-out attrition at each of the follow-ups, further limiting the sample size, it is possible these analyses are underpowered to detect a significant mediation

Appendix B Discussion of Recruitment Approach

The main recruitment pathway involved contacting university departments around the UK by email and asking them to circulate an advert to their undergraduate students (as successfully used by Kingston, Watkins, & O'Mahen, 2013). This contact took place between 14/11/13 and 10/12/14. In total, 1834 departments were contacted, with a repeat contact made to 1527 of these in the following academic year. A total of 336 departments (18.32% of total contacts) confirmed that the advertisement had been circulated to their students (either by email or displayed in the department as a poster).

A Twitter account and paid Facebook advertising were also set up to help circulate the advert to young people who had previously expressed an interest in the following terms: stress; worry; rumination; mental health; self-esteem; wellbeing; research; psychology; cognitive-behavioural therapy; online therapy. Additionally, three of fourteen contacted organisations working with young people and/or in the field of mental health agreed to advertise the study.

Despite employing several recruitment strategies, the only successful approach was via direct contact with university departments. The lack of help-seeking and stigmatization (as discussed in Chapter 1), may explain why the Facebook advertising did not reach the desired sample, as many students may not have explicitly expressed an interest in mental health on their Facebook account. In addition, even though there is evidence that students like to seek health information online, viewing the advertisement on a charity website would still require an individual to be actively seeking help. Given the range of barriers to help-seeking expressed by students (see Chapter 1), it is likely that students only seek help once symptoms are causing significant distress or functional

impairment and those who may be eligible for preventive interventions are therefore less likely to be actively viewing mental health sites.

The recruitment procedure involved loss of potential participants at each stage. At the online screening phase, 30.76% of potential participants were both eligible and consented to further contact. However, only 20.75% of individuals sent further information about the trial then completed the telephone screening. Of those who completed the interview, 76.8% were recruited to the trial. These figures demonstrate the large reach needed to recruit to sufficient numbers for prevention trials as, overall, 4.9% of visitors to the screening site were recruited into the trial. One area to investigate further in order to increase the numbers for future trials may be to include a question in the screener and in the invitation to interview asking why participants who screened as potentially eligible on the online screener then declined to provide contact details for the next stage of screening or provided contact details but then declined the interview. Approximately 1 in 3 visitors to the screener were eligible for further screening but did not provide contact details and, of the participants who did consent to be contacted, 79.25% then did not respond or declined the interview. Understanding the barriers to further engagement with the trial were for individuals who had shown an initial interest may improve recruitment rates for future trials of i-RFCBT.

Eligible participants were from a total of 65 different UK HE institutions, with a median of 2 students recruited per institution. Several universities were particularly well represented among the sample, with 19 students (8.1%) studying at Cambridge, 14 (6.0%) at Exeter and 12 (5.1%) at both Reading and York.

Seven participants were studying short courses or in employment, with the remaining 228 in either undergraduate or postgraduate education. Of these, 96.5% were undergraduates, with almost a third (31.1%) in first year. Table 6.9 presents a breakdown of students by year of study.

Table 6.9. Year of academic study of RESPOND participants.

Academic year	N (%)
First year undergraduate	71 (31.1)
Second year undergraduate	64 (28.1)
Third year undergraduate	58 (25.4)
Fourth year undergraduate	24 (10.5)
Fifth year undergraduate	3 (1.3)
First year taught postgraduate	4 (1.8)
Second year taught postgraduate	1 (0.4)
Third year taught postgraduate	1 (0.4)
First year PhD	2 (0.9)

While there was a wide variety in the courses the participants were studying, with 116 different degree courses represented, over one quarter were studying either Psychology (*n* = 42, 17.9%) or Medicine (*n* = 22, 9.4%). These students may have been particularly willing to participate in the RESPOND trial due to a greater prior knowledge of mental health interventions, as well as an awareness of the clinical trial process (Davies, Morris, & Glazebrook, 2014). In addition, a previous qualitative study assessing help-seeking among medical students found high levels of perceived stigma, due to not wanting to be viewed as weak in such a competitive environment, an unwillingness to disclose mental distress to tutors and concerns about any record of mental health difficulties

impacting on future career progression (Chew-Graham, Rogers, & Yassin, 2003). This may explain why medical students may be more willing to engage in online interventions, delivered outside their own university or clinical placement settings. For efficiency, future trials may therefore specifically target Medical Schools and Psychology departments to recruit students for iCBT trials, although this necessarily limits the generalizability of findings to the wider student body.

Appendix C Overview of stressful events

The Episodic Life Events Interview (Hammen, 2004) was administered during the screening interview to ascertain how many significant events (from the standardised list, or self-identified) the participant had experienced in the previous 3 months, and re-administered at each follow-up interview to record stressful events experienced during the follow-up period. As stress was not the primary outcome of the trial, the interview was not administered for each event. Instead, participants were asked to identify which event had been the most stressful, provide some more detail of this individual event and provide a subjective rating of the stress or negative impact experienced as a result.

As baseline stress is an important covariate in the Cox models, the baseline data is discussed in detail, followed by a brief overview of the stress reported during the follow-up interviews. For baseline stress, the events were also rated for objective stress or negative impact as well as the level of independence or dependence of the stressful event. The objective stress rating was coded based on the factual information provided about the event (what happened, any contextual details, consequences of the event), disregarding any reported details about emotional reactions to the event. For the independence rating, the individual's contribution to the event was rated (as defined by Hammen, 2004), such that events outside one's control (e.g. exams) were rated independent, unless the individual's behaviour impacted on the situation (e.g. not revising sufficiently), in which case the event was rated as mixed.

Full team ratings were beyond the scope of the thesis, but inter-rater reliability was established by two coders independently rating 20 transcripts (10% of the sample), discussing any disagreements and agreeing some rules

for coding. A further random 10% of the sample was coded and inter-rater reliability was good for both objective stress (Cohen's kappa = .74) and independence (Cohen's kappa = .82).

Participants in the RESPOND trial reported a mean of 3.62 events in the 3 months prior to screening (*SD* = 2.19) and a median of 3.00 events. Participants who reported no events (*n* = 13) are excluded from the subsequent descriptive statistics. Of the participants reporting at least one event (*n* = 222), the mean number of events was 3.83 (*SD* = 2.06) and the median number was 4.00.

For the independence ratings, almost all events were classified as either 'almost completely independent' (*n* = 101, 45.7%) or mixed (*n* = 104, 47.1%). Only one event was classed as 'almost completely dependent'. Successfully completing a degree course involves managing a range of independent stressors (e.g. coursework, exams). However, the majority of stressors involve some degree of personal responsibility for the situation. Over half of the events reported by the sample involved particular personal choices, such as choosing to apply for postgraduate courses, and behaviours, such as procrastination, that contributed to the stressful event. Interpersonal problems were also classed as mixed unless it was clear that one or other party was responsible for the situation.

Previous research suggests certain cognitive styles, such as a negative attributional style, in which stressors are attributed to stable, global, internal causes, typical of depressive rumination, may lead individuals to experience more stressful events (Cohen, Murphy, & Prather, 2019) as this negative attributional style may engender more interpersonal problems (Liu & Alloy,

2010). In addition, avoidance as a coping strategy, which is associated with depressive rumination, predicted increased interpersonal problems four weeks later in university students (Barker, 2007). This suggests that students with a tendency to worry or ruminate may exacerbate the negative impact of objectively stressful events through their maladaptive coping strategies.

For the worst event, the subjective and objective ratings were significantly correlate (*rs*(221) = .43, p < .001). Mean subjective ratings of stress were significantly higher (*M* = 2.59, *SD* = .83) than the mean objective stress rating (*M* = 2.19, *SD* = .74): *t* (440) = 5.33, *p* < .001. The distribution of stress ratings for the worst event, across all event types, are reported in Table 6.10.

Table 6.10. Frequencies of stress ratings.

Stress rating	Subjective frequency (%)	Objective frequency (%)
None	4 (1.8)	3 (1.4)
Mild	12 (5.4)	18 (8.1)
Mild to Moderate	7 (3.2)	0
Moderate	61 (27.6)	150 (67.9)
Moderate to Marked	17 (7.7)	0
Marked	92 (41.6)	34 (15.4)
Marked to Severe	6 (2.7)	0
Severe	22 (10.0)	16 (7.2)

Two thirds of the events were rated as moderately stressful by the independent coder, whereas the subjective ratings indicate that over half the sample rated their subjective stress as marked or above.

The stress ratings for each category of event are presented in Table 6.11 and the most frequent events (reported by ≥5% sample) in Table 6.12. While the original rating ranges from 1 ‘None’ to 5 ‘Severe’, for consistency, the recoded ratings of 0 ‘None’ to 4 ‘Severe’ (see Chapter 6) are used to calculate the mean stress.

Table 6.11. Mean stress ratings for each event category.

Event Category	N	Mean subjective stress (SD)	Mean objective stress (SD)
Work	32	2.44 (.90)	1.91 (.64)
Education	92	2.66 (.68)	2.01 (.41)
Financial	9	1.72 (.91)	1.67 (.87)
Health	18	3.00 (.82)	3.17 (.71)
Bereavement	10	2.55 (.76)	3.50 (.85)
Migration	15	2.50 (.60)	2.13 (.52)
Courtship and Cohabitation	13	2.38 (.98)	2.00 (.82)
Legal	1	4.00	3.00
Family and Social	27	2.78 (.84)	2.30 (.72)
Other	4	1.75 (1.71)	2.00 (.82)

Table 6.12. Mean stress ratings for the most frequently reported events.

Event	N	Subjective Mean (SD)	Objective Mean (SD)
Prepare for or take an important exam	45	2.72 (.61)	1.98 (.15)
Begin full time or half time education	19	2.37 (.68)	1.89 (.32)
Change to a new line of work, or get a new job	13	2.19 (.52)	1.85 (.55)
Physical or emotional illness, injury or accident to close family member, friend, romantic partner (not leading to death)	11	2.82 (.84)	3.45 (.52)
Serious argument or problem with family member	11	2.77 (.82)	1.91 (.30)
Serious argument or problem with friend	11	2.77 (.93)	2.64 (.67)

These descriptive statistics demonstrate that the most frequently reported stressful events among students at high risk of depression are related to academia, employment and social relationships. This is consistent with previous surveys, in which academic demands, career prospects and difficulties with interpersonal relationships predicted poor mental health (Alonso et al., 2019, Wörfel et al., 2015).

Stress across the follow-up period

At each follow-up interview, participants were asked to report stressful events experienced since the previous interview (i.e. all periods were 3 months except the final follow-up, which covered the preceding 9 months). The number of stressful events (Table 6.13) and subjective stress ratings of the worst event (Table 6.14) experienced, split by randomisation arm were explored to examine any changes in stress across time. There were no significant between-group differences in the number of events experienced at any timepoint.

Table 6.13. Mean number of stressful events in each trial arm across time.

	Baseline		Follow-up 1 (3 months)		Follow-up 2 (6 months)		Follow-up 3 (15 months)	
Trial arm	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Usual care control	77	3.64 (2.31)	66	2.53 (1.78)	61	2.70 (1.96)	63	3.59 (2.08)
Guided i-RFCBT	82	3.77 (2.41)	59	2.85 (2.00)	52	2.29 (1.86)	50	3.36 (2.38)
Unguided i-RFCBT	76	3.43 (1.80)	57	2.70 (1.46)	49	2.31 (1.62)	48	3.29 (1.83)

Of those participants reporting at least one stressful life event, the mean stress ratings for the worst event experienced are presented in Table 6.14.

Table 6.14. Mean subjective stress in each trial arm across time.

	Baseline		Follow-up 1 (3 months)		Follow-up 2 (6 months)		Follow-up 3 (15 months)	
Condition	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Usual care control	70	2.41 (.91)	58	2.18 (.99)	54	2.35 (1.07)	59	2.50 (.97)
Guided i-RFCBT	77	2.74 (.72)	52	2.62 (.88)	43	2.42 (1.02)	48	2.64 (.93)
Unguided i-RFCBT	74	2.59 (.83)	54	2.27 (.88)	43	2.23 (.83)	47	2.30 (.89)

Of those participants who reported at least one stressful life event at every follow-up point (N = 119), there was no significant difference between the mean subjective rating of stress at baseline or 6 months or 15 months. There was a significant between-group difference at 3 months (post-intervention): F (2,161) = 3.34, p = .038. Post-hoc pairwise comparisons found that only the mean difference between the guided i-RFCBT arm and usual care control was significant, indicating the stress ratings for guided i-RFCBT were significantly higher than usual care controls. Taken together, these findings suggest that the

significant preventive effects of guided i-RFCBT relative to usual care cannot be explained by the guided participants experiencing fewer stressors or lower perceived stress during the follow-up period. One possibility is that the i-RFCBT intervention is providing a protective function mitigating the effect of stressful events on producing depression.

Appendix D Decomposing the Stress Interaction

For the Cox models, due to the small number of participants that would be in each cell for a categorical variable, as well as the inclusion of participants who had scored their stress level between two categories, stress was treated as a continuous rather than a categorical variable in the Cox models. The derivatives of the hazard ratio are calculated using a continuum vector. If stress were a categorical variable, we would have had four covariates in the model (mild, moderate, marked, severe), each separately compared to the baseline category (no stress). We therefore did not test the simple effects at the different levels of the moderator, as the baseline stress covariate in the original Cox model was continuous. The survival curves (Figure 6.3) are plotted at stress levels 0 to 4, but these are probabilities based on stress as a continuum and are included for visual representation of the interaction effect.

This stress interaction is a secondary analysis, and the trial was not powered to detect subgroup effects. Whilst this may result in Type I errors, the literature has highlighted stress as an important risk factor. We acknowledge that this interaction effect requires further testing in a fully powered trial.

The pattern of the survival curves suggest that the interaction effect may be driven by the usual care control group worsening with increasing stress (survival probability for usual care controls across the 65 weeks drops from almost 100% to approximately 20% between no stress and severe stress), rather than the guided i-RFCBT particularly improving with increased stress (survival probability rises from approximately 60% to approximately 80%). At low stress levels, the intervention appears to have a detrimental effect relative to usual care controls. However, very few participants with low stress experienced an MDE within the follow-up period, so this pattern of findings is

based on low power and needs to be interpreted with caution. The overall pattern suggests that high ruminators with high stress levels are most at risk of MDE, and intervening with i-RFCBT significantly reduces this risk, but a further trial with larger samples and/or a longer follow-up period is needed in order to fully unpack this interaction effect. In addition, trials comparing i-RFCBT to other preventive interventions would help to further unpack this relationship. For example, Haeffel (2010) tested a traditional cognitive workbook (focused on thought challenging), an adapted cognitive therapy (without thought challenging) and an academic skills training for at-risk students. A three-way interaction between stress, rumination, and intervention indicated students with both high rumination and high stress experienced more depression after completing traditional CBT than after the other two interventions. This suggests that traditional CBT is not helpful for the high-ruminators with high stress, so it may be that i-RFCBT produces better clinical outcomes than other interventions currently provided to this high-risk subgroup of students.

Appendix E ANCOVA tables including Multiple Imputation and Effect sizes

The primary outcome was onset of depression so the effects of the intervention on symptom measures were secondary analyses. The RESPOND trial reported case completers rather than multiple imputation for simplicity as the overall pattern of effects indicated short- to medium-term effects on symptom measures. To further investigate this overall trend, Cohen's *d* effect sizes are calculated and presented in Tables 6.15 and 6.16. These effect sizes are conducted on the raw mean and SD scores and not adjusted for baseline score (Lakens, 2013) Overall, these effect sizes indicate the intervention has positive effects on symptoms of depression and anxiety and measures of worry and rumination up to 6 months post-intervention, but these effects are not maintained up to the 15-month follow-up period.

Table 6.15. Baseline adjusted symptom measures at 3, 6 and 15 months with multiple imputation and effect sizes: guided i-RFCBT vs. usual care controls

Time-point	Measure	Guided i-RFCBT	Usual care			
		Mean [95% CI]	Mean [95% CI]	Difference [95% CI]	Cohen's d	MI-Difference [95% CI]
Follow-up 1 (3 months) *N* = 114	PHQ9	4.75 [3.74, 5.76]	5.40 [4.48, 6.33]	-0.65[b] [-2.02; 0.72]	-0.13	-0.55[b] [-2.05-0.96]
	GAD7	5.58 [4.51, 6.66]	6.27 [5.28, 7.25]	-0.69[b] [-2.15; 0.78]	-0.06	-0.53[b] [-2.14, 1.09]
	PSWQ	57.27 [54.85, 59.69]	58.45 [56.23, 60.67]	-1.18[b] [-4.46, 2.11]	-0.09	-0.75[b] [-4.35, 2.86]
	RRS[a]	44.34 [41.66; 47.02]	48.21 [45.73, 50.68]	-3.87[c] [-7.53, -0.21]	-0.22	-3.69[b] [-8.01, 0.63]
Follow-up 2 (6 months) *N* = 105	PHQ9	3.70 [2.48, 4.92]	5.52 [4.42, 6.62]	-1.82[c] [-3.46, -0.18]	-0.40	-1.97[c] [-3.87, -.063]
	GAD7	4.72 [3.44, 5.99]	6.06 [4.91, 7.20]	-1.34[b] [-3.05, 0.38]	-0.26	-1.15[b] [-3.16, 0.85]
	PSWQ	54.83 [52.19, 57.48]	58.41 [56.03, 60.79]	-3.58[c] [-7.14, -0.02]	-0.41	-2.71[b] [-6.68, 1.25]
	RRS	41.74 [38.15, 45.34]	46.35 [43.12, 49.58]	-4.60[b] [-9.47, 0.26]	-0.25	-3.98[b] [-9.48, 1.52]
Follow-up 3 (15 months) *N* = 108	PHQ9	4.47 [3.23, 5.71]	4.82 [3.73, 5.91]	-0.35[b] [-2.00, 1.30]	-0.06	-0.38[b] [-2.30, 1.55]
	GAD7	4.42 [3.16, 5.68]	5.73 [4.62, 6.83]	-1.31[b] [-2.99, 0.38]	-0.18	-1.10[b] [-2.10, 0.80]
	PSWQ	54.81 [51.71, 57.91]	58.11 [55.39, 60.84]	-3.30[b] [-7.43, 0.82]	-0.25	-1.74[b] [-6.53, 3.06]
	RRS	46.15 [42.59, 49.72]	44.65 [41.53, 47.78]	1.50[b] [-3.28, 6.28]	-0.19	1.16[b] [-3.99, 6.31]

Note. PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalised Anxiety Disorder Screener; PSWQ = Penn State Worry Questionnaire; RRS = Ruminative Response Scale.

[a]*N* = 115 for RRS at 3 months due to one partially completed questionnaire set; [b]not significant; [c]*P <.05*.

Cohen's d are based on raw mean/SD scores and not adjusted for baseline score

Table 6.16. Baseline adjusted symptom measures at 3, 6 and 15 months with multiple imputation and effect sizes: unguided i-RFCBT vs. usual care controls

Time-Point	Measure	Unguided i-RFCBT	Usual care			
		Mean [95% CI]	Mean [95% CI]	Difference [95% CI]	Cohen's d	MI-Difference [95% CI]
Follow-up 1 (3 months) *N* = 116	PHQ9	4.02 [3.07, 4.96]	5.21 [4.33, 6.10]	-1.20 [-2.49, 0.10]	-0.37	-1.18 [-2.65, 0.28]
	GAD7	4.94 [3.90, 5.99]	5.98 [5.01, 6.96]	-1.04 [-2.47, 0.39]	-0.29	-1.06 [-2.60, 0.49]
	PSWQ	55.77 [53.26, 58.28]	57.60 [55.26, 59.95]	-1.84 [-5.28, 1.61]	-0.3	-1.35 [-4.87, 2.17]
	RRS	44.47 [41.89, 47.06]	47.01 [44.60, 49.42]	-2.54 [-6.08, 1.01]	-0.32	-2.42 [-6.19, 1.34]
Follow-up 2 (6 months) *N* = 104	PHQ9	4.38 [3.20, 5.56]	5.35 [4.30, 6.40]	-0.97 [-2.56, 0.61]	-0.28	-1.04 [-2.89, -0.81]
	GAD7	4.20 [2.96, 5.44]	5.93 [4.83, 7.03]	-1.73 [-3.38, -0.07]	-0.42	-2.09 [-3.92, -0.28]
	PSWQ	54.51 [51.60, 57.42]	58.06 [55.47, 60.65]	-3.55 [-7.46, 0.36]	-0.44	-3.35 [-7.36, 0.67]
	RRS	41.27 [38.07, 44.47]	45.20 [42.35, 48.04]	-3.93 [-8.22, 0.37]	-0.42	-4.12 [-8.94, 0.69]
Follow-up 3 (15 months) *N* = 107	PHQ9	4.20 [3.00, 5.40]	4.69 [3.64, 5.73]	-0.49 [-2.08, 1.11]	-0.17	-0.92 [-2.61, 0.77]
	GAD7	4.49 [3.28, 5.70]	5.52 [4.46, 6.57]	-1.03 [-2.63, 0.58]	-0.23	-1.36 [-3.23, 0.52]
	PSWQ	53.78 [50.75, 56.81]	57.56 [54.93, 60.19]	-3.78 [-7.79, 0.24]	-0.39	-4.34 [-8.57, -0.09]
	RRS	42.07 [38.59, 45.54]	43.85 [40.84, 46.86]	-1.78 [-6.40, 2.83]	-0.23	-2.61 [-7.93, 2.71]

Note. PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalised Anxiety Disorder Screener; PSWQ = Penn State Worry Questionnaire; RRS = Ruminative Response Scale.
Cohen's d are based on raw mean/SD scores and not adjusted for baseline score

Appendix F Data Management and Cleaning

Efforts were made during each interview to reduce errors in the data. The lead researcher made notes on paper during each telephone interview, detailing the participant's response to the diagnostic questions and noting any additional information that may be relevant for further discussion with the clinical supervisor in order to confirm a diagnosis. Logic checks were ongoing during the data collection process. For example, where questionnaires were completed during the telephone interview, the researcher queried any responses that did not fit with previous responses (e.g. items that contained a double negative such as 'If I don't have enough time to do everything, I don't worry about it.'). In addition, if symptoms reported on the PHQ-9 differed from those discussed in the diagnostic interview, the researcher asked for further information to ensure accurate and consistent recording of current symptoms. Where questionnaires were returned by email, missing items or items that were not consistent with the interview data were followed up by email for clarification.

The data entry was conducted during the trial, as soon as possible after each interview. The data was entered into Excel by a visiting researcher or the lead researcher, using the paper notes from the interviews and electronic copies of questionnaire measures where necessary.

At the end of the trial, the data was combined in a single SPSS database and checked by the lead researcher to ensure individual participants' data matched their records from each interview. Range checks were conducted prior to sharing the database with the statistician.

Appendix G Comorbid Anxiety Disorders

The proportion of participants meeting criteria for a co-morbid anxiety disorder prior to study entry are outlined in Table X. These diagnoses are not necessarily current at baseline. The frequency data includes participants who have met diagnostic criteria at any point prior to the RESPOND trial, with the exception of GAD, which must have occurred in the past 6 months.

Table 6.17: Proportions of participants meeting the diagnostic criteria for a co-morbid anxiety disorder at baseline.

	Usual Care (n=77) N Yes (%)	Guided i-RFCBT (n=82) N Yes (%)	Unguided i-RFCBT (n=76) N Yes (%)
Panic Disorder	10 (13)	11 (13.4)	8 (10.5)
Panic Disorder with Agoraphobia	6 (7.7)	7 (8.5)	4 (5.3)
Agoraphobia without Panic Disorder	10 (13)	12 (14.6)	11 (14.5)
Social Phobia	21 (27.3)	19 (23.2)	14 (18.4)
Obsessive Compulsive Disorder (OCD)	4 (5.2)	4 (4.9)	4 (5.3)
Generalised Anxiety Disorder (GAD)	24 (31.2)	39 (47.6)	23 (30.2)

GAD was not an exclusion criterion for the trial, so separate survival analyses for GAD were not conducted as the numbers were too low. However, an exploratory analysis of the subgroup of participants with GAD at baseline suggests the effects of co-morbid GAD warrant testing in future trials.

For the exploratory GAD analysis, only participants who were eligible for the Cox survival analyses are included (usual care control n = 69; guided i-RFCBT n = 63; unguided i-RFCBT n = 57). Of these, seventy students met

criteria for GAD at baseline (usual care control n = 22 (31.9%); unguided i-RFCBT n = 16 (28.1%); guided i-RFCBT n = 32 (50.8%).

For the primary comparison of guided i-RFCBT to usual care controls, students with GAD at baseline were over twice as likely to experience MDE during the follow-up period (OR = 2.47, 95% CI [1.16, 5.26], p =.02).

For the unguided i-RFCBT compared to usual care controls, there was no significant difference between MDE risk for those with or without GAD (OR = 1.84, 95% CI [0.82, 4.13], p = .14).

When analysed separately, baseline GAD was only significantly associated with MDE risk for guided i-RFCBT (OR = 3.55, 95% CI [1.08, 11.68], p = .04). However, this condition had a higher base rate of GAD and there may not have been sufficient power to detect an effect of GAD in the other intervention groups.

CHAPTER 7: General Discussion

This general discussion chapter is structured as follows: the overall aims of the full programme of the PhD are outlined in Section 7.1. The main findings from each study are discussed individually in Section 7.2. These findings are then synthesised into a more detailed discussion of the clinical outcomes and acceptability of guided i-RFCBT in comparison to the literature considering: diagnostic status; symptom severity; acceptability and compliance; and in comparison to the preliminary finding for unguided i-RFCBT. The theoretical implications of the thesis findings are discussed in Section 7.3, followed by the clinical implications (Section 7.4). The General Discussion then outlines the main strengths (Section 7.5) and limitations (Section 7.6) of the studies. Recommendations for further research are made in Section 7.7. Finally, Section 7.8 outlines the final conclusions.

7.1 Overview of the thesis

The aim of the PhD was to assess internet-based rumination-focused cognitive-behavioural therapy (i-RFCBT) as an intervention to reduce the impact of depression in university students. I-RFCBT was tested as both a treatment and preventive intervention using a range of settings and methodologies. Firstly, an audit and an open multiple baseline case series tested the effectiveness of i-RFCBT for the treatment of depression and anxiety in the Wellbeing Services at the University of Exeter. Secondly, a qualitative study using an online focus group investigated the acceptability of intenet-based preventive interventions for depression with specific reference to i-RFCBT. Finally, the RESPOND randomised-controlled trial aimed to replicate and extend the findings of Topper et al. (2017) in a UK university sample, by assessing whether guided i-RFCBT prevented incidence of depression relative to usual care. An additional quasi

phase II pilot arm was included in the RESPOND trial to test the feasibility and estimate effect sizes of unguided i-RFCBT relative to usual care to aid planning for a fully powered trial.

7.2 Summary of findings

7.2.1 Audit and open multiple baseline case series

The audit tested the usage and clinical outcomes of guided i-RFCBT delivered at the Wellbeing Centre, University of Exeter, from January 2014 to June 2016. Overall, 108 students completed an average of 3.19 modules (*SD* = 2.35), with 51 (47.2%) treatment compliers (completing at least four modules). The audit tested the hypothesis that i-RFCBT would be efficacious in treating acute symptoms of depression and anxiety within a routine clinical service. Pre- and post-treatment scores were available for 82 students and supported this hypothesis, with significant reductions in both depression and anxiety. There was a significant correlation between the number of modules completed and improvement in symptoms, suggesting a dose-response relationship.

The case series subsample also showed improvement in clinical outcomes, across a range of different start points in the academic year, length of baseline, course studied and initial symptom severity. Additionally, we found significant reductions in rumination in support of the hypothesised mechanism of change. Plotting symptom levels across the course of treatment demonstrated that symptom reductions only occurred after treatment had commenced and not during a baseline assessment phase, and showed a similar trajectory across participants. Furthermore, changes in depression and anxiety tended to occur in parallel, suggesting that targeting rumination had a similar impact on both disorders.

7.2.2 Qualitative analysis of acceptability of i-RFCBT

This online focus group study aimed to assess the acceptability of i-RFCBT as a preventive, rather than treatment, intervention. The focus group identified benefits of internet-based interventions including their increased convenience of use and it being easier to express oneself in writing. However, students also highlighted that completing unguided internet interventions requires significant self-discipline and, for some, guided interventions would be easier to engage with, as the supporter would provide accountability, interaction and empathy. Participants also discussed the benefits of face-to-face therapy that cannot be replicated online: the use of non-verbal cues and the fluidity of the interaction so that the therapist can easily prompt for further information. For some individuals, the therapeutic alliance achieved by face-to-face interaction cannot be matched by online interventions.

In terms of specific aspects of the platform, participants highlighted the benefits of a simple clear design to enhance credibility, although some variety in layout may be needed to maintain interest. The majority of participants liked having the case studies in video format as this reduced reading fatigue, although one participant preferred written transcripts. Views on the content of the videos were along a continuum, depending on how much an individual personally identified with the examples. Participants valued the security of the platform, but one disconfirming case suggested this security should not come at the cost of being able to easily log in to the platform.

Participants recommended shorter, clearer sections and greater flexibility in terms of navigation, including providing the modules in any order, to further improve the design and delivery and personalise the content. With specific

reference to the RFCBT content, participants liked the conceptualisation of rumination as a habit and the range of techniques to reduce this habit and acknowledged that providing a variety of techniques allowed them to personalise the intervention. They also highlighted the tone as being gentle and supportive, indicating the language used was able to convey some common therapeutic factors such as empathy and warmth. Some participants found the tone patronising, although they were able to overlook this if the content was sufficiently engaging.

7.2.3 RESPOND randomised controlled trial

A phase-III randomised-controlled trial compared guided i-RFCBT to usual care for the prevention of depression. Overall, there was no significant difference in the risk of MDE between guided i-RFCBT and usual care over the 12-month follow-up period. However, a significant interaction between treatment and baseline levels of stress was found, indicating guided i-RFCBT significantly reduced risk by 57% relative to usual care for participants experiencing above average levels of stress at the start of study. Significant short- to medium-term improvements in rumination, worry and depressive symptoms were found for case completers for guided i-RFCBT relative to usual care, although only the short-term effects on depressive symptoms remained significant in the multiple imputation analyses. Effect sizes (Table 6.15) indicated the largest effects on symptom measures were at 6 months, but these effects were not maintained over the full follow-up period (15 months).

Prevention requires widespread dissemination and interventions that are highly scalable to reach large numbers of people. As guided interventions are necessarily limited by clinician availability, we also investigated the potential for

i-RFCBT to be delivered as an unguided self-help intervention. As this format was previously untested, a quasi phase-II pilot feasibility study was conducted, comparing unguided i-RFCBT to usual care aimed to assess acceptability and estimate effect sizes of this intervention. No formal statistical analyses were conducted, but estimated hazard ratios indicated unguided i-RFCBT was associated with a 36% reduced risk of MDE relative to usual care, a similar effect size to that of guided i-RFCBT. There was also a similar interaction effect between intervention (unguided i-RFCBT) and baseline stress. In addition, the pattern of between-group differences between unguided i-RFCBT and usual care indicated similar short- to medium-term benefits of unguided i-RFCBT to those found for guided i-RFCBT.

7.2.4 Evaluating the efficacy and acceptability of guided i-RFCBT in comparison to the wider literature

7.2.4.1 Diagnostic status

Diagnostic status in the audit case series was assessed using clinical cut-offs on the PHQ-9 (≥10) and GAD-7 (≥8) reflecting the same thresholds used in NHS England IAPT services. IAPT adopts a definition of recovery to incorporate overall wellbeing rather than treating depression or anxiety in isolation, such that clients may be above clinical cut-offs on either PHQ-9 or GAD-7 at assessment but must be below clinical cut-offs on both measures post-treatment to be classed as recovered. Using this definition, the audit sample achieved 46.67% recovery for individuals meeting caseness for depression at baseline and 40.32% recovery for individual meeting caseness for GAD at baseline. These recovery rates are comparable to the overall IAPT rates during the same time period (Community and Mental Health team, 2015,

2016). Among the subsample participating in the case series, recovery was higher than the 50% target for IAPT services, at 62.5% for those meeting caseness for depression at baseline and 52.2% for those meeting caseness for GAD at baseline. This benchmarking suggests that i-RFCBT is achieving similar outcomes to other treatments offered within IAPT services. Recovery rates may have been higher for those in the case series because they were more motivated and engaged in the treatment.

The RESPOND trial measured diagnostic status using a standardised diagnostic interview (SCID-I; First et al., 2002) to assess the onset of new cases of MDE during the follow-up period. This was a specific improvement on the prior Topper et al., (2017) trial, which had only assessed caseness by using cut-offs on the PHQ-9 and GAD-7. The reduction in risk for onset of MDE in the current trial (34% for guided i-RFCBT relative to usual care) was smaller than that found in the Topper et al., (2017) study (47% reduction in incidence).

One possible explanation for this observed difference in effect sizes between the two trials is the different measures used in each study. RESPOND used a well-validated diagnostic interview surveying the onset of MDE across the entire follow-up period, whereas Topper et al., (2017) used clinical cut-offs on self-report measures at particular cross-sectional points in time. Topper et al. (2017) acknowledged that their use of clinical cut-offs on self-report measures may have resulted in more false positives than would be obtained from diagnostic interviews, since it is possible to score above the clinical threshold on the questionnaire without necessarily meeting all the criteria for a MDE. Furthermore, the Topper et al., (2017) approach could only capture elevated depression or anxiety that occurred at the point of the assessment and could

not detect any episodes of MDE that had occurred and then improved between assessment points. By influencing the detected base rate of “incidence” of MDE, these measurement differences could influence the sensitivity of each trial to detect genuine changes. Overall, the structured clinical interview used in RESPOND is the more conservative and more accurate approach.

Another possible explanation for the difference is the different ages of the samples (Cook, Mostazir, & Watkins, 2019). The developmental stage of participants could influence the base rate of incidence of MDE and thus the sensitivity of the trials or the responsiveness of participants to the interventions. Because cases of depression begin to rise steeply at 14 (Hankin et al., 2015), i-RFCBT may be more efficacious for prevention in mid-to-late adolescence than in undergraduates. It is possible that the ruminative habit has become stronger and more entrenched by the time individuals attend university and may therefore be more resistant to intervention than in younger participants.

Nonetheless, the effect size for prevention found in the RESPOND trial is consistent with those found in previous meta-analyses of prevention interventions for depression. For example, Van Zoonen et al. (2014) found a 21% decrease in incidence on average. Cuijpers et al. (2008) found an average incidence rate ratio (IRR) of 0.72 for selective interventions, indicating a 28% reduction in risk of MDE. The effects of i-RFCBT thus seem to be on a par with other evidence-based psychological interventions to prevent depression. From a probability-based framework, this increases the likelihood that the observed findings are genuine, because they are consistent with these prior findings.

Major depression is highly recurrent, with 50 to 80% of cases experiencing multiple episodes (Judd, 1997). As expected, past MDE

significantly increased risk (by two and a half times) of a further episode during the follow-up period. As many prevention trials do not assess past depression, a common criticism is that outcomes cannot distinguish between first onset and relapse (Merry et al., 2011). This limitation was rectified in the RESPOND trial because a baseline assessment of past history of depression was included. Importantly, in the RESPOND trial, past MDE did not interact with intervention arm, indicating there was no differential effect of i-RFCBT on the prevention of either first onset of MDE or relapse.

A significant interaction between intervention arm and stress indicated the preventive effects of i-RFCBT improved as baseline subjective stress increased. This is an important finding as previous research in students has found that it is the combination of stress and rumination that prospectively predicts the highest levels of hopelessness, dysphoria and suicidal thoughts in students (Morrison & O'Connor, 2008), indicating that this is a subgroup at particularly high risk of mental ill health.

However, more traditional CBT techniques may not be suitable for managing this risk. For example, a preventive trial of self-help prevention workbooks for at-risk students found a 3-way interaction between intervention by stress by rumination (Haeffel, 2010), in which students with high stress and high rumination who completed a traditional cognitive workbook (thought challenging and generating adaptive cognitions) experienced more depression four months later than students who had completed an adapted cognitive therapy (generating adaptive cognitions without any challenging of negative thoughts) or an academic skills workbook. This suggests that traditional

cognitive self-help approaches are not effective, and may even be harmful, for students with high levels of both stress and rumination.

Preventive approaches that successfully reduce rumination have shown more promise in individuals with high stress. For example, in adolescents aged 13-15, a school-based mindfulness intervention for the indicated prevention of depression was most beneficial for those with more severe baseline symptoms, including perceived stress (Fung et al., 2019). The intervention effects were mediated by reductions in rumination, indicating that reducing rumination, particularly in youth with higher levels of stress, improves mental wellbeing.

In a web-based stress management universal prevention for undergraduates, the intervention was most effective at reducing stress in a subgroup identified as high-risk (due to a history of interpersonal violence) (Nguyen-Feng et al., 2015). Rumination was elevated in this subgroup and the intervention effects were mediated by a decrease in rumination. Taken together, these studies and the findings from RESPOND indicate that targeting rumination in high stress individuals may be particularly beneficial in preventing depression.

In sum, the results of the audit and RESPOND trial provide convergent evidence that guided i-RFCBT can be efficacious at both reducing caseness of current depression and at preventing the onset of future MDE, with clinical outcomes similar to those observed in IAPT services and in recent meta-analyses of prevention interventions. In addition, guided i-RFCBT is particularly efficacious at preventing depression in high-risk students who present with a combination of high rumination and high levels of stress.

7.2.4.2 Symptom severity

In the audit and case series, guided i-RFCBT was associated with significant reductions in acute symptoms of depression and anxiety, as well as reductions in rumination and worry from pre- to post-treatment. For those at clinical levels prior to intervention, the mean difference in PHQ-9 scores from pre-to post-intervention was 6 points. A 6-point reduction on PHQ-9 is the IAPT threshold for reliable change. Mean change on GAD-7 (3.86 points) almost met the IAPT threshold for reliable change (4 points). This suggests that the symptom improvements in the audit sample were not only statistically, but also clinically, significant.

In the RESPOND trial, we found that guided i-RFCBT reduced rumination (post-treatment), worry and depressive symptoms relative to usual care but only for the first 3 to 6 months. Effect sizes were small-to-moderate at 6 months, but only small effects were found on symptom measures at the 15-month follow-up. This pattern of short-to-medium term symptom improvement is consistent with a meta-analysis of iCBT for prevention, in which small but significant effects in favour of the intervention over waitlist control or usual care were found for depressive symptoms, but where effect sizes reduced over time and were no longer significant after 6 months, indicating that benefits were not maintained (Sander et al., 2016). Similarly, in a relapse prevention trial, the addition of mobile-based cognitive therapy to maintenance treatment as usual (TAU) significantly reduced symptoms of depression at 3-month follow-up compared to TAU only (Kok et al., 2015). However, there was no evidence of long-term effects. At 24 months post-intervention, cumulative relapse rates were not significantly different between TAU plus mobile-based cognitive therapy and

TAU alone (Klein et al., 2018), indicating the short-term benefits of the intervention on symptom severity did not translate into significant relapse prevention. As trials of preventive interventions often have only short-term follow-ups, measuring only symptom severity may overestimate the positive effects of an intervention.

Taken together, these findings suggest guided i-RFCBT is able to produce clinically reliable change in acute symptoms of depression and anxiety and reduce short-to medium-term severity of subclinical depressive symptoms in a high-risk preventive sample, but further adaptations may be needed to ensure these effects are maintained over the longer term.

7.2.4.3 Acceptability, adherence and compliance rates for guided i-RFCBT

Usage data, including number of log-ins and number and percentage of modules completed is often used as a measure of treatment adherence and, indirectly, as a measure of acceptability of a treatment: the more modules a participant completes, the more acceptable and engaging to them, the intervention is assumed to be. By examining this data, we are able to infer whether the intervention as a whole is acceptable.

Where attitudes have been assessed qualitatively, there is evidence of a link with engagement. For example, in a trial of iCBT in routine clinical settings, Knowles et al. (2015) found participants with positive attitudes used the intervention an average of 9.1 times, those rated as ambivalent used it 6.7 times and those with negative attitudes used it an average of 3.2 times.

Overall in the audit sample, participants completed a mean number of 3.19 modules (*SD* = 2.35), and 47.2% of participants were treatment compliers. Within the case series sample, the average number of modules completed was 3.81 (*SD* = 2.01) and compliance rates were higher at 62.5%.

Similar rates were found when guided i-RFCBT was delivered as a preventive intervention rather than an acute treatment. Within the full ITT sample participants completed an average of 3.46 modules (*SD* = 2.25), with 46% of participants classified as compliers. The rate of compliance was higher (60%) for the participants who provided follow-up outcome data indicating participants who were more engaged in the research procedures were also more engaged with the intervention.

We would have liked to assess which modules were completed the most often as a measure of acceptability of individual techniques (Cook & Watkins, 2016). However, the fixed presentation order makes this difficult to interpret as, by definition, completion will be highest for the earlier modules.

Previous research has found compliance tends to be lower for guided iCBT than for face-to-face CBT. For example, in a meta-analysis of 24 studies (26 treatment conditions: 14 face-to-face CBT, 12 guided iCBT), van Ballegooijen et al. (2014) reported significantly lower completion rates for guided iCBT (65.1%) than face-to-face CBT (84.7%). However, no significant differences were found in terms of the percentage of content completed (80.8% guided iCBT vs. 83.9% face-to-face CBT), suggesting an adequate dosage was achieved for guided iCBT.

While the average percentage of content completed in RESPOND (58%) is lower than that reported by van Ballegooijen et al. (2014), it is comparable to

a mean of 3.96 modules completed (equivalent to 66% of content) in a previous trial of guided i-RFCBT (Topper et al., 2017). Topper et al. (2017) found compliance was lower in the internet version than the (face-to-face) group version of RFCBT but observed no difference in clinical outcomes, suggesting a minimum necessary level of dose was achieved in the internet format. This finding that younger adolescents benefitted from minimal exposure could reflect the findings of O'Kearney et al. (2009) who found no relationship between rate of symptom decline and number of modules completed in younger participants (14-16).

In contrast, the current findings provide some evidence that compliance was associated with clinical outcomes in student samples, at least for the treatment of acute symptoms. In the Wellbeing audit sample, greater compliance was associated with larger improvements in symptom severity, indicating a dose-response effect. In the RESPOND trial, there was no significant difference between compliers and non-compliers on incidence of depression. However, there was a significant interaction between stress and compliance, indicating those participants with higher baseline stress who complied to the intervention achieved the greatest benefit (65% reduction in risk of MDE).

These findings that increased compliance to the therapy results in better outcomes (a dose-response effect) is consistent with the wider literature on interventions, especially in adults. For example, when iCBT programmes for depression and anxiety were delivered in routine clinical settings, the number of modules completed and baseline symptom severity were predictors of clinical outcomes (Hadjistavropoulos, Pugh, Hesser, & Andersson, 2016).

Taken together, these findings provide evidence that guided i-RFCBT is acceptable to students when delivered as either a treatment or a preventive intervention, with similar compliance rates to previous studies of iCBT and i-RFCBT. The evidence of a dose-response effect in both the acute sample and the high-stress preventive subsample suggests further actions to encourage treatment compliance would boost the clinical effects of i-RFCBT.

7.2.4.4 Comparison of unguided i-RFCBT to guided i-RFCBT and the wider literature regarding unguided iCBT

Although only designed as a feasibility pilot, and thus needing to be treated with caution, the RESPOND results provide a preliminary suggestion that unguided i-RFCBT may have similar clinical effects to guided i-RFCBT for the prevention of depression. In addition, the findings from RESPOND that compliance rates were not significantly different between guided and unguided i-RFCBT suggests students were able to successfully complete modules without support.

Previous research has found that guided iCBT interventions are significantly more effective than unguided in the acute treatment of depression (Andersson & Cuijpers, 2009; Gellatly et al., 2007; Spek et al., 2007). One proposed reason for this is lower adherence to unguided interventions. Several trials of internet interventions for acute depression have reported high levels of attrition or non-adherence to the intervention (57% attrition across 40 studies; Richards & Richardson, 2012), particularly when interventions are unguided (74% attrition; Richards & Richardson, 2012) and provided in an open access way (less than 1% completing the intervention; Christensen et al., 2004). However, there is emerging evidence that the differences between guided and

unguided interventions may be smaller than suggested by the earlier reviews (Dear et al., 2015b; Königbauer, Letsch, Doebler, Ebert, & Baumeister, 2017; Mira et al., 2017; Olthuis, Watt, Bailey, Hayden, & Stewart, 2016).

Shim, Mahaffey, Bleidestel and Gonzalez (2017) conducted a scoping review of human support factors in internet-provided interventions for the treatment of depression or anxiety disorders in adults and found mixed results for trials directly comparing guided and unguided interventions. In some trials, guided interventions were superior to unguided interventions (Farrer et al., 2011; Kleiboer et al., 2015; Titov et al., 2009; Titov et al., 2008), while in other studies, no significant difference was found (Berger et al., 2011a; Berger et al., 2011b; Dear et al., 2015b; Kobak et al., 2015; Santucci et al., 2014). Four of these trials found lower treatment adherence for unguided interventions relative to guided interventions, with the remaining five finding no difference between them. Clinician expertise did not affect outcomes. However, Shim et al. (2017) did find a significant effect of the schedule of support, with support provided at predetermined fixed intervals in a structured schedule (e.g. weekly) associated with better clinical outcomes than unstructured support (i.e. only provided in response to client requests).

Indeed, where iCBT is utilised for prevention, it is still unclear how much added value support provides (Bolinski et al., 2018). Specifically, while guided interventions are generally more clinically effective, Bolinski et al. (2018) hypothesised that unguided iCBT for prevention will be more cost-effective (as measured in terms of healthcare use, presenteeism, absenteeism and disorder free days). Even if an unguided intervention has a smaller effect size or higher drop-out rate than a guided intervention, unguided preventive interventions

have the potential to result in a larger public health benefit simply because the numbers who can access the intervention are much higher (Muñoz et al., 2015; Weisel et al., 2019).

While this argument for implementing unguided prevention centres on scaling up small effect sizes to achieve population-level effects, the current findings suggest that guidance and support may not be necessary for i-RFCBT when used as a preventive intervention and that similar effect sizes may be achievable using the intervention without guidance. Results from the focus group, whose participants only saw the unguided version, suggested unguided i-RFCBT was largely acceptable to a high-risk student population.

Demographic or intervention factors may explain the similar effect sizes of guided and unguided i-RFCBT in the current study. Other studies in university students have found similar effects for guided versus unguided interventions. For example, in a meta-analysis of 48 studies assessing internet interventions for mental health in university students (aimed at symptoms of depression, anxiety, stress, sleep problems or eating disorders, as well as overall functioning and wellbeing), there was no evidence that guidance moderated effect size (Harrer et al., 2018). Young adults are particularly computer literate and may therefore be less reliant on support for iCBT than older adults. In addition, university students in particular are required to engage in a large amount of independent study in order to complete their degree so may be better able to self-motivate than non-students.

With regard to intervention factors, the transdiagnostic focus may have improved the efficacy of unguided i-RFCBT. An RCT of transdiagnostic iCBT (for depression and anxiety) in young adults aged 18-24 (60% students)

compared guided and self-administered versions of the intervention (Dear et al., 2018). Significant improvements in depression and anxiety were found for both versions as well as improvements in general distress, life satisfaction and disability. No significant differences were found between the two versions, indicating a transdiagnostic intervention delivered either with or without support may be effective for young adults. Like the RESPOND trial, this study involved telephone contact with the research team for baseline and follow-up assessments and participants were monitored for risk, so different findings might occur when using fully automated, unguided iCBT.

A third potential reason for the unguided version of i-RFCBT having similar adherence and effect sizes to the guided version of i-RFCBT could be the targeting of both interventions only to participants with elevated levels of worry and rumination. It may also be that the particular focus of the intervention on rumination and worry as a non-stigmatising and common problem that many young people may want to address. By delivering a treatment specifically targeting rumination only to individuals who reported high levels of rumination, the treatment may have been more credible, relevant and engaging to participants, and this may have mitigated any of the benefits of support. In cases where interventions match the user's needs through being credible, relevant and high quality, there will be less need for support and unguided formats may be as acceptable as guided (Dear et al., 2015b). For example, treatment credibility was a predictor of adherence to an unguided Social Anxiety Disorder (SAD) intervention, but not to guided SAD treatment, indicating that users who view the intervention as credible are able to successfully adhere without the support of a coach (Nordgreen et al., 2012).

The convergent evidence from the qualitative study and compliance rates suggest unguided i-RFCBT is sufficiently credible, relevant and of high enough quality to engage students who are identified as being prone to rumination.

Our preliminary evidence suggests that unguided i-RFCBT may be as acceptable and efficacious as guided i-RFCBT in the preventive context in undergraduate samples. We need to be cautious about giving too much weight to this finding as this was a feasibility study and not a properly powered evaluation. Nonetheless, our findings are consistent with other data that unguided internet interventions may do as well as guided internet interventions in young adults. There also remains the question of whether guidance is more essential for the success of acute treatment of depression than the prevention of depression.

7.3 Theoretical implications

The primary focus of this thesis was the evaluation of i-RFCBT as an intervention in university students (i.e., clinical utility) rather than on directly testing theoretical hypotheses. Nonetheless, the findings are supportive of and consistent with several prominent theories of rumination.

First, a number of accounts have posited that rumination is a transdiagnostic risk factor, involved in the onset and maintenance of a range of emotional disorders (Ehring & Watkins, 2008; Watkins, 2008; Nolen-Hoeksema & Watkins, 2011). Consistent with this model, i-RFCBT reduced both symptoms of depression and anxiety, in an acute treatment setting (see Study 1, Chapter 3) and a trial of i-RFCBT as a preventive intervention (see Study 3, Chapter 6).

Second, I-RFCBT is derived from a number of theoretical models including a conceptualisation of pathological rumination as a habit (Watkins & Nolen-Hoeksema, 2014) and as involving a maladaptive style of abstract processing (Watkins, 2008). I-RFCBT explicitly has principles and techniques designed to break the habitual nature of rumination and to shift patients out of the unhelpful thinking style to the helpful thinking style. Evidence from RESPOND that i-RFCBT does reduce the onset of depression is at least consistent with these theoretical models. However, evidence that an intervention is effective is not necessarily sufficient evidence that the processes targeted by the intervention are either causal in the disorder, nor that these processes are the active mechanisms of the treatment. Interventions like i-RFCBT are complex interventions consisting of many components, and we are unable to tell from a parallel-arm RCT which elements or components were responsible for symptom change.

The MRC guidelines recommend process evaluations alongside outcome evaluations. These serve to clarify intermediate causal mechanisms and contextual factors that explain variability in outcomes (Craig et al., 2008). Process evaluations would inform further adaptations to i-RFCBT to optimise its impact on student wellbeing.

While there is growing evidence of the effectiveness of iCBT for a range of mental health conditions, more research is needed to understand which aspects of iCBT work for whom and the underlying mechanisms (Andersson, Carlbring, Titov, & Lindefors, 2019). Parallel-group RCTs provide evidence of the overall intervention effects, but do not assess the effects of individual components or any interactions between components (Watkins et al., 2016). There are

hypothesised mechanisms of change for each of the intervention components included in i-RFCBT, for example, concreteness training is hypothesised to reduce overgeneralisation and negative cognitive biases and functional analysis is hypothesised to target the habitual nature of rumination (see Watkins et al., 2016). However, this thesis did not explore individual components. A factorial design in which specific components are either present or absent (Watkins et al., 2016) would provide evidence for which specific components of i-RFCBT exert the strongest effect on clinical outcomes, either as a main effect or in interaction with other components. Such a study would potentially allow the formation of a briefer, more potent form of i-RFCBT. In addition, such an approach can also be used to test the hypothesised mechanism of change underlying individual intervention components. As described by Watkins et al. (2016), this involves testing whether the presence of a specific treatment component has an effect on the secondary outcome measure of the predicted mechanism of change, and whether this change in turn mediates the relationship between treatment component and outcome. An example within i-RFCBT would be to test whether the presence (versus absence) of the concreteness module reduces overgeneralisation and whether change in overgeneralisation mediates outcomes for the concreteness module.

Understanding the underlying processes of i-RFCBT is important to improving the longer-term outcomes of the intervention. The pattern of findings for symptoms severity suggest effects may be short-to medium-term but not sustained over the longer term. Further research should therefore test methods for boosting the longer-term effects of i-RFCBT.

The mediation analyses (Appendix A, Chapter 6) did not find that change in rumination (as measured using RRS) during the intervention period (baseline to 3-month follow-up) mediated the effect of guided i-RFCBT on depression (symptom severity or MDE onset). However, it is possible that the analyses were underpowered to detect a mediation effect as the main intervention effect was not significant and the sample size diminished across the follow-up period. Topper et al. (2017) found the reduction in rumination mediated the intervention effect on depression, so it is possible that RESPOND was not sufficiently powered to detect such an effect. The mediation models outlined in Chapter 6 could be utilised in further trials to test whether the observed intervention effects are mediated by change in rumination.

The mediation analyses in Chapter 6 used trait rumination as the putative mediator, but other measures of rumination may provide further insight into the underlying mechanisms of change. One proposed underlying mechanism is the weakening of ruminative habit. Rumination is conceptualised as a habit (Watkins & Nolen-Hoeksema, 2014) which requires consistent and long-term practice to change, particularly when habits are strong and longstanding. Consistent with this conceptualisation of rumination as a habit (Watkins & Nolen-Hoeksema, 2014), the case series participants demonstrated a significant reduction in habit scores from pre-to post-intervention indicating that rumination had become less habitual over the course of the intervention. However, no follow-up assessment was conducted in this study, so it is unclear whether such changes persisted over the longer term.

In contrast, i-RFCBT did include a long-term follow-up but found the short- to medium-term benefits of i-RFCBT on depression, anxiety and rumination were

not maintained longer term. Watkins & Nolen-Hoeksema (2014) hypothesised that the change in underlying habit may determine whether an intervention has a short or long-term benefit. This is because some interventions may temporarily reduce rumination by removing the context that triggers the habitual behaviour, but if the context-response linkage is unchanged, there is a risk that the ruminative response will be reactivated on encountering such contexts in the future. The techniques within i-RFCBT are designed to be practised repeatedly as a new helpful response to cues that trigger rumination so that these new responses eventually become the habitual responses to the original context. Given that changing a long-held habit requires repeated and persistent practice of any new behaviour, it may be the case that many participants in RESPOND did not practise sufficiently to achieve lasting change in their underlying ruminative habit. In a trial of a single treatment component from RFCBT (concreteness training), the treatment effects were greater in participants who reported that this new technique had become a habit (Watkins et al., 2012).

Future research could therefore investigate ways to encourage practising the new, helpful techniques both more frequently and in response to a wider range of situations to help strengthen these helpful habits, thereby boosting the longer-term effects of the intervention. This could take the form of a booster session several months post-intervention to remind participants to practise, using practical reminders such as flashcards or reminder texts/emails. In addition, as rumination is likely to be triggered by a wide range of contexts, booster sessions could work on pairing the newer, helpful habits to a wider range of contexts (Hertel & Mathews, 2011).

Consistent with the rumination-as-a-habit hypothesis (Watkins & Nolen-Hoeksema, 2014), we would expect ruminative habit to predict incidence and symptoms of depression. As the intervention aims to countercondition rumination with more helpful responses, we hypothesise that both a reduction in ruminative habit and an increase in If-Then as a habit would significantly mediate the effects of i-RFCBT on clinical outcomes. In addition, the maintenance of ruminative habit should predict the future onset of depression. In order to test mediation using the ruminative habit measures, we would need to collect the same habit measures already built into the intervention (RH, HINT) in the control as well as the intervention arm.

Third, the Response Styles Theory (RST; Nolen-Hoeksema, 1991) conceptualises rumination as a stable, habitual, trait-like, repetitive, self-focused response to low mood (Nolen-Hoeksema et al., 2008; Watkins & Nolen-Hoeksema, 2014). This theory, supported by experimental findings, posits that this trait rumination exacerbates and prolongs negative affect and has a deleterious effect on problem solving and the ability to engage in more helpful behaviours (Nolen-Hoeksema, 1991; Nolen-Hoeksema et al., 2008). RST therefore argues that rumination is an unhelpful habitual response to low mood, such as emerges when faced with a loss or stressor. Diathesis-stress models propose that cognitive vulnerabilities (such as rumination) have a particularly negative effect on mental health when triggered by stressful life events (Morrison & O'Connor, 2005).

Indeed, experimental studies have shown that rumination only has deleterious effects in the context of low mood or stressful events. In experimental manipulations of rumination versus distraction, the deleterious

effects of rumination are only found when participants are in a dysphoric mood prior to the manipulation (Nolen-Hoeksema et al., 2008; Watkins, 2016). A similar effect of rumination exacerbating the effects of low mood or stress has been found in ecological momentary assessment studies and prospective longitudinal studies.

In a university sample, the combination of high perceived stress and high baseline rumination prospectively predicted greater hopelessness, dysphoria and suicidal thinking three weeks later (Morrison & O'Connor, 2008), while high trait rumination in the absence of perceived stress predicted lower levels of suicidal thinking, indicating rumination does not always have a negative impact on measures of distress. This relationship between stress and rumination has also been found over longer periods, with exposure to stressful events predicting higher levels of rumination a year later, and rumination mediating the relationship between previous stress exposure and increased symptoms of depression and anxiety (Michl, McLaughlin, Shepherd, & Nolen-Hoeksema, 2013).

In ecological momentary assessment studies, momentary rumination has been found to have a bidirectional relationship with negative affect, such that they reinforce each other (Moberly & Watkins, 2008a; Selby et al., 2016; Takano et al., 2013; Takano et al., 2014). This momentary rumination also mediates the relationship between stressful events and subsequent negative affect and depressive symptoms over a short-term period in both nonclinical and clinical samples (Genet & Siemer, 2012; Moberly & Watkins, 2008b; Ruscio et al., 2015). A recent study in undergraduates (Connolly & Alloy, 2017) found that momentary rumination moderated the effect between stress and

depression such that the deleterious effects of stressful events were amplified by rumination. On days when students experienced a high number of stressful events but did not engage in rumination, or on days when they engaged in rumination but experienced few stressful events, depressive symptoms were lower than on days when both stressful events and rumination were high.

In an undergraduate sample, measuring weekly rumination and stressful events over a 4-week exam period, Vanderhasselt, Brose, Koster, and De Raedt (2016) found the covariation between stress and rumination predicted depressive symptoms 3 and 15 months later, after controlling for baseline depressive symptoms. Additionally, this phasic rumination, in response to discrete stressful events, predicted depressive symptoms over and above the effects of a stable, trait tendency to ruminate. Stress may be difficult to avoid in academia (Morrison & O'Connor, 2008) but interventions that specifically target rumination in response to stressful events may improve clinical outcomes by training alternative coping strategies to use in place of rumination when faced with such events, thereby reducing the co-occurrence of stress and rumination (Vanderhasselt et al., 2016).

The findings in the RESPOND trial are consistent with these diathesis-stress models of rumination. The sample in RESPOND were specifically selected for elevated RNT and, across the sample as a whole, stress was a marginally significant predictor of MDE, increasing the risk of MDE by 40% for each one-point increase in stress (as rated on a 5-point Likert scale), indicating that high ruminators with high perceived stress were at greater risk of depression. In addition, stress significantly interacted with intervention arm, such that those with higher stress obtained the greatest preventive benefit from the intervention.

This suggests that directly targeting the tendency to ruminate in response to stressful events may have reduced the negative impact of these stressful events.

7.4 Clinical implications

There is considerable evidence of elevated rates of poor mental health in students but also of this group being underserved, with a treatment provision gap. There is thus a pressing need for evidence-based, scalable and accessible interventions relevant to students. The results of the RESPOND trial provide some preliminary evidence that i-RFCBT may be a useful addition to addressing this treatment gap. In this section, the evidence for the clinical need is briefly recapped and the potential benefits of i-RFCBT reviewed.

Students are a demographic not well catered for by current NHS mental health services. Demand for mental health services at university has increased considerably in recent years (Thorley, 2017). However, there is also a significant treatment gap. In a survey of 1093 students, 54% of those in need of treatment did not access university services and 33% reported not knowing where to access support if needed (National Union of Students, 2015). For those students who do access support, a significant proportion do not benefit. For example, almost half felt GP appointments were too short to adequately discuss their mental health and 41% of students who had received talking therapy reported it as not being helpful. Suggested improvements to NHS services included reduced waiting times, a lower threshold for treatment and more follow-up to ensure continuity of care. (Batchelor et al., 2019).

Students face some unique barriers to accessing timely mental health treatment. While waiting times in HE institutions (6-7 working days for

assessment followed by 17-18 days for ongoing treatment; (Broglia, Millings, & Barkham, 2017) are comparable to the average wait time of 20.7 days in IAPT services (Community and Mental Health Team & NHS Digital, 2018), this amounts to approximately half an academic term without intervention and the potential for the student to fall behind on academic work. In addition, the majority of these appointments are for high intensity interventions, demonstrating that students are already experiencing significant levels of distress by the time they seek help (Broglia et al., 2017).

Students also face geographical barriers. Once a student commences treatment at their university, they may face lengthy periods without support during the holidays. These structural barriers are particularly important to support staff (mental health advisors and university counselling services), who cite inadequate NHS services, difficult referral procedures and a lack of joined up care between home and university location as being particularly detrimental (Student Minds, 2014). However, for students structural barriers were rated as less important than attitudes towards mental health and help seeking, with the top priorities being: fear of judgment, stress, finding it difficult to be open with others that you are struggling, perceiving mental health problems as a weakness and feeling lonely (Student Minds, 2014).

i-RFCBT has the potential to address some of the structural and attitudinal priorities identified by Student Minds (2014) to improve the mental health of university students. Firstly, as i-RFCBT can be accessed at any time, it is not subject to the same scheduling restrictions and waiting lists as face-to-face appointments. This may facilitate students taking a more active approach to their mental wellbeing. Patients with depression have previously highlighted

accessibility as a key facilitator to becoming an active agent in their recovery, rather than passively waiting for treatment to begin while on a waiting list (Lillevol et al., 2013).

As well as lowering the initial threshold for accessing treatment, i-RFCBT can also provide greater continuity of care across the academic year. In the case series sample (Study 1) over one third of modules were completed during holiday periods, demonstrating that students continued to engage with the intervention outside term time. The inclusion of digital or telephone support that can be accessed remotely, such as i-RFCBT, within the university setting has the potential to both increase the number of students that can be supported each academic year and improve the continuity of care across the year.

I-RFCBT also has the potential to address some of the attitudinal or help-seeking challenges rated as top priorities by students. In the qualitative study, participants spoke about it being easier to express oneself online as this removed the fear of being judged and facilitated a more honest disclosure of one's feelings. Secondly, they identified specific techniques within i-RFCBT that helped them to manage stress more effectively. Furthermore, the focus on targeting worry and rumination, rather than on clinical disorders or symptoms, may have benefits in terms and user engagement and reducing stigma. Worry and rumination, particularly in response to setbacks, are frequently reported in surveys of student wellbeing (McIntosh & Shaw, 2017; Pereira et al., 2019) so i-RFCBT is relevant to the concerns expressed by this population. Seeking an intervention for these common experiences of worry or rumination may involve less fear of judgement and of being labelled as mentally ill and less concern that this reflects a weakness.

The RESPOND trial found that, among a student population specifically selected for being at-risk of depression due to elevated rumination, students with higher stress levels benefitted most from guided i-RFCBT. This highlights the value in routine screening of students to identify those most in need of intervention. The World Health Organisation (2017) recommends routinely screening for depression and anxiety in university students, as these disorders are both highly prevalent and associated with significant impacts among first-year students. Screening and prevention early in a student's course has the potential to improve their entire university experience. Findings from RESPOND suggest that screening measures could focus on the risk factors of rumination and stress, rather than clinical symptoms. Such an approach to screening and intervention would avoid the medicalisation of students' experiences. I-RFCBT has the potential to engage students at an earlier stage in their symptom trajectory and reduce the demand for acute treatment services.

Although there is evidence from RESPOND that guided i-RFCBT is effective for prevention of depression in high-risk students, the scalability is necessarily limited by the availability of therapists to support the intervention. Preliminary findings from RESPOND suggest unguided i-RFCBT may also be an effective and acceptable preventive intervention for university students. A fully powered effectiveness trial is needed to confirm these effects but, if found to be robust, there is potential for both guided and unguided i-RFCBT to be offered within HE institutions. Unguided interventions are highly scalable and non-consumable (i.e. the same content can be used by unlimited numbers without losing therapeutic value; Muñoz et al., 2010). Given this scalability, even small effect sizes can provide considerable preventive effects on a population level (Muñoz et al., 2015; Weisel et al., 2019). Even if unguided i-RFCBT is associated with

smaller preventive effects than guided i-RFCBT, providing access to the entire student body has the potential to reduce the considerable burden of disease of depression within this population. An effective unguided i-RFCBT intervention could be utilised as a public health intervention with near universal coverage.

The findings from RESPOND suggest guided i-RFCBT may be usefully implemented as a preventive intervention in UK universities. Universities UK (2017) advocate a Whole University Approach to mental health, such that the focus on mental wellbeing and resilience permeate throughout the entire organisation, rather than relying solely on acute treatment services. Recommendations to implement this approach include a focus on prevention and early intervention rather than intervening only once symptoms are severe; focusing on important transitions such as that from school to university and university to employment as these are high risk periods; greater emphasis on staff training to identify students with early symptoms as well as how to better manage their own mental health and greater collection of data to assess both need and efficacy of interventions. I-RFCBT is consistent with this Whole University Approach, prioritising prevention in undergraduates, and the findings from RESPOND provide evidence that this intervention is effective in the relevant university context.

7.5 Strengths of research

As a programme of work, the studies reported in this thesis provide convergent evidence of the acceptability and efficacy of i-RFCBT for undergraduates. I-RFCBT was tested as both a treatment and preventive intervention for university students. For the treatment study, i-RFCBT was implemented within the Wellbeing Services and provided as one treatment

option during the standard assessment. Participants were therefore not actively seeking iCBT. As the study only analysed data that was collected during the routine assessment and automatically recorded by the intervention platform, the study had good ecological validity.

In the overall audit sample, i-RFCBT was associated with significant improvements in symptoms of depression and GAD. Within the case series sample, these positive effects were found across different times of the academic year and differing lengths of baseline period. Participants also ranged in age, were roughly equally distributed in terms of gender and were also studying a wide range of subjects. These findings are therefore generalisable across a range of students and time periods.

For the RESPOND trial, participants were specifically selected for elevated RNT and recruited through advertisements and are therefore a more self-selecting sample. This may have resulted in a more engaged sample than those in the Wellbeing study. However, the design of the trial, including randomisation and the usual care control arm, allow us to make stronger causal inference about the effects of i-RFCBT. Taken together, these findings provide convergent evidence that i-RFCBT is acceptable and efficacious for both the treatment and prevention of depression and anxiety in a university student population.

The RESPOND trial addressed several key criticisms identified in the prevention literature reviewed in Chapter 1. The majority of studies use self-report measures to assess symptom severity as the primary outcome. Reductions in symptom severity are more accurately classed as treatment trials. In order to demonstrate preventive effects using symptom severity requires an

increase in severity in the control arm and no increase or a reduced increase in the intervention arm (Horowitz & Garber, 2006). A further confound is the lack of ceiling cut-off for symptoms in many eHealth trials, so a proportion of participants would likely be classed as clinical cases prior to intervention. Those who are currently within the clinical range are likely to differ from at-risk or subclinical users in both motivation to engage and responsiveness to the intervention (Deady et al., 2017).

The aim of preventive interventions is to reduce incidence (Muñoz et al., 2010). In order to measure incidence, diagnostic status must be determined, both at baseline and during the follow-up period. Even in cases where diagnostic interviews are used to screen out current clinical cases, these interviews often neglect to assess past depression, so it is unclear whether the intervention aims to prevent first onset or prevent relapse.

The inclusion of diagnostic interviews in RESPOND addressed these limitations from the Topper et al (2017) study by administering the SCID at both baseline assessment and each follow-up. At baseline, this ensured participants were excluded from the trial if currently meeting criteria for MDE and provided with appropriate information about seeking help, thereby encouraging help seeking in students who did not perceive their symptoms as being at clinical levels. The baseline assessment also recorded past diagnosis of MDE so that a distinction could be made between first onset and relapse prevention over the course of the follow-up period. While clinical cut-offs on the PHQ-9 provide 88% sensitivity and 88% specificity for the diagnosis of MDE (Kroenke et al., 2001), these are only able to measure point prevalence and not retrospective incidence. The use of the SCID interview at each follow-up therefore allowed us to assess

both current MDE and any episodes occurring during the interim period, providing greater sensitivity and a more accurate measure of time to onset.

7.6 Limitations of research

The main limitation of the Wellbeing study (Chapter 3) is that, because of the lack of control and the lack of any randomisation to treatment condition, we cannot infer causality as to the effect of the intervention. However, the reduction in symptoms was only found once treatment commenced, across a range of start dates and waitlist periods, reducing the likelihood that these improvements were simply due to timing effects or spontaneous remission.

The guided versus usual care effect size in RESPOND was smaller than that found by Topper et al. (2017). It may be therefore that RESPOND was underpowered to detect a main preventive effect of i-RFCBT in undergraduates as the sample size was calculated on the basis of the larger effect size previously demonstrated for i-RFCBT (Topper et al., 2017). In RESPOND, the reported HR was 0.65 i.e. a 35% reduced risk for the experimental group. However, the study was not fully powered to detect such effect size. Following the method suggested by Schoenfeld (1983) and Collett (2014), assuming an overall accrual period of 52 weeks and a follow-up period of 65 weeks (the same timeframe as used for RESPOND), a sample size of N = 712 (356 per group) would detect a similar effect size with 0.8 power (Alpha = .05), allowing for 20% dropout. This equates to recruiting 13 to 14 participants per week. Overall approximately 170 events are expected to be observed during the follow-up period.

Since beginning the RESPOND trial, an alternative recommendation for power calculations is not to rely on prior effect sizes but rather on calculations

based on minimally clinically important differences (e.g. Buntrock et al., 2016). Given the low number of prevention trials using incidence rates as outcome measures, there is little evidence on what effect size constitutes a minimally clinically important difference for users of preventive internet interventions. However, in consultation with clinicians, Buntrock et al. (2016) recommend an absolute risk reduction of 10% between the intervention arm and control arm would represent a meaningful clinical difference. Using an estimate of 25% incidence in the control group, Buntrock et al. (2016) calculated the required sample size at 406 participants, allowing for 20% drop out. Because the base rate for the incidence of depression in high worriers/ruminators is higher (32.4% Topper et al., 2017; 33% in the RESPOND trial) than this estimate of 25%, the Buntrock et al. (2016) calculation would provide a conservative estimate of the number needed for evaluating guided i-RFCBT. On this basis, the current trial was still under-powered.

It is also noted that dropout was higher than the predicted 20% from Topper et al. (2017), again reducing the overall power to detect a significant effect. The higher than expected drop-out may be because the use of diagnostic interviews relative to self-report requires the scheduling of a specific time and place for the telephone interview and the participant's attendance, whereas self-report measures can be completed at the participant's convenience. Students have a particularly variable timetable (Fleischmann et al., 2017) and participants in RESPOND reported forgetting the booked telephone call or having conflicting priorities. In a larger trial, missed assessments would produce considerable administrative costs in terms of lost researcher time and rebooking appointments. The NHS now uses text reminders to reduce non-attendance of

appointments. It is recommended that these be incorporated into future trials of i-RFCBT.

One limitation of the qualitative study is that the sample included only one male student so the acceptability of i-RFCBT to males is still unclear. Additionally, only a single online focus group was conducted and not all participants contributed to all topics, so the views are limited to a small number of participants. However, the overall findings are consistent with other qualitative studies of students' attitudes towards iCBT, suggesting high ruminating students face the same barriers and facilitators as the wider student population. A further limitation concerns the practicalities of implementing the suggested improvements to the intervention. One of the aims of the qualitative study was to inform changes prior to testing the intervention in the RESPOND trial. Due to problems with recruiting for an in-person focus group and subsequently conducting the focus group online, the focus group was conducted at the same time as recruitment commenced for the trial. Given the time needed to analyse the qualitative data and the technological challenges in making large, structural changes to the intervention, it was not possible to implement these changes in time for these changes to be implemented in the RESPOND trial. Future trials of i-RFCBT should therefore include the suggested adaptations (e.g. smaller sections, simpler navigation, flexible module order, options for written or video case studies) in order to further tailor the intervention to a student sample. One approach to achieving these changes may be to develop a mobile application that students can more easily complete in bitesize chunks and in the environmental contexts that typically trigger their rumination.

There was a high proportion of females compared to males in RESPOND. This distribution was expected, as rumination and depression are more common in females than males (Nolen-Hoeksema, Larson, & Grayson, 1999). This sample is therefore consistent with the intended target population of high ruminators at elevated risk for depression, but potentially limits the generalisability of the preventive findings to male students. However, in the treatment sample of the Wellbeing study the gender distribution was more equal. Although a rumination-focussed intervention will necessarily attract more females, the online delivery has the scope to reach some male students who would not choose face-to-face talking therapies. Calear et al. (2009) suggested that males may prefer the structured logical approach of internet-based CBT interventions. Despite this, male gender is a significant predictor of dropout from self-guided interventions (Karyotaki et al., 2015), possibly because females are more conscientious about health problems and engage a greater effort to manage depression, suggesting they may better able to self-motivate in the absence of a supporter. Additionally, mature students and international students are subgroups who are particularly at risk and may face unique barriers to help-seeking. Qualitatively assessing the opinions of more males, a wider range of ethnicities and including mature students would therefore be an important consideration prior to implementation to ensure the intervention meets the needs of a wide range of students.

7.7 Plans for future research

The MRC provides guidelines for research into Complex interventions (Craig et al., 2008), consisting of four interlinked domains: development, feasibility or piloting, evaluation and implementation. The studies reported in this thesis

address various stages of this process and recommendations for completing further stages are discussed.

7.7.1 Further evaluation of guided i-RFCBT

The Phase-III RCT comparing guided i-RFCBT to care as usual falls under the evaluation domain, specifically testing effectiveness. As it is possible that RESPOND was underpowered to detect an overall prevention effect, one future plan for research is to conduct a further fully-powered phase III trial, as outlined in section 7.6.

One advantage of a larger-scale trial would be the potential to assess any delay in onset of MDE as well as overall incidence rates. Even in the absence of a significant overall reduction in number of cases, any delay to onset could still be beneficial in reducing the disease burden of depression (Buntrock et al., 2016), particularly in young people due to the developmental and academic demands at this age. Buntrock et al. (2016) found average time to onset was increased by 6 weeks in the intervention group relative to controls. Even such a relatively short delay would reduce the overall disease burden in the student population.

A further area of research could be to investigate the wider effects of i-RFCBT in terms of preventing GAD, as well as investigating the impact on broader aspects of student wellbeing, such as academic achievement and social functioning. If shown to be effective on such measures, this would provide a stronger case for widespread implementation in university settings.

The primary interest of the RESPOND trial was the prevention of depressive episodes (MDE) but, in support of the theory that rumination is a

transdiagnostic risk factor, Topper et al. (2017) found preventive effects of RFCBT on the onset of GAD as well as MDE. A further trial should test these transdiagnostic effects in students. While anxiety disorders were assessed in RESPOND, these were not exclusion criteria at baseline. It was therefore not possible to assess whether i-RFCBT had similar effects on preventing anxiety disorders (as found with GAD by Topper et al., 2017) in university students. The pattern of changes on the symptom measures (reductions in symptoms of anxiety and worry) suggest that i-RFCBT does have a transdiagnostic effect among students but a future trial should exclude participants with a diagnosable episode of GAD at baseline to confirm this.

Demonstrating an effect on more than just clinical symptoms is also important evidence of the intervention's effectiveness, as highlighted by a meta-analysis of fourteen trials of iCBT for depression (totalling sixteen comparisons), which found significant short-term effects on symptoms but no evidence of improvements in functioning (So et al., 2013). Although functioning was assessed as a secondary outcome, and trials may not have been adequately powered to detect an effect on functioning, a demonstration of positive outcomes on measures other than clinical symptoms might strengthen the case for implementation of an intervention increase implementation, thereby reducing the research to practice gap (Mohr, Lyon, Lattie, Reddy, & Schueller, 2017).

Functional impairment in students covers a range of domains (academic, social, domestic; Alonso et al., 2019). In terms of academic functioning, poor mental health may lead to lower achievement, dropout and poorer employment prospects. Eight percent of UK undergraduates drop out of their course within the first year and more than 20% do not complete their degree (Papadatou-

Pastou et al., 2017). As these are the key criteria that universities are judged on, demonstrating that an intervention improves academic achievement and retention rates would provide a strong case for widespread implementation in the Higher Education sector. However, while the academic impact may be particularly valuable to the institution, on a more personal level, a recent WHO survey found that, while students with depressive symptoms reported role impairments across a range of domains, the greatest role impairments were in social (e.g. close relationships, socialising) rather than academic domains (Alonso et al., 2019). As rumination has negative consequences in both the academic (e.g. lack of motivation, procrastination) and social domains (e.g. negative social evaluations, lack of assertiveness and disconnection from one's surroundings) (Watkins, 2016), it is hypothesised that i-RFCBT would have a positive impact on both academic achievement and social functioning.

One specific area of interest with regard to the rumination-as-a-habit hypothesis is to analyse the nature of the If-Then implementation intentions to investigate whether encouraging a more concrete and specific If-Then plan facilitates implementation. Previous research has shown that highly specific cues and responses are more likely to achieve the desired behaviour as they are less open to interpretation (de Vet, Oenema, & Brug, 2011; Gollwitzer, 1999). Concrete plans specify the what, when, where, how and with whom of the desired behaviour (Watkins, 2016) so researchers could rate the concreteness of plans against these criteria. We hypothesise that participants who formulated more concrete and specific If-Then plans would have been more successful in implementing the desired counter-ruminative behaviour and would achieve greater reduction in ruminative habit. If this is the case, further adaptations to i-RFCBT could encourage highly specific If-Then plans. Previous

research has demonstrated that implementation intentions formed in collaboration with a therapist are more effective (Armitage, 2009; Ziegelmann, Lippke, & Schwarzer, 2006). However, methods that could be used without a therapist, such as volitional help-sheets to support correct formulation have been developed for public health interventions (Armitage, 2008). These volitional help-sheets list specific triggers and responses that may be relevant to the user and can therefore be used as a template for developing idiosyncratic plans (Adriaanse & Verhoeven, 2018). I-RFCBT includes questionnaires about common trigger situations so it would be possible to adapt these into a volitional help-sheet where users pair their selected triggers with specific techniques from the intervention.

Another important consideration in effective implementation intentions for changing existing habits is identifying the critical cue to the undesired behaviour, so that the new, helpful behaviour can be practised in direct competition with the undesired behaviour (Adriaanse & Verhoeven, 2018). One method that may help is cue monitoring, where participants record their behaviour as it happens, using a diary, and the specifics of the situation (e.g. place, people, task) in order to identify which contextual elements are the strongest triggers of the behaviour. I-RFCBT incorporates a mood diary for this purpose, but users complete this retrospectively for the day as a whole. Further research could evaluate the number of diary entries and how concrete the descriptions of the situations are to examine whether participants who made greater use of the diary were more successful at implementing later If-Then plans. If the mood diary is shown to be helpful, a further adaptation could be to include a mood diary app that could be completed in situ, thereby reducing any reliance on retrospective memory to identify the critical cue.

Even when implementation intentions are sufficiently well formulated and strong, the resultant changes are usually relatively small (Adriaanse & Verhoeven, 2018). While such changes are likely to be more sustainable over the longer term, individuals may be demotivated by a perceived lack of quick progress. The inclusion of motivational enhancers, such as motivational interviewing, and reminders may therefore be required in interventions that use implementation intentions (Adriaanse & Verhoeven, 2018).

In terms of boosting motivation to continue practising the techniques, some participants in the qualitative study recommended building in more reminders (either from the coach or automated). However, findings from the habit literature suggest such reminders may be counter-productive as they encourage reliance on the technology, thereby interrupting the automaticity of linking the response to an environmental cue. Recommendations from Stawarz, Cox, and Blandford (2015) for reinforcing new habits within an intervention are: (a) focus on trigger events and include a post event reflection to check whether the desired behaviour was enacted; (b) use reminders only to reinforce implementation intentions e.g. “remember to do Y after X” rather than in the form of “remember to do Y” as this will strengthen the cue-response linkage by forming an association between the trigger and the behaviour and gradually reduce the number of reminders so users do not become reliant on the reminders; (c) do not include features that will make users reliant on the technology, such as self-tracking and general reminders. This suggests that simply reminding participants to log in is insufficient and that reminders should be more idiosyncratic and specifically designed to reinforce If-Then plans. It is hypothesised that such reminders focussed specifically on reinforcing the implementation intentions would improve the long-term effects of i-RFCBT by

increasing the likelihood that positive alternative behaviours are enacted in stressful situations.

7.7.2 Evaluation of unguided i-RFCBT

Unguided i-RFCBT was a novel intervention developed specifically for this thesis. While it contains the same content as guided i-RFCBT, the lack of previous evidence necessitated taking a feasibility or pilot approach in order to determine acceptability and estimate effect size to inform a full-scale evaluation. Future trials should therefore focus on a proper phase III evaluation of unguided i-RFCBT relative to usual care.

As the observed effect size in RESPOND for the unguided i-RFCBT compared to usual care was of the same magnitude as that for guided i-RFCBT, the power calculations in Section 7.6 can be utilised to plan a phase III trial of unguided i-RFCBT. For efficiency, a 3-arm trial would allow the same control group to be used to test the clinical outcomes of both versions of i-RFCBT separately. Including cost-effectiveness measures of healthcare use, presenteeism, absenteeism and disorder free days (as used by Bolinski et al., 2018) would provide important evidence of the relative benefits of guided and unguided i-RFCBT. Based on the literature and the effect sizes from RESPOND, it is hypothesised that unguided i-RFCBT would have significant preventive effects on the incidence of depression in a phase III trial and, given the wider scalability of unguided prevention, demonstrate greater cost-effectiveness than guided i-RFCBT.

7.7.3 Further qualitative assessments of i-RFCBT

Another avenue for further research is to qualitatively assess the opinions of trial participants to further improve the acceptability of i-RFCBT. The qualitative focus group assessed acceptance of i-RFCBT but the participants were asked to read rather than complete the intervention. While participants were selected on the basis of elevated RNT and responses suggested that they did practise some of the techniques, evaluating an intervention for a focus group study may be a different experience from actively using i-RFCBT as a preventive intervention. For example, Bendelin et al. (2011) identified three categories of iCBT users: those who read but did not engage with the material 'readers'; those who found some elements helpful 'strivers' and those who actively engaged with the intervention 'doers'. Participating in the online focus group may have inadvertently pushed participants towards being 'readers' rather than 'doers' and their opinions of the intervention may have been impacted.

The inclusion of qualitative interviews within RESPOND was beyond the scope of the thesis. Qualitative interviewing would ideally be undertaken immediately post-treatment to minimise recall bias. As the researcher responsible for the follow-up assessments was blind to intervention condition until all participants had completed their final follow-up assessment, an additional, unblinded researcher would have been required to conduct qualitative interviews post-treatment.

Further research should therefore collect qualitative data from the trial participants in a mixed-methods approach (as used by Sugg et al., 2020). This could be achieved by conducting semi-structured interviews with a subset of

trial participants, using the same questions focused on barriers and facilitators to using i-RFCBT and which techniques participants found more or less helpful, as well as more detailed questions about engagement with the techniques, such as how helpful particular techniques were in session, how easy or difficult it was to make and implement their If-Then plans, and the amount of time they spent practicing the new techniques. Having both attitudinal and outcome measures from the same participants would help us to identify who would benefit the most from the intervention and inform future adaptations.

One advantage of incorporating qualitative methods into future trials would be the assessment of any differences in opinions between guided and unguided participants. While the responses from the focus group suggested students may prefer supported interventions, past research has criticized the written feedback received from the supporter as being too generic or scripted. (e.g. Fleischmann et al., 2017). It would therefore be informative to test whether the same criticism arose for guided i-RFCBT to aid further tailoring of the support provided.

As well as investigating users' acceptability of i-RFCBT, another important consideration is how acceptable the intervention is to the therapists supporting guided i-RFCBT. One barrier to implementing internet-based therapies is the stakeholders' (e.g. care providers, policy makers) acceptance of such interventions. A recent European survey (Topooco et al., 2017) found iCBT was only recommended for mild depression and by only 47% of stakeholders, whereas 70% would recommend blended therapy (whereby the technology is used as an adjunct to face-to-face sessions). Concerns centred

largely on the loss of face-to-face contact in iCBT and whether a therapeutic alliance could be formed.

Negative therapist attitudes could therefore be a barrier to implementation. Further qualitative research should therefore explore the benefits and barriers of i-RFCBT to those providing the intervention and, where possible, resolve any barriers they may face to supporting the therapy.

7.8 Final summary and conclusions

Despite the theoretical benefits of iCBT for university students, relatively few studies have assessed the acceptability and effectiveness of such interventions. The findings from this thesis contribute to this field by providing evidence for the acceptability and effectiveness of guided i-RFCBT for the treatment of acute symptoms of depression and anxiety when delivered within existing university Wellbeing services. While the provision of effective treatments is vital, greater benefits are achieved with effective preventive interventions. The findings from RESPOND provide evidence that guided i-RFCBT prevents the onset of depression, particularly in students with the combined risk factors of high rumination and high stress. The findings also provide preliminary evidence for unguided i-RFCBT, which, if confirmed in a fully powered trial, has the potential to be implemented as an open access public health intervention available to all registered students, thereby increasing the overall numbers who benefit from evidence-based prevention, as well as potentially attracting students who do not want to communicate with a therapist. Additionally, the recurrent nature of depression considerably increases the disease burden. The findings reported in this thesis provide evidence for the benefits of i-RFCBT at different stages of depression: preventing first onset, reducing risk of relapse, and treatment of

acute episodes. This suggests i-RFCBT is appropriate for use across all stages of the trajectory of depression, thereby potentially considerably reducing the disease burden of depression in UK universities.

References

Aalto-Setälä, T., Marttunen, M., Tuulio-Henriksson, A., Poikolainen, K., & Lönnqvist, J. (2001). One-month prevalence of depression and other DSM-IV disorders among young adults. *Psychological Medicine, 31*(5), 791-801. doi:10.1017/s0033291701004081

Abela, J. R., Brozina, K., & Haigh, E. P. (2002). An examination of the response styles theory of depression in third- and seventh-grade children: a short-term longitudinal study. *Journal of Abnormal Child Psychology, 30*(5), 515-527. doi:10.1023/a:1019873015594

Adriaanse, M. A., & Verhoeven, A. (2018). Breaking Habits Using Implementation Intentions. In B. Verplanken (Ed.), *The Psychology of Habit: Theory, Mechanisms, Change, and Contexts* (pp. 169-188). Cham, Switzerland: Springer International Publishing.

Allison, P.D. (2010). Survival analysis. In G.R. Hancock & R.O. Mueller (Eds.), *The Reviewer's Guide to Quantitative Methods in the Social Sciences* (pp. 413-425). New York: Routledge.

Alonso, J., Vilagut, G., Mortier, P., Auerbach, R. P., Bruffaerts, R., Cuijpers, P., . . . WHO WMH-ICS Collaborators. (2019). The role impairment associated with mental disorder risk profiles in the WHO World Mental Health International College Student Initiative. *International Journal of Methods in Psychiatric Research, 28*(2), e1750. doi:10.1002/mpr.1750

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.). Arlington, VA: APA.

Andersson, G. (2010). The promise and pitfalls of the internet for cognitive behavioral therapy. *BMC Medicine, 8*, 82. doi:10.1186/1741-7015-8-82

Andersson, G., Carlbring, P., Titov, N., & Lindefors, N. (2019). Internet Interventions for Adults with Anxiety and Mood Disorders: A Narrative Umbrella Review of Recent Meta-Analyses. *The Canadian Journal of Psychiatry, 64*(7), 465-470. doi:10.1177/0706743719839381

Andersson, G., & Cuijpers, P. (2009). Internet-based and other computerized psychological treatments for adult depression: a meta-analysis. *Cognitive Behaviour Therapy, 38*(4), 196-205. doi:10.1080/16506070903318960

Andersson, G., Cuijpers, P., Carlbring, P., Riper, H., & Hedman, E. (2014). Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. *World Psychiatry, 13*(3), 288-295. doi:10.1002/wps.20151

Andersson, G., & Titov, N. (2014). Advantages and limitations of Internet-based interventions for common mental disorders. *World Psychiatry, 13*(1), 4-11. doi:10.1002/wps.20083

Andrews, G., Basu, A., Cuijpers, P., Craske, M. G., McEvoy, P., English, C. L., & Newby, J. M. (2018). Computer therapy for the anxiety and depression disorders is effective, acceptable and practical health care: An updated meta-analysis. *Journal of Anxiety Disorders, 55*, 70-78. doi:10.1016/j.janxdis.2018.01.001

Andrews, G., Cuijpers, P., Craske, M. G., McEvoy, P., & Titov, N. (2010). Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis. *PloS one, 5*(10), e13196. doi:10.1371/journal.pone.0013196

Andrews, G., Issakidis, C., Sanderson, K., Corry, J., & Lapsley, H. (2004). Utilising survey data to inform public policy: comparison of the cost-

effectiveness of treatment of ten mental disorders. *The British Journal of Psychiatry, 184*, 526-533. doi:10.1192/bjp.184.6.526

Angrist, J. D., Imbens, G. W., & Rubin, D. B. (1996). Identification of Causal Effects Using Instrumental Variables. *Journal of the American Statistical Association, 91*(434), 444-455. doi:10.1080/01621459.1996.10476902

Armitage, C. J. (2008). A volitional help sheet to encourage smoking cessation: a randomized exploratory trial. *Health Psychology, 27*(5), 557-566. doi:10.1037/0278-6133.27.5.557

Armitage, C. J. (2009). Effectiveness of experimenter-provided and self-generated implementation intentions to reduce alcohol consumption in a sample of the general population: a randomized exploratory trial. *Health Psychology, 28*(5), 545-553. doi:10.1037/a0015984

Auerbach, R. P., Mortier, P., Bruffaerts, R., Alonso, J., Benjet, C., Cuijpers, P., . . . WHO WMH-ICS Collaborators (2018). WHO World Mental Health Surveys International College Student Project: Prevalence and distribution of mental disorders. *Journal of Abnormal Psychology, 127*(7), 623-638. doi:10.1037/abn0000362

Barbour, R. S. (2001). Checklists for improving rigour in qualitative research: a case of the tail wagging the dog? *BMJ, 322*(7294), 1115-1117. doi:10.1136/bmj.322.7294.1115

Barbour, R. S. (2005). Making sense of focus groups. *Medical Education, 39*(7), 742-750. doi:10.1111/j.1365-2929.2005.02200.x

Barbour, R. S. (2008). *Doing focus groups*. London: Sage.

Barker, D. B. (2007). Antecedents of stressful experiences: Depressive symptoms, self-esteem, gender, and coping. *International Journal of Stress Management, 14*(4), 333-349.

Batchelor, R., Pitman, E., Sharpington, A., Stock, M., & Cage, E. (2019). Student perspectives on mental health support and services in the UK. *Journal of Further and Higher Education*, 1-15. doi:10.1080/0309877x.2019.1579896

Bebbington, P. E., & Nyani, T. (1995). The Psychosis Screening Questionnaire. *International Journal of Methods in Psychiatric Research, 5*, 11-19. doi:10.1037/t30040-000

Beck, A. T., Rush, A. J., Shaw, B. F., & Emery, G. (1979). *Cognitive Therapy of Depression*. New York: Guilford Press.

Beekman, A. T., Smit, F., Stek, M. L., Reynolds, C. F., 3rd, & Cuijpers, P. C. (2010). Preventing depression in high-risk groups. *Current Opinion in Psychiatry, 23*(1), 8-11. doi:10.1097/YCO.0b013e328333e17f

Bendelin, N., Hesser, H., Dahl, J., Carlbring, P., Nelson, K. Z., & Andersson, G. (2011). Experiences of guided Internet-based cognitive-behavioural treatment for depression: a qualitative study. *BMC Psychiatry, 11*(1), 107. doi:10.1186/1471-244X-11-107

Bentley, A., Virgo, M. &Hastings, D. (2016) Reaching out to enhance the wellbeing of international students. Are university counselling and wellbeing services accessible and inclusive? In *Research into the international student experience in the UK2015-16.* pp. 46-69. London: UKCISA. Available at: https://www.ukcisa.org.uk/Research--Policy/Grants-research/UKCISA-grants-for-research

Berger, T. (2016). The therapeutic alliance in internet interventions: A narrative review and suggestions for future research. *Psychotherapy Research, 27*(5), 511-524. doi:10.1080/10503307.2015.1119908

Berger, T., Caspar, F., Richardson, R., Kneubuhler, B., Sutter, D., & Andersson, G. (2011a). Internet-based treatment of social phobia: a randomized controlled trial comparing unguided with two types of guided self-help. *Behaviour Research and Therapy, 49*(3), 158-169. doi:10.1016/j.brat.2010.12.007

Berger, T., Hammerli, K., Gubser, N., Andersson, G., & Caspar, F. (2011b). Internet-based treatment of depression: a randomized controlled trial comparing guided with unguided self-help. *Cognitive Behaviour Therapy, 40*(4), 251-266. doi:10.1080/16506073.2011.616531

Bewick, B. M., Gill, J., Mulhern, B., Barkham, M., & Hill, A. J. (2008). Using electronic surveying to assess psychological distress within the UK student population: a multi-site pilot investigation. *E-Journal of Applied Psychology, 4*(2). doi:10.7790/ejap.v4i2.120

Bolinski, F., Kleiboer, A., Karyotaki, E., Bosmans, J. E., Zarski, A. C., Weisel, K. K., . . . Riper, H. (2018). Effectiveness of a transdiagnostic individually tailored Internet-based and mobile-supported intervention for the indicated prevention of depression and anxiety (ICare Prevent) in Dutch college students: study protocol for a randomised controlled trial. *Trials, 19*(1), 118. doi:10.1186/s13063-018-2477-y

Borkovec, T. D., Alcaine, O. M., & Behar, E. (2004). Avoidance theory of worry and generalized anxiety disorder. In R. G. Heimberg, C. L. Turk, & D. S. Mennin (Eds.), *Generalized anxiety disorder: Advances in research and practice* (pp. 77–108). New York, NY: Guilford.

Borkovec, T. D., Robinson, E., Pruzinsky, T., & DePree, J. A. (1983). Preliminary exploration of worry: Some characteristics and processes.

Behaviour Research and Therapy, 21(1), 9-16. doi:https://doi.org/10.1016/0005-7967(83)90121-3

Bradley, G. (2000). Responding effectively to the mental health needs of international students. *Higher Education, 39*(4), 417-433. doi:10.1023/a:1003938714191

Breedvelt, J. J. F., Kandola, A., Kousoulis, A. A., Brouwer, M. E., Karyotaki, E., Bockting, C. L. H., & Cuijpers, P. (2018). What are the effects of preventative interventions on major depressive disorder (MDD) in young adults? A systematic review and meta-analysis of randomized controlled trials. *Journal of Affective Disorders, 239*, 18-29. doi:10.1016/j.jad.2018.05.010

Broderick, P. C., & Korteland, C. (2004). A Prospective Study of Rumination and Depression in Early Adolescence. *Clinical Child Psychology & Psychiatry, 9*(3), 383-394. doi:10.1177/1359104504043920

Broglia, E., Millings, A., & Barkham, M. (2017). Challenges to addressing student mental health in embedded counselling services: a survey of UK higher and further education institutions. *British Journal of Guidance & Counselling, 46*(4), 441-455. doi:10.1080/03069885.2017.1370695

Bruffaerts, R., Mortier, P., Auerbach, R. P., Alonso, J., Hermosillo De la Torre, A. E., Cuijpers, P., . . . WHO WMH-ICS Collaborators. (2019). Lifetime and 12-month treatment for mental disorders and suicidal thoughts and behaviors among first year college students. *International Journal of Methods in Psychiatric Research, 28*(2), e1764. doi:10.1002/mpr.1764

Buntrock, C., Ebert, D. D., Lehr, D., Smit, F., Riper, H., Berking, M., & Cuijpers, P. (2016). Effect of a Web-Based Guided Self-help Intervention for Prevention of Major Depression in Adults With Subthreshold Depression:

A Randomized Clinical Trial. *JAMA, 315*(17), 1854-1863. doi:10.1001/jama.2016.4326

Butler, L. D., & Nolen-hoeksema, S. (1994). Gender differences in responses to depressed mood in a college sample. *Sex Roles, 30*(5-6), 331-346. doi:10.1007/bf01420597

Cage, E., Stock, M., Sharpington, A., Pitman, E., & Batchelor, R. (2018). Barriers to accessing support for mental health issues at university. *Studies in Higher Education*, 1-13. doi:10.1080/03075079.2018.1544237

Calear, A. L., & Christensen, H. (2010). Systematic review of school-based prevention and early intervention programs for depression. *Journal of Adolescence, 33*(3), 429-438. doi:10.1016/j.adolescence.2009.07.004

Calear, A. L., Christensen, H., Mackinnon, A., & Griffiths, K. M. (2013). Adherence to the MoodGYM program: outcomes and predictors for an adolescent school-based population. *Journal of Affective Disorders, 147*(1-3), 338-344. doi:10.1016/j.jad.2012.11.036

Calear, A. L., Christensen, H., Mackinnon, A., Griffiths, K. M., & O'Kearney, R. (2009). The YouthMood Project: a cluster randomized controlled trial of an online cognitive behavioral program with adolescents. *Journal of Consulting and Clinical Psychology, 77*(6), 1021-1032. doi:10.1037/a0017391

Carolan, S., & de Visser, R. O. (2018). Employees' Perspectives on the Facilitators and Barriers to Engaging With Digital Mental Health Interventions in the Workplace: Qualitative Study. *JMIR Mental Health, 5*(1), e8. doi:10.2196/mental.9146

Carver, C. S. (1998). Generalization, adverse events, and development of depressive symptoms. *Journal of Personality, 66*(4), 607-619.

Carver, C. S. (2013). *Attitudes Toward Self (ATS). Measurement Instrument Database for the Social Sciences*. Retrieved from http://www.midss.org/content/attitudes-toward-self-ats

Cavanagh, K., Herbeck Belnap, B., Rothenberger, S. D., Abebe, K. Z., & Rollman, B. L. (2018). My care manager, my computer therapy and me: The relationship triangle in computerized cognitive behavioural therapy. *Internet Interventions, 11*, 11-19. doi:https://doi.org/10.1016/j.invent.2017.10.005

Chan, J. K., Farrer, L. M., Gulliver, A., Bennett, K., & Griffiths, K. M. (2016). University Students' Views on the Perceived Benefits and Drawbacks of Seeking Help for Mental Health Problems on the Internet: A Qualitative Study. *JMIR Human Factors, 3*(1), e3. doi:10.2196/humanfactors.4765

Chew-Graham, C. A., Rogers, A., & Yassin, N. (2003). 'I wouldn't want it on my CV or their records': medical students' experiences of help-seeking for mental health problems. *Medical Education, 37*(10), 873-880. doi:10.1046/j.1365-2923.2003.01627.x

Christensen, H., Griffiths, K. M., & Farrer, L. (2009). Adherence in internet interventions for anxiety and depression. *Journal of Medical Internet Research, 11*(2), e13. doi:10.2196/jmir.1194

Christensen, H., Griffiths, K. M., & Jorm, A. F. (2004). Delivering interventions for depression by using the internet: randomised controlled trial. *BMJ, 328*(7434), 265. doi:10.1136/bmj.37945.566632.EE

Christensen, H., Griffiths, K. M., Korten, A. E., Brittliffe, K., & Groves, C. (2004). A Comparison of Changes in Anxiety and Depression Symptoms of Spontaneous Users and Trial Participants of a Cognitive Behavior

Therapy Website. *Journal of Medical Internet Research, 6*(4), e46. doi:10.2196/jmir.6.4.e46

Ciesla, J. A., Felton, J. W., & Roberts, J. E. (2011). Testing the cognitive catalyst model of depression: does rumination amplify the impact of cognitive diatheses in response to stress? *Cognition & Emotion, 25*(8), 1349-1357. doi:10.1080/02699931.2010.543330

Ciesla, J. A., & Roberts, J. E. (2002). Self-directed thought and response to treatment for depression: A preliminary investigation. *Journal of Cognitive Psychotherapy, 16*(4), 435-453. doi:10.1891/jcop.16.4.435.52528

Ciesla, J. A., & Roberts, J. E. (2007). Rumination, negative cognition, and their interactive effects on depressed mood. *Emotion, 7*(3), 555-565. doi:10.1037/1528-3542.7.3.555

Clarke, A. M., Kuosmanen, T., & Barry, M. M. (2015). A systematic review of online youth mental health promotion and prevention interventions. *Journal of Youth and Adolescence, 44*(1), 90-113. doi:10.1007/s10964-014-0165-0

Clarke, G., Kelleher, C., Hornbrook, M., Debar, L., Dickerson, J., & Gullion, C. (2009). Randomized effectiveness trial of an Internet, pure self-help, cognitive behavioral intervention for depressive symptoms in young adults. *Cognitive Behaviour Therapy, 38*(4), 222-234. doi:10.1080/16506070802675353

Cohen, S., Murphy, M. L. M., & Prather, A. A. (2019). Ten Surprising Facts About Stressful Life Events and Disease Risk. *Annual Review of Psychology, 70*, 577-597. doi:10.1146/annurev-psych-010418-102857

Collett, D. (2014). *Modelling Survival Data in Medical Research* (3rd ed.). New York: Chapman and Hall/CRC.

Collins, M. E., & Mowbray, C. T. (2005). Higher education and psychiatric disabilities: national survey of campus disability services. *American Journal of Orthopsychiatry, 75*(2), 304-315. doi:10.1037/0002-9432.75.2.304

Community and Mental Health team. (2015). *Psychological Therapies, Annual Report on the use of IAPT services - England, 2014-15*. Leeds: Health and Social Care Information Centre Retrieved from http://digital.nhs.uk/catalogue/PUB19098.

Community and Mental Health team. (2016). *Psychological Therapies: Annual report on the use of IAPT services. England, 2015-16*. Leeds: NHS Digital Retrieved from http://digital.nhs.uk/catalogue/PUB22110.

Community and Mental Health Team, & NHS Digital. (2018). *Annual report on the use of IAPT services, England 2017-18*. Retrieved from https://files.digital.nhs.uk/52/D3168F/psych-ther-2017-18-ann-rep.pdf.

Conley, C. S., Durlak, J. A., & Kirsch, A. C. (2015). A Meta-analysis of Universal Mental Health Prevention Programs for Higher Education Students. *Prevention Science, 16*(4), 487-507. doi:10.1007/s11121-015-0543-1

Conley, C. S., Durlak, J. A., Shapiro, J. B., Kirsch, A. C., & Zahniser, E. (2016). A Meta-Analysis of the Impact of Universal and Indicated Preventive Technology-Delivered Interventions for Higher Education Students. *Prevention Science, 17*(6), 659-678. doi:10.1007/s11121-016-0662-3

Conley, C. S., Shapiro, J. B., Kirsch, A. C., & Durlak, J. A. (2017). A meta-analysis of indicated mental health prevention programs for at-risk higher

education students. *Journal of Counseling Psychology, 64*(2), 121-140. doi:10.1037/cou0000190

Connolly, S. L., & Alloy, L. B. (2017). Rumination interacts with life stress to predict depressive symptoms: An ecological momentary assessment study. *Behaviour Research and Therapy, 97*, 86-95. doi:10.1016/j.brat.2017.07.006

Cook, J., & Doyle, C. (2002). *Working Alliance in Online Therapy as Compared to Face-to-Face Therapy: Preliminary Results* (Vol. 5).

Cook, L., Mostazir, M., & Watkins, E. (2019). Reducing Stress and Preventing Depression (RESPOND): Randomized Controlled Trial of Web-Based Rumination-Focused Cognitive Behavioral Therapy for High-Ruminating University Students. *Journal of Medical Internet Research, 21*(5), e11349. doi:10.2196/11349

Cook, L., & Watkins, E. (2016). Guided, internet-based, rumination-focused cognitive behavioural therapy (i-RFCBT) versus a no-intervention control to prevent depression in high-ruminating young adults, along with an adjunct assessment of the feasibility of unguided i-RFCBT, in the REducing Stress and Preventing Depression trial (RESPOND): study protocol for a phase III randomised controlled trial. *Trials, 17*, 1. doi:10.1186/s13063-015-1128-9

Corrigan, P. W., Watson, A. C., & Barr, L. (2006). The self-stigma of mental illness: Implications for self-esteem and self-efficacy. *Journal of Social and Clinical Psychology, 25*(8), 875-884. doi:10.1521/jscp.2006.25.8.875

Coulson, N. S., Smedley, R., Bostock, S., Kyle, S. D., Gollancz, R., Luik, A. I., . . . Espie, C. A. (2016). The Pros and Cons of Getting Engaged in an Online Social Community Embedded Within Digital Cognitive Behavioral

Therapy for Insomnia: Survey Among Users. *Journal of Medical Internet Research, 18*(4), e88. doi:10.2196/jmir.5654

Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., & Petticrew, M. (2008). Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ, 337*, a1655. doi:10.1136/bmj.a1655

Craske, M. G. (2012). Transdiagnostic treatment for anxiety and depression. *Depression and Anxiety, 29*(9), 749-753. doi:10.1002/da.21992

Cuijpers, P. (2009). Prevention: an achievable goal in personalized medicine. *Dialogues in Clinical Neuroscience, 11*(4), 447-454.

Cuijpers, P., & Christensen, H. (2017). Are personalised treatments of adult depression finally within reach? *Epidemiology and Psychiatric Sciences, 26*(1), 40-42. doi:10.1017/S204579601600007X

Cuijpers, P., Riper, H., & Andersson, G. (2015). Internet-based treatment of depression. *Current Opinion in Psychology, 4*, 131-135. doi:https://doi.org/10.1016/j.copsyc.2014.12.026

Cuijpers, P., van Straten, A., Smit, F., Mihalopoulos, C., & Beekman, A. (2008). Preventing the onset of depressive disorders: a meta-analytic review of psychological interventions. *American Journal of Psychiatry, 165*(10), 1272-1280. doi:10.1176/appi.ajp.2008.07091422

Cukrowicz, K. C., & Joiner, T. E. (2007). Computer-Based Intervention for Anxious and Depressive Symptoms in a Non-Clinical Population. *Cognitive Therapy and Research, 31*(5), 677-693. doi:10.1007/s10608-006-9094-x

Culjak, G., Kowalenko, N., & Tennant, C. (2016). Awareness, Access and Use of Internet Self-Help Websites for Depression by University Students. *JMIR Mental Health, 3*(4), e48. doi:10.2196/mental.5311

Davies, E. B., Morriss, R., & Glazebrook, C. (2014). Computer-delivered and web-based interventions to improve depression, anxiety, and psychological well-being of university students: a systematic review and meta-analysis. *Journal of Medical Internet Research, 16*(5), e130. doi:10.2196/jmir.3142

Day, V., McGrath, P. J., & Wojtowicz, M. (2013). Internet-based guided self-help for university students with anxiety, depression and stress: a randomized controlled clinical trial. *Behaviour Research and Therapy, 51*(7), 344-351. doi:10.1016/j.brat.2013.03.003

De Graaf, R., Bijl, R. V., Ravelli, A., Smit, F., & Vollebergh, W. A. (2002). 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 Psychiatrica Scandinavica, 106*(4), 303-313. doi:10.1034/j.1600-0447.2002.01397.x

de Vet, E., Oenema, A., & Brug, J. (2011). More or better: Do the number and specificity of implementation intentions matter in increasing physical activity? *Psychology of Sport and Exercise, 12*(4), 471-477. doi:https://doi.org/10.1016/j.psychsport.2011.02.008

Deady, M., Choi, I., Calvo, R. A., Glozier, N., Christensen, H., & Harvey, S. B. (2017). eHealth interventions for the prevention of depression and anxiety in the general population: a systematic review and meta-analysis. *BMC Psychiatry, 17*(1), 310. doi:10.1186/s12888-017-1473-1

Dear, B. F., Fogliati, V. J., Fogliati, R., Johnson, B., Boyle, O., Karin, E., . . . Titov, N. (2018). Treating anxiety and depression in young adults: A randomised controlled trial comparing clinician-guided versus self-guided Internet-delivered cognitive behavioural therapy. *Australian and New Zealand Journal of Psychiatry, 52*(7), 668-679. doi:10.1177/0004867417738055

Dear, B. F., Gandy, M., Karin, E., Staples, L. G., Johnston, L., Fogliati, V. J., . . . Titov, N. (2015a). The Pain Course: a randomised controlled trial examining an internet-delivered pain management program when provided with different levels of clinician support. *Pain, 156*(10), 1920-1935. doi:10.1097/j.pain.0000000000000251

Dear, B. F., Johnson, B., Singh, A., Wilkes, B., Brkic, T., Gupta, R., . . . Titov, N. (2019). Examining an internet-delivered intervention for anxiety and depression when delivered as a part of routine care for university students: A phase IV trial. *Journal of Affective Disorders, 256*, 567-577. doi:https://doi.org/10.1016/j.jad.2019.06.044

Dear, B. F., Staples, L. G., Terides, M. D., Karin, E., Zou, J., Johnston, L., . . . Titov, N. (2015b). Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for generalized anxiety disorder and comorbid disorders: A randomized controlled trial. *Journal of Anxiety Disorders, 36*, 63-77. doi:10.1016/j.janxdis.2015.09.003

Doblyte, S., & Jimenez-Mejias, E. (2017). Understanding Help-Seeking Behavior in Depression: A Qualitative Synthesis of Patients' Experiences. *Qualitative Health Research, 27*(1), 100-113. doi:10.1177/1049732316681282

Doherty, G., Coyle, D., & Sharry, J. (2012). *Engagement with online mental health interventions*. Paper presented at the Proceedings of the 2012 ACM annual conference on Human Factors in Computing Systems.

Donaldson, C., & Lam, D. (2004). Rumination, mood and social problem-solving in major depression. *Psychological Medicine, 34*(7), 1309-1318. doi:10.1017/s0033291704001904

Donkin, L., & Glozier, N. (2012). Motivators and motivations to persist with online psychological interventions: a qualitative study of treatment completers. *Journal of Medical Internet Research, 14*(3), e91-e91. doi:10.2196/jmir.2100

Dorow, M., Löbner, M., Pabst, A., Stein, J., & Riedel-Heller, S. G. (2018). Preferences for Depression Treatment Including Internet-Based Interventions: Results From a Large Sample of Primary Care Patients. *Frontiers in Psychiatry, 9*(181). doi:10.3389/fpsyt.2018.00181

Downs, M. F., & Eisenberg, D. (2012). Help seeking and treatment use among suicidal college students. *Journal of American College Health, 60*(2), 104-114. doi:10.1080/07448481.2011.619611

Dunbar, M. S., Sontag-Padilla, L., Kase, C. A., Seelam, R., & Stein, B. D. (2018). Unmet Mental Health Treatment Need and Attitudes Toward Online Mental Health Services Among Community College Students. *Psychiatric Services, 69*(5), 597-600. doi:10.1176/appi.ps.201700402

Dunn, G., Maracy, M., & Tomenson, B. (2005). Estimating treatment effects from randomized clinical trials with noncompliance and loss to follow-up: the role of instrumental variable methods. *Statistical Methods in Medical Research, 14*(4), 369-395. doi:10.1191/0962280205sm403oa

Earley, C., Joyce, C., McElvaney, J., Richards, D., & Timulak, L. (2017). Preventing depression: Qualitatively examining the benefits of depression-focused iCBT for participants who do not meet clinical thresholds. *Internet Interventions, 9*, 82-87. doi:10.1016/j.invent.2017.07.003

Ebert, D. D., Cuijpers, P., Muñoz, R. F., & Baumeister, H. (2017). Prevention of Mental Health Disorders Using Internet- and Mobile-Based Interventions: A Narrative Review and Recommendations for Future Research. *Frontiers in Psychiatry, 8*, 116. doi:10.3389/fpsyt.2017.00116

Ebert, D. D., Mortier, P., Kaehlke, F., Bruffaerts, R., Baumeister, H., Auerbach, R. P., . . . Kessler, R. C. (2019). Barriers of mental health treatment utilization among first-year college students: First cross-national results from the WHO World Mental Health International College Student Initiative. *International Journal of Methods in Psychiatric Research, 28*(2). doi:10.1002/mpr.1782

Eells, T. D., Barrett, M. S., Wright, J. H., & Thase, M. (2014). Computer-assisted cognitive-behavior therapy for depression. *Psychotherapy, 51*(2), 191-197. doi:10.1037/a0032406

Ehring, T., & Watkins, E. R. (2008). Repetitive Negative Thinking as a Transdiagnostic Process. *International Journal of Cognitive Therapy, 1*(3), 192-205. doi:10.1521/ijct.2008.1.3.192

Ehring, T., Zetsche, U., Weidacker, K., Wahl, K., Schonfeld, S., & Ehlers, A. (2011). The Perseverative Thinking Questionnaire (PTQ): validation of a content-independent measure of repetitive negative thinking. *Journal of Behavior Therapy and Experimental Psychiatry, 42*(2), 225-232. doi:10.1016/j.jbtep.2010.12.003

Eisenberg, D., Golberstein, E., & Hunt, J. B. (2009). Mental Health and Academic Success in College. *The B.E. Journal of Economic Analysis & Policy, 9*(1). doi:10.2202/1935-1682.2191

Eisenberg, D., Gollust, S. E., Golberstein, E., & Hefner, J. L. (2007). Prevalence and correlates of depression, anxiety, and suicidality among university students. *American Journal of Orthopsychiatry, 77*(4), 534-542. doi:10.1037/0002-9432.77.4.534

Eisenberg, D., Hunt, J., Speer, N., & Zivin, K. (2011). Mental health service utilization among college students in the United States. *The Journal of Nervous and Mental Disease, 199*(5), 301-308. doi:10.1097/NMD.0b013e3182175123

Eisenberg, D., Speer, N., & Hunt, J. B. (2012). Attitudes and beliefs about treatment among college students with untreated mental health problems. *Psychiatric Services, 63*(7), 711-713. doi:10.1176/appi.ps.201100250

Eysenck, S. B. G., Eysenck, H. J., & Barrett, P. (1985). A revised version of the psychoticism scale. *Personality and Individual Differences, 6*(1), 21-29. doi:10.1016/0191-8869(85)90026-1

Farrand, P., & Woodford, J. (2013). Impact of support on the effectiveness of written cognitive behavioural self-help: a systematic review and meta-analysis of randomised controlled trials. *Clinical Psychology Review, 33*(1), 182-195. doi:10.1016/j.cpr.2012.11.001

Farrer, L., Christensen, H., Griffiths, K. M., & Mackinnon, A. (2011). Internet-Based CBT for Depression with and without Telephone Tracking in a National Helpline: Randomised Controlled Trial. *PloS one, 6*(11), e28099. doi:10.1371/journal.pone.0028099

Farrer, L., Gulliver, A., Chan, J. K., Batterham, P. J., Reynolds, J., Calear, A., . . . Griffiths, K. M. (2013). Technology-based interventions for mental health in tertiary students: systematic review. *Journal of Medical Internet Research, 15*(5), e101. doi:10.2196/jmir.2639

Farrer, L. M., Gulliver, A., Katruss, N., Fassnacht, D. B., Kyrios, M., & Batterham, P. J. (2019). A novel multi-component online intervention to improve the mental health of university students: Randomised controlled trial of the Uni Virtual Clinic. *Internet Interventions, 18*, 100276. doi:https://doi.org/10.1016/j.invent.2019.100276

Fava, M., Rankin, M. A., Wright, E. C., Alpert, J. E., Nierenberg, A. A., Pava, J., & Rosenbaum, J. F. (2000). Anxiety disorders in major depression. *Comprehensive Psychiatry, 41*(2), 97-102. doi:10.1016/s0010-440x(00)90140-8

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (2002). *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition With Psychotic Screen (SCID-I/P W/ PSY SCREEN)*. New York: Biometrics Research, New York State Psychiatric Institute.

Fleischmann, R. J., Harrer, M., Zarski, A. C., Baumeister, H., Lehr, D., & Ebert, D. D. (2017). Patients' experiences in a guided Internet- and App-based stress intervention for college students: A qualitative study. *Internet Interventions*. doi:10.1016/j.invent.2017.12.001

Fox, F. E., Morris, M., & Rumsey, N. (2007). Doing Synchronous Online Focus Groups With Young People:Methodological Reflections. *Qualitative Health Research, 17*(4), 539-547. doi:10.1177/1049732306298754

Freeman, D., Sheaves, B., Goodwin, G. M., Yu, L.-M., Nickless, A., Harrison, P. J., . . . Espie, C. A. (2017). The effects of improving sleep on mental

health (OASIS): a randomised controlled trial with mediation analysis. *The Lancet Psychiatry, 4*(10), 749-758. doi:10.1016/S2215-0366(17)30328-0

Fung, J., Kim, J. J., Jin, J., Chen, G., Bear, L., & Lau, A. S. (2019). A Randomized Trial Evaluating School-Based Mindfulness Intervention for Ethnic Minority Youth: Exploring Mediators and Moderators of Intervention Effects. *Journal of Abnormal Child Psychology, 47*(1), 1-19. doi:10.1007/s10802-018-0425-7

Gega, L., Smith, J., & Reynolds, S. (2013). Cognitive behaviour therapy (CBT) for depression by computer vs. therapist: patient experiences and therapeutic processes. *Psychotherapy Research, 23*(2), 218-231. doi:10.1080/10503307.2013.766941

Gellatly, J., Bower, P., Hennessy, S., Richards, D., Gilbody, S., & Lovell, K. (2007). What makes self-help interventions effective in the management of depressive symptoms? Meta-analysis and meta-regression. *Psychological Medicine, 37*(9), 1217-1228. doi:10.1017/S0033291707000062

Genet, J. J., & Siemer, M. (2012). Rumination moderates the effects of daily events on negative mood: results from a diary study. *Emotion, 12*(6), 1329-1339. doi:10.1037/a0028070

Gerhards, S. A., Abma T.A., Arntz, A., de Graaf, L. E., Evers, S. M., Huibers, M. J., & Widdershoven, G. A. (2011). Improving adherence and effectiveness of computerised cognitive behavioural therapy without support for depression: a qualitative study on patient experiences. *Journal of Affective Disorders*(1573-2517 (Electronic)).

Gollwitzer, P. M. (1999). Implementation Intentions: Strong Effects of Simple Plans. *American Psychologist, 54*, 493-503. doi:10.1037/0003-066X.54.7.493

Gollwitzer, P. M. (2014). Weakness of the will: Is a quick fix possible? *Motivation and Emotion, 38*(3), 305-322. doi:10.1007/s11031-014-9416-3

Gollwitzer, P. M., & Sheeran, P. (2006). Implementation Intentions and Goal Achievement: A Meta-analysis of Effects and Processes. *Advances in Experimental Social Psychology, 38*, 69-119. doi:https://doi.org/10.1016/S0065-2601(06)38002-1

Gotlib, I. H., Hamilton, J. P., Cooney, R. E., Singh, M. K., Henry, M. L., & Joormann, J. (2010). Neural processing of reward and loss in girls at risk for major depression. *Archives of General Psychiatry, 67*(4), 380-387. doi:10.1001/archgenpsychiatry.2010.13

Griffiths, C. A., & Griffiths, L. J. (2015). Recovery and reliable change rates for patients scoring severe on depression, anxiety or impaired functioning in a psychological therapies service: IAPT. *Mental Health Review Journal, 20*(1), 28-35. doi:10.1108/mhrj-06-2014-0022

Hadjistavropoulos, H. D., Faller, Y. N., Klatt, A., Nugent, M. N., Dear, B. F., & Titov, N. (2018). Patient Perspectives on Strengths and Challenges of Therapist-Assisted Internet-Delivered Cognitive Behaviour Therapy: Using the Patient Voice to Improve Care. *Community Mental Health Journal, 54*(7), 944-950. doi:10.1007/s10597-018-0286-0

Hadjistavropoulos, H. D., Pugh, N. E., Hesser, H., & Andersson, G. (2016). Predicting Response to Therapist-Assisted Internet-Delivered Cognitive Behavior Therapy for Depression or Anxiety Within an Open

Dissemination Trial. *Behavior Therapy, 47*(2), 155-165. doi:10.1016/j.beth.2015.10.006

Hadjistavropoulos, H. D., Schneider, L. H., Edmonds, M., Karin, E., Nugent, M. N., Dirkse, D., . . . Titov, N. (2017). Randomized controlled trial of internet-delivered cognitive behaviour therapy comparing standard weekly versus optional weekly therapist support. *Journal of Anxiety Disorders, 52*, 15-24. doi:10.1016/j.janxdis.2017.09.006

Haeffel, G. J. (2010). When self-help is no help: Traditional cognitive skills training does not prevent depressive symptoms in people who ruminate. *Behaviour Research and Therapy, 48*(2), 152-157. doi:https://doi.org/10.1016/j.brat.2009.09.016

Hammen, C. (2004). *Episodic Life Event Interview: UCLA Stress Interview*. Los Angeles, CA: UCLA Department of Psychology.

Hammen, C. (2005). Stress and Depression. *Annual Review of Clinical Psychology, 1*(1), 293-319. doi:10.1146/annurev.clinpsy.1.102803.143938

Hankin, B. L. (2008). Rumination and depression in adolescence: investigating symptom specificity in a multiwave prospective study. *Journal of Clinical Child & Adolescent Psychology, 37*(4), 701-713. doi:10.1080/15374410802359627

Hankin, B. L., Young, J. F., Abela, J. R., Smolen, A., Jenness, J. L., Gulley, L. D., . . . Oppenheimer, C. W. (2015). Depression from childhood into late adolescence: Influence of gender, development, genetic susceptibility, and peer stress. *Journal of Abnormal Psychology, 124*(4), 803-816. doi:10.1037/abn0000089

Hankin, B. L., Young, J. F., Gallop, R., & Garber, J. (2018). Cognitive and Interpersonal Vulnerabilities to Adolescent Depression: Classification of Risk Profiles for a Personalized Prevention Approach. *Journal of Abnormal Child Psychology, 46*(7), 1521-1533. doi:10.1007/s10802-018-0401-2

Hardeveld, F., Spijker, J., De Graaf, R., Nolen, W. A., & Beekman, A. T. (2010). Prevalence and predictors of recurrence of major depressive disorder in the adult population. *Acta Psychiatrica Scandinavica, 122*(3), 184-191. doi:10.1111/j.1600-0447.2009.01519.x

Harrer, M., Adam, S. H., Baumeister, H., Cuijpers, P., Karyotaki, E., Auerbach, R. P., . . . Ebert, D. D. (2019). Internet interventions for mental health in university students: A systematic review and meta-analysis. *International Journal of Methods in Psychiatric Research, 28*(2), e1759. doi:10.1002/mpr.1759

Harrer, M., Adam, S. H., Fleischmann, R. J., Baumeister, H., Auerbach, R., Bruffaerts, R., . . . Ebert, D. D. (2018). Effectiveness of an Internet- and App-Based Intervention for College Students With Elevated Stress: Randomized Controlled Trial. *Journal of Medical Internet Research, 20*(4), e136. doi:10.2196/jmir.9293

Harvey, A. G., Watkins, E., Mansell, W., & Shafran, R. (2004). *Cognitive behavioural processes across psychological disorders: A transdiagnostic approach to research and treatment*. Oxford, UK: Oxford University Press.

Hayes, S. C. (1981). Single case experimental design and empirical clinical practice. *Journal of Consulting and Clinical Psychology, 49*(2), 193-211. doi:10.1037//0022-006x.49.2.193

Healthcare Safety Investigation Branch. (2018). *Investigation into the transition from child and adolescent mental health services to adult mental health services*. Farnborough, UK: HSIB Retrieved from https://www.hsib.org.uk/investigations-cases/transition-from-child-and-adolescent-mental-health-services-to-adult-mental-health-services/final-report/.

Hertel, P. T., & Mathews, A. (2011). Cognitive Bias Modification: Past Perspectives, Current Findings, and Future Applications. *Perspectives on Psychological Science, 6*(6), 521-536. doi:10.1177/1745691611421205

Hetrick, S. E., Cox, G. R., Witt, K. G., Bir, J. J., & Merry, S. N. (2016). Cognitive behavioural therapy (CBT), third-wave CBT and interpersonal therapy (IPT) based interventions for preventing depression in children and adolescents. *Cochrane Database of Systematic Reviews*(8), CD003380. doi:10.1002/14651858.CD003380.pub4

Higgins, J. P. T., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., . . . Sterne, J. A. C. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ, 343*, d5928. doi:10.1136/bmj.d5928

Hilgart, M., Thorndike, F. P., Pardo, J., & Ritterband, L. M. (2012). Ethical issues of web-based interventions and online therapy. In *The Oxford Handbook of International Psychological Ethics.* (pp. 161-175). New York, NY, US: Oxford University Press.

Hind, D., O'Cathain, A., Cooper, C. L., Parry, G. D., Isaac, C. L., Rose, A., . . . Sharrack, B. (2010). The acceptability of computerised cognitive behavioural therapy for the treatment of depression in people with chronic physical disease: a qualitative study of people with multiple

sclerosis. *Psychology & Health, 25*(6), 699-712. doi:10.1080/08870440902842739

Hoek, W., Schuurmans, J., Koot, H. M., & Cuijpers, P. (2012). Effects of Internet-based guided self-help problem-solving therapy for adolescents with depression and anxiety: a randomized controlled trial. *PloS one, 7*(8), e43485. doi:10.1371/journal.pone.0043485

Hoffmann, T. C., Glasziou, P. P., Boutron, I., Milne, R., Perera, R., Moher, D., . . . Michie, S. (2014). Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ, 348*, g1687. doi:10.1136/bmj.g1687

Hong, R. Y. (2007). Worry and rumination: differential associations with anxious and depressive symptoms and coping behavior. *Behaviour Research and Therapy, 45*(2), 277-290. doi:10.1016/j.brat.2006.03.006

Hoorelbeke, K., Koster, E. H., Vanderhasselt, M. A., Callewaert, S., & Demeyer, I. (2015). The influence of cognitive control training on stress reactivity and rumination in response to a lab stressor and naturalistic stress. *Behaviour Research and Therapy, 69*, 1-10. doi:10.1016/j.brat.2015.03.010

Horowitz, J. L., & Garber, J. (2006). The prevention of depressive symptoms in children and adolescents: A meta-analytic review. *Journal of Consulting and Clinical Psychology, 74*(3), 401-415. doi:10.1037/0022-006X.74.3.401

Hysenbegasi, A., Hass, S. L., & Rowland, C. R. (2005). The impact of depression on the academic productivity of university students. *The Journal of Mental Health Policy and Economics, 8*(3), 145-151.

Ibrahim, A. K., Kelly, S. J., Adams, C. E., & Glazebrook, C. (2013). A systematic review of studies of depression prevalence in university students. *Journal of Psychiatric Research, 47*(3), 391-400. doi:10.1016/j.jpsychires.2012.11.015

Imamura, K., Kawakami, N., Furukawa, T. A., Matsuyama, Y., Shimazu, A., Umanodan, R., . . . Kasai, K. (2015). Does Internet-based cognitive behavioral therapy (iCBT) prevent major depressive episode for workers? A 12-month follow-up of a randomized controlled trial. *Psychological Medicine, 45*(9), 1907-1917. doi:10.1017/s0033291714003006

Johansson, O., Michel, T., Andersson, G., & Paxling, B. (2015). Experiences of non-adherence to Internet-delivered cognitive behavior therapy: A qualitative study. *Internet Interventions, 2*(2), 137-142. doi:10.1016/j.invent.2015.02.006

Jorm, A., & Yap, M. (2019). The future of Mental Health & Prevention. *Mental Health & Prevention, 14*, 200168. doi:https://doi.org/10.1016/j.mhp.2019.200168

Judd, L. L. (1997). The clinical course of unipolar major depressive disorders. *Archives of general psychiatry, 54*(11), 989-991. doi:10.1001/archpsyc.1997.01830230015002

Just, N., & Alloy, L. B. (1997). The response styles theory of depression: tests and an extension of the theory. *Journal of Abnormal Psychology, 106*(2), 221-229. doi:10.1037//0021-843x.106.2.221

Karyotaki, E., Kleiboer, A., Smit, F., Turner, D. T., Pastor, A. M., Andersson, G., . . . Cuijpers, P. (2015). Predictors of treatment dropout in self-guided web-based interventions for depression: an 'individual patient data' meta-

analysis. *Psychological Medicine, 45*(13), 2717-2726. doi:10.1017/S0033291715000665

Kazdin, A. E. (1996). Dropping Out of Child Psychotherapy: Issues for Research and Implications for Practice. *Clinical Child Psychology and Psychiatry, 1*(1), 133-156. doi:10.1177/1359104596011012

Kazdin, A. E. (2003). *Methodological issues and strategies in clinical research 3rd ed*. Washington D.C.: American Psychological Association.

Kazdin, A. E., & Blase, S. L. (2011). Rebooting Psychotherapy Research and Practice to Reduce the Burden of Mental Illness. *Perspectives on Psychological Science, 6*(1), 21-37. doi:10.1177/1745691610393527

Kenardy, J., McCafferty, K., & Rosa, V. (2003). Internet-Delivered Indicated Prevention For Anxiety Disorders: A Randomized Controlled Trial. *Behavioural and Cognitive Psychotherapy, 31*(3), 279-289. doi:10.1017/S1352465803003047

Kenardy, J., McCafferty, K., & Rosa, V. (2006). Internet-delivered indicated prevention for anxiety disorders: Six-month follow-up. *Clinical Psychologist, 10*(1), 39-42. doi:10.1080/13284200500378746

Kerr, C., Murray, E., Stevenson, F., Gore, C., & Nazareth, I. (2006). Internet interventions for long-term conditions: patient and caregiver quality criteria. *Journal of Medical Internet Research, 8*(3), e13. doi:10.2196/jmir.8.3.e13

Kerr, H. (2013). Mental Distress Survey Overview. Retrieved from http://www.nus.org.uk/Global/Campaigns/20130517%20Mental%20Distress%20Survey%20%20Overview.pdf

Kessler, R. C., Amminger, G. P., Aguilar-Gaxiola, S., Alonso, J., Lee, S., & Ustün, T. B. (2007). Age of onset of mental disorders: a review of recent

literature. *Current Opinion in Psychiatry, 20*(4), 359-364. doi:10.1097/YCO.0b013e32816ebc8c

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry, 62*(6), 593-602. doi:10.1001/archpsyc.62.6.593

Kessler, R. C., van Loo, H. M., Wardenaar, K. J., Bossarte, R. M., Brenner, L. A., Ebert, D. D., . . . Zaslavsky, A. M. (2017). Using patient self-reports to study heterogeneity of treatment effects in major depressive disorder. *Epidemiology and Psychiatric Sciences, 26*(1), 22-36. doi:10.1017/S2045796016000020

Kingston, R., Watkins, E., & O'Mahen, H. (2013). An Integrated Examination of Risk Factors for Repetitive Negative Thought. *Journal of Experimental Psychopathology, 4*(2), 161-181. doi:10.5127/jep.027712

Kitzinger, J. (1995). Qualitative research. Introducing focus groups. *BMJ, 311*(7000), 299-302. doi:10.1136/bmj.311.7000.299

Kleiboer, A., Donker, T., Seekles, W., van Straten, A., Riper, H., & Cuijpers, P. (2015). A randomized controlled trial on the role of support in Internet-based problem solving therapy for depression and anxiety. *Behaviour Research and Therapy, 72*, 63-71. doi:https://doi.org/10.1016/j.brat.2015.06.013

Klein, N. S., Kok, G. D., Burger, H., van Valen, E., Riper, H., Cuijpers, P., . . . Bockting, C. L. H. (2018). No Sustainable Effects of an Internet-Based Relapse Prevention Program over 24 Months in Recurrent Depression: Primary Outcomes of a Randomized Controlled Trial. *Psychotherapy and Psychosomatics, 87*(1), 55-57. doi:10.1159/000485039

Knauper, B., McCollam, A., Rosen-Brown, A., Lacaille, J., Kelso, E., & Roseman, M. (2011). Fruitful plans: adding targeted mental imagery to implementation intentions increases fruit consumption. *Psychology & Health, 26*(5), 601-617. doi:10.1080/08870441003703218

Knowles, S. E., Lovell, K., Bower, P., Gilbody, S., Littlewood, E., & Lester, H. (2015). Patient experience of computerised therapy for depression in primary care. *BMJ Open, 5*(11), e008581. doi:10.1136/bmjopen-2015-008581

Knowles, S. E., Toms, G., Sanders, C., Bee, P., Lovell, K., Rennick-Egglestone, S., . . . Bower, P. (2014). Qualitative meta-synthesis of user experience of computerised therapy for depression and anxiety. *PloS one, 9*(1), e84323. doi:10.1371/journal.pone.0084323

Kobak, K. A., Greist, R., Jacobi, D. M., Levy-Mack, H., & Greist, J. H. (2015). Computer-assisted cognitive behavior therapy for obsessive-compulsive disorder: a randomized trial on the impact of lay vs. professional coaching. *Annals of General Psychiatry, 14*(1), 10. doi:10.1186/s12991-015-0048-0

Kok, G., Burger, H., Riper, H., Cuijpers, P., Dekker, J., van Marwijk, H., . . . Bockting, C. L. (2015). The Three-Month Effect of Mobile Internet-Based Cognitive Therapy on the Course of Depressive Symptoms in Remitted Recurrently Depressed Patients: Results of a Randomized Controlled Trial. *Psychotherapy and Psychosomatics, 84*(2), 90-99. doi:10.1159/000369469

Königbauer, J., Letsch, J., Doebler, P., Ebert, D., & Baumeister, H. (2017). Internet- and mobile-based depression interventions for people with diagnosed depression: A systematic review and meta-analysis. *Journal*

of Affective Disorders, 223, 28-40. doi:https://doi.org/10.1016/j.jad.2017.07.021

Kraemer, H. C., Wilson, G. T., Fairburn, C. G., & Agras, W. S. (2002). Mediators and moderators of treatment effects in randomized clinical trials. *Archives of General Psychiatry, 59*(10), 877-883. doi:10.1001/archpsyc.59.10.877

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: validity of a brief depression severity measure. *Journal of General Internal Medicine, 16*(9), 606-613. doi:10.1046/j.1525-1497.2001.016009606.x

Kroenke, K., Spitzer, R. L., Williams, J. B., Monahan, P. O., & Löwe, B. (2007). Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Annals of Internal Medicine, 146*(5), 317-325. doi:10.7326/0003-4819-146-5-200703060-00004

Kroenke, K., Strine, T. W., Spitzer, R. L., Williams, J. B., Berry, J. T., & Mokdad, A. H. (2009). The PHQ-8 as a measure of current depression in the general population. *Journal of Affective Disorders, 114*(1-3), 163-173. doi:10.1016/j.jad.2008.06.026

Lakens, D. (2013). Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. *Frontiers in Psychology, 4*, 863. doi:10.3389/fpsyg.2013.00863

Lange, T., & Hansen, J. (2011). Direct and Indirect Effects in a Survival Context. *Epidemiology, 22*(4), 575-581.

Lattie, E. G., Adkins, E. C., Winquist, N., Stiles-Shields, C., Wafford, Q. E., & Graham, A. K. (2019). Digital Mental Health Interventions for Depression, Anxiety, and Enhancement of Psychological Well-Being Among College

Students: Systematic Review. *Journal of Medical Internet Research, 21*(7), e12869. doi:10.2196/12869

Leary, M. R., Adams, C. E., & Tate, E. B. (2006). Hypo-egoic self-regulation: exercising self-control by diminishing the influence of the self. *Journal of Personality, 74*(6), 1803-1831. doi:10.1111/j.1467-6494.2006.00429.x

Lee, D. H., Kang, S., & Yum, S. (2005). A qualitative assessment of personal and academic stressors among Korean College students: an exploratory study. *College Student Journal, 39*, 442+.

Levin, M. E., Krafft, J., & Levin, C. (2018). Does self-help increase rates of help seeking for student mental health problems by minimizing stigma as a barrier? *Journal of American College Health, 66*(4), 302-309. doi:10.1080/07448481.2018.1440580

Lewinsohn, P. M., Rohde, P., & Seeley, J. R. (1998). Major depressive disorder in older adolescents: prevalence, risk factors, and clinical implications. *Clinical Psychology Review, 18*(7), 765-794. doi:10.1016/s0272-7358(98)00010-5

Lillevoll, K. R., Wilhelmsen, M., Kolstrup, N., Høifødt, R. S., Waterloo, K., Eisemann, M., & Risør, M. B. (2013). Patients' Experiences of Helpfulness in Guided Internet-Based Treatment for Depression: Qualitative Study of Integrated Therapeutic Dimensions. *Journal of Medical Internet Research, 15*(6), e126. doi:10.2196/jmir.2531

Lintvedt, O. K., Griffiths, K. M., Sørensen, K., Østvik, A. R., Wang, C. E., Eisemann, M., & Waterloo, K. (2013). Evaluating the effectiveness and efficacy of unguided internet-based self-help intervention for the prevention of depression: a randomized controlled trial. *Clinical Psychology & Psychotherapy, 20*(1), 10-27. doi:10.1002/cpp.770

Lintvedt, O. K., Sørensen, K., Østvik, A. R., Verplanken, B., & Wang, C. E. (2008). The Need for Web-Based Cognitive Behavior Therapy Among University Students. *Journal of Technology in Human Services, 26*(2-4), 239-258. doi:10.1080/15228830802096705

Liu, R. T., & Alloy, L. B. (2010). Stress generation in depression: A systematic review of the empirical literature and recommendations for future study. *Clinical Psychology Review, 30*(5), 582-593. doi:10.1016/j.cpr.2010.04.010

Lobbestael, J., Leurgans, M., & Arntz, A. (2011). Inter-rater reliability of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I) and Axis II Disorders (SCID II). *Clinical Psychology & Psychotherapy, 18*(1), 75-79. doi:10.1002/cpp.693

Loeys, T., & Goetghebeur, E. (2003). A causal proportional hazards estimator for the effect of treatment actually received in a randomized trial with all-or-nothing compliance. *Biometrics, 59*(1), 100-105. doi:10.1111/1541-0420.00012

Lyubomirsky, S., Caldwell, N. D., & Nolen-Hoeksema, S. (1998). Effects of ruminative and distracting responses to depressed mood on retrieval of autobiographical memories. *Journal of Personality and Social Psychology, 75*(1), 166-177. doi:10.1037//0022-3514.75.1.166

Lyubomirsky, S., Kasri, F., & Zehm, K. (2003). Dysphoric Rumination Impairs Concentration on Academic Tasks. *Cognitive Therapy and Research, 27*(3), 309-330.

Lyubomirsky, S., & Nolen-Hoeksema, S. (1995). Effects of self-focused rumination on negative thinking and interpersonal problem solving.

Journal of Personality and Social Psychology, 69(1), 176-190. doi:10.1037//0022-3514.69.1.176

Lyubomirsky, S., Tucker, K. L., Caldwell, N. D., & Berg, K. (1999). Why ruminators are poor problem solvers: clues from the phenomenology of dysphoric rumination. *Journal of Personality and Social Psychology, 77*(5), 1041-1060. doi:10.1037//0022-3514.77.5.1041

MacGregor, A. D., Hayward, L., Peck, D. F., & Wilkes, P. (2009). Empirically Grounded Clinical Interventions Clients' and Referrers' Perceptions of Computer-Guided CBT (FearFighter). *Behavioural and Cognitive Psychotherapy, 37*(1), 1-9. doi:10.1017/S135246580800492X

Mackinnon, D. P., Lockwood, C. M., & Williams, J. (2004). Confidence Limits for the Indirect Effect: Distribution of the Product and Resampling Methods. *Multivariate Behavioral Research, 39*(1), 99-99. doi:10.1207/s15327906mbr3901_4

Malhi, G. S., & Mann, J. J. (2018). Depression. *The Lancet, 392*(10161), 2299-2312. doi:10.1016/s0140-6736(18)31948-2

Marcus, M., Yasamy, M. T., van Ommeren, M., Chisholm, D., & Saxena, S. (2012). *Depression, A Global Public Health Concern.* Geneva, Switzerland: World Health Organization.

Martell, C. R., Addis, M. E., & Jacobson, N. S. (2001). *Depression in context: Strategies for guided action*. New York: Norton.

Martell, C. R., Dimidjian, S., & Herman-Dunn, R. (2013). *Behavioral Activation for Depression: A Clinician's Guide*. New York: Guilford Press.

Martin, L. L., & Tesser, A. (1996). Some ruminative thoughts. In R. S. Wyer (Ed.), *Advances in Social Cognition* (Vol. 9). Hillsdale, NJ: Erlbaum.

McEvoy, P. M., Grove, R., & Slade, T. (2011). Epidemiology of anxiety disorders in the Australian general population: findings of the 2007 Australian National Survey of Mental Health and Wellbeing. *Australian and New Zealand Journal of Psychiatry, 45*(11), 957-967. doi:10.3109/00048674.2011.624083

McIntosh, E., & Shaw, J. (2017). *Student Resilience: Exploring the positive case for resilience*. Bristol, UK: Unite Students Retrieved from http://www.unite-group.co.uk/sites/default/files/2017-05/student-resilience.pdf.

McIntyre, J. C., Worsley, J., Corcoran, R., Harrison Woods, P., & Bentall, R. P. (2018). Academic and non-academic predictors of student psychological distress: the role of social identity and loneliness. *Journal of Mental Health, 27*(3), 230-239. doi:10.1080/09638237.2018.1437608

McLaughlin, K. A., & Hatzenbuehler, M. L. (2009). Mechanisms linking stressful life events and mental health problems in a prospective, community-based sample of adolescents. *Journal of Adolescent Health, 44*(2), 153-160. doi:10.1016/j.jadohealth.2008.06.019

McManus, S., Bebbington, P., Jenkins, R., & Brugha, T. (2016). *Mental health and wellbeing in England: Adult Psychiatric Morbidity Survey 2014*. Leeds, UK: NHS Digital Retrieved from https://digital.nhs.uk/catalogue/PUB21748.

Mendelson, T., & Eaton, W. W. (2018). Recent advances in the prevention of mental disorders. *Social Psychiatry and Psychiatric Epidemiology, 53*(4), 325-339. doi:10.1007/s00127-018-1501-6

Merry, S., & Hetrick, S. (2017). Prevention of depression and anxiety: is the whole better than the sum of the parts? *Evidence-Based Mental Health, 20*(1), e1. doi:10.1136/eb-2016-102425

Merry, S. N., Hetrick, S. E., Cox, G. R., Brudevold-Iversen, T., Bir, J. J., & McDowell, H. (2011). Psychological and educational interventions for preventing depression in children and adolescents. *Cochrane Database of Systematic Reviews*(12), CD003380. doi:10.1002/14651858.CD003380.pub3

Meyer, T. J., Miller, M. L., Metzger, R. L., & Borkovec, T. D. (1990). Development and validation of the Penn State Worry Questionnaire. *Behaviour Research and Therapy, 28*(6), 487-495. doi:10.1016/0005-7967(90)90135-6

Michael, K. D., Hueisman, T. J., Gerard, C., Gilligan, T. M., & Gustafson, M. R. (2006). Depression Among College Students: Trends in Prevalence and Treatment Seeking. *Counseling and Clinical Psychology Journal, 3*(2), 60-70.

Michie, S., Richardson, M., Johnston, M., Abraham, C., Francis, J., Hardeman, W., . . . Wood, C. E. (2013). The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. *Annals of Behavioral Medicine, 46*(1), 81-95. doi:10.1007/s12160-013-9486-6

Michl, L. C., McLaughlin, K. A., Shepherd, K., & Nolen-Hoeksema, S. (2013). Rumination as a mechanism linking stressful life events to symptoms of depression and anxiety: longitudinal evidence in early adolescents and adults. *Journal of Abnormal Psychology, 122*(2), 339-352. doi:10.1037/a0031994

Minddistrict. Retrieved from https://www.minddistrict.com

http://www.webcitation.org/70IFG4ZML

Mira, A., Bretón-López, J., García-Palacios, A., Quero, S., Baños, R. M., & Botella, C. (2017). An Internet-based program for depressive symptoms using human and automated support: a randomized controlled trial. *Neuropsychiatric Disease and Treatment, 13*, 987-1006. doi:10.2147/NDT.S130994

Mitchell, N., & Gordon, P. K. (2007). Attitudes Towards Computerized CBT for Depression Amongst a Student Population. *Behavioural and Cognitive Psychotherapy, 35*(04), 421-430. doi:10.1017/s1352465807003700

Moberly, N. J., & Watkins, E. R. (2008a). Ruminative self-focus and negative affect: an experience sampling study. *Journal of Abnormal Psychology, 117*(2), 314-323. doi:10.1037/0021-843X.117.2.314

Moberly, N. J., & Watkins, E. R. (2008b). Ruminative self-focus, negative life events, and negative affect. *Behaviour Research and Therapy, 46*(9), 1034-1039. doi:10.1016/j.brat.2008.06.004

Moffitt, T. E., Caspi, A., Taylor, A., Kokaua, J., Milne, B. J., Polanczyk, G., & Poulton, R. (2010). How common are common mental disorders? Evidence that lifetime prevalence rates are doubled by prospective versus retrospective ascertainment. *Psychological Medicine, 40*(6), 899-909. doi:10.1017/S0033291709991036

Mohr, D. C., Cuijpers, P., & Lehman, K. (2011). Supportive Accountability: A Model for Providing Human Support to Enhance Adherence to eHealth Interventions. *Journal of Medical Internet Research, 13*(1), e30. doi:10.2196/jmir.1602

Mohr, D. C., Lyon, A. R., Lattie, E. G., Reddy, M., & Schueller, S. M. (2017). Accelerating Digital Mental Health Research From Early Design and Creation to Successful Implementation and Sustainment. *Journal of Medical Internet Research, 19*(5), e153. doi:10.2196/jmir.7725

Mohr, D. C., Riper, H., & Schueller, S. M. (2018). A Solution-Focused Research Approach to Achieve an Implementable Revolution in Digital Mental Health. *JAMA Psychiatry, 75*(2), 113-114. doi:10.1001/jamapsychiatry.2017.3838

Morrison, R., & O'Connor, R. C. (2005). Predicting psychological distress in college students: the role of rumination and stress. *Journal of Clinical Psychology, 61*(4), 447-460. doi:10.1002/jclp.20021

Morrison, R., & O'Connor, R. C. (2008). The role of rumination, attentional biases and stress in psychological distress. *British Journal of Psychology, 99*(Pt 2), 191-209. doi:10.1348/000712607X216080

Mrazek, P. J., & Haggerty, R. J. (1994). In *Reducing Risks for Mental Disorders: Frontiers for Preventive Intervention Research*. Washington (DC): National Academies Press (US)

Mullin, A., Dear, B. F., Karin, E., Wootton, B. M., Staples, L. G., Johnston, L., . . . Titov, N. (2015). The UniWellbeing course: A randomised controlled trial of a transdiagnostic internet-delivered cognitive behavioural therapy (CBT) programme for university students with symptoms of anxiety and depression. *Internet Interventions, 2*(2), 128-136. doi:10.1016/j.invent.2015.02.002

Muñoz, R. F. (2017). The Efficiency Model of Support and the Creation of Digital Apothecaries. *Clinical Psychology: Science and Practice, 24*(1), 46-49. doi:10.1111/cpsp.12174

Muñoz, R. F., Bunge, E. L., Chen, K., Schueller, S. M., Bravin, J. I., Shaughnessy, E. A., & Pérez-Stable, E. J. (2015). Massive Open Online Interventions: A Novel Model for Delivering Behavioral-Health Services Worldwide. *Clinical Psychological Science, 4*(2), 194-205. doi:10.1177/2167702615583840

Muñoz, R. F., Cuijpers, P., Smit, F., Barrera, A. Z., & Leykin, Y. (2010). Prevention of major depression. *Annual Review of Clinical Psychology, 6*, 181-212. doi:10.1146/annurev-clinpsy-033109-132040

Muris, P., Roelofs, J., Meesters, C., & Boomsma, P. (2004). Rumination and Worry in Nonclinical Adolescents. *Cognitive Therapy and Research, 28*(4), 539-554. doi:10.1023/B:COTR.0000045563.66060.3e

Nathan, P. E., & Gorman, J. M. (2015). *A guide to treatments that work*. Oxford, UK: Oxford University Press.

National Institute of Clinical Excellence. (2009). Depression in adults: the treatment and management of depression in adults (Update-NICE clinical guideline 90). Retrieved from https://www.nice.org.uk/guidance/cg90/chapter/1-Guidance

National Institute of Mental Health. (2003). *Depression and college students*. (NIH Publication No. 15-4266). Bethesda, MD: NIMH Retrieved from https://www.nimh.nih.gov/health/publications/depression-and-college-students/index.shtml.

National Research Council, & Institute of Medicine. (2009). *Preventing mental, emotional, and behavioral disorders among young people: Progress and possibilities*. Washington (DC), USA: National Academies Press (US) Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK32775/

Nehmy, T. (2010). School-based prevention of depression and anxiety in Australia: Current state and future directions. *Clinical Psychologist, 14*(3), 74-83. doi:10.1080/13284207.2010.524884

Newby, J. M., Mackenzie, A., Williams, A. D., McIntyre, K., Watts, S., Wong, N., et al. (2013). Internet cognitive behavioural therapy for mixed anxiety and depression: A randomized controlled trial and evidence of effectiveness in primary care. *Psychological Medicine*, 1-14. doi: 10.1017/s0033291713000111.

Newman, D. L., Moffitt, T. E., Caspi, A., Magdol, L., Silva, P. A., & Stanton, W. R. (1996). Psychiatric disorder in a birth cohort of young adults: prevalence, comorbidity, clinical significance, and new case incidence from ages 11 to 21. *Journal of Consulting and Clinical Psychology, 64*(3), 552-562. doi:10.1037//0022-006x.64.3.552

Newman, M. G., Szkodny, L. E., Llera, S. J., & Przeworski, A. (2011). A review of technology-assisted self-help and minimal contact therapies for anxiety and depression: is human contact necessary for therapeutic efficacy? *Clinical Psychology Review, 31*(1), 89-103. doi:10.1016/j.cpr.2010.09.008

Nguyen-Feng, V. N., Greer, C. S., & Frazier, P. (2017). Using online interventions to deliver college student mental health resources: Evidence from randomized clinical trials. *Psychological Services, 14*(4), 481-489. doi:10.1037/ser0000154

NHS. (2019). Child and adolescent mental health services (CAMHS). Retrieved from https://www.nhs.uk/using-the-nhs/nhs-services/mental-health-services/child-and-adolescent-mental-health-services-camhs/

Nolen-Hoeksema, S. (1991). Responses to depression and their effects on the duration of depressive episodes. *Journal of Abnormal Psychology, 100*(4), 569-582. doi:10.1037//0021-843x.100.4.569

Nolen-Hoeksema, S. (2000). The role of rumination in depressive disorders and mixed anxiety/depressive symptoms. *Journal of Abnormal Psychology, 109*(3), 504-511. doi:10.1037//0021-843x.109.3.504

Nolen-Hoeksema, S. (2001). Gender Differences in Depression. *Current Directions in Psychological Science, 10*(5), 173-176. doi:10.1111/1467-8721.00142

Nolen-Hoeksema, S., Larson, J., & Grayson, C. (1999). Explaining the gender difference in depressive symptoms. *Journal of Personality and Social Psychology, 77*(5), 1061-1072. doi:10.1037//0022-3514.77.5.1061

Nolen-Hoeksema, S., & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster: the 1989 Loma Prieta Earthquake. *Journal of Personality and Social Psychology, 61*(1), 115-121. doi:10.1037/0022-3514.61.1.115

Nolen-Hoeksema, S., & Morrow, J. (1993). Effects of rumination and distraction on naturally occurring depressed mood. *Cognition and Emotion, 7*(6), 561-570. doi:10.1080/02699939308409206

Nolen-Hoeksema, S., Stice, E., Wade, E., & Bohon, C. (2007). Reciprocal relations between rumination and bulimic, substance abuse, and depressive symptoms in female adolescents. *Journal of Abnormal Psychology, 116*(1), 198-207. doi:10.1037/0021-843X.116.1.198

Nolen-Hoeksema, S., & Watkins, E. R. (2011). A Heuristic for Developing Transdiagnostic Models of Psychopathology: Explaining Multifinality and

Divergent Trajectories. *Perspectives on Psychological Science, 6*(6), 589-609. doi:10.1177/1745691611419672

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking Rumination. *Perspectives on Psychological Science, 3*(5), 400-424. doi:10.1111/j.1745-6924.2008.00088.x

Nordgreen, T., Havik, O. E., Ost, L. G., Furmark, T., Carlbring, P., & Andersson, G. (2012). Outcome predictors in guided and unguided self-help for social anxiety disorder. *Behaviour Research and Therapy, 50*(1), 13-21. doi:10.1016/j.brat.2011.10.009

Nordin, S., Carlbring, P., Cuijpers, P., & Andersson, G. (2010). Expanding the Limits of Bibliotherapy for Panic Disorder: Randomized Trial of Self-Help Without Support but With a Clear Deadline. *Behavior Therapy, 41*(3), 267-276. doi:https://doi.org/10.1016/j.beth.2009.06.001

Nubel, J., Mullender, S., Hapke, U., & Jacobi, F. (2019). Epidemic of depression? : Development of prevalence and help-seeking behaviour. *Nervenarzt, 90*(11), 1177-1186. doi:10.1007/s00115-019-0681-y

NUS. (2015). *Lost in transition? – provision of mental health support for year olds moving to further and higher education.* Paper presented at the All Party Parliamentary Group on Students, London, UK.

O'Kearney, R., Kang, K., Christensen, H., & Griffiths, K. (2009). A controlled trial of a school-based Internet program for reducing depressive symptoms in adolescent girls. *Depression and Anxiety, 26*(1), 65-72. doi:10.1002/da.20507

Odondi, L., & McNamee, R. (2010). Performance of statistical methods for analysing survival data in the presence of non-random compliance. *Statistics in Medicine, 29*(29), 2994-3003. doi:10.1002/sim.4070

OECD/EU. (2018). *Health at a Glance: Europe 2018: State of Health in the EU Cycle*. Paris, France: OECD Publishing.

Olthuis, J. V., Watt, M. C., Bailey, K., Hayden, J. A., & Stewart, S. H. (2016). Therapist-supported Internet cognitive behavioural therapy for anxiety disorders in adults. *Cochrane Database of Systematic Reviews*(3). doi:10.1002/14651858.CD011565.pub2

Ormel, J., Kessler, R. C., & Schoevers, R. (2019). Depression: more treatment but no drop in prevalence: how effective is treatment? And can we do better? *Current Opinion in Psychiatry, 32*(4), 348-354. doi:10.1097/YCO.0000000000000505

Palacios, J. E., Richards, D., Palmer, R., Coudray, C., Hofmann, S. G., Palmieri, P. A., & Frazier, P. (2018). Supported Internet-Delivered Cognitive Behavioral Therapy Programs for Depression, Anxiety, and Stress in University Students: Open, Non-Randomised Trial of Acceptability, Effectiveness, and Satisfaction. *JMIR Mental Health, 5*(4), e11467-e11467. doi:10.2196/11467

Papadatou-Pastou, M., Goozee, R., Payne, E., Barrable, A., & Tzotzoli, P. (2017). A review of web-based support systems for students in higher education. *International Journal of Mental Health Systems, 11*(1), 59. doi:10.1186/s13033-017-0165-z

Patten, S. B. (2003). Recall bias and major depression lifetime prevalence. *Social Psychiatry and Psychiatric Epidemiology, 38*(6), 290-296. doi:10.1007/s00127-003-0649-9

Paykel, E. S. (2003). Life events and affective disorders. *Acta Psychiatrica Scandinavica, 108*(s418), 61-66. doi:10.1034/j.1600-0447.108.s418.13.x

Pereira, S., Reay, K., Bottell, J., Walker, L., Dzikiti, C., Platt, C., & Goodrham, C. (2019). *University Student Mental Health Survey 2018*. London: UK: The Insight Network and Dig-In.

Pine, D. S. (2003). Developmental psychobiology and response to threats: relevance to trauma in children and adolescents. *Biological Psychiatry, 53*(9), 796-808. doi:10.1016/s0006-3223(03)00112-4

Pine, D. S., Cohen, P., Gurley, D., Brook, J., & Ma, Y. (1998). The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. *Archives of General Psychiatry, 55*(1), 56-64. doi:10.1001/archpsyc.55.1.56

Praharso, N. F., Tear, M. J., & Cruwys, T. (2017). Stressful life transitions and wellbeing: A comparison of the stress buffering hypothesis and the social identity model of identity change. *Psychiatry Research, 247*, 265-275. doi:https://doi.org/10.1016/j.psychres.2016.11.039

Pratschke, J., Haase, T., Comber, H., Sharp, L., de Camargo Cancela, M., & Johnson, H. (2016). Mechanisms and mediation in survival analysis: towards an integrated analytical framework. *BMC Medical Research Methodology, 16*, 27. doi:10.1186/s12874-016-0130-6

Pressler, S. J., Subramanian, U., Perkins, S. M., Gradus-Pizlo, I., Kareken, D., Kim, J., . . . Sloan, R. (2011). Measuring depressive symptoms in heart failure: Validity and reliability of the Patient Health Questionnaire–8. *American Journal of Critical Care, 20*(2), 146-152.

Prestwich, A., Sheeran, P., Webb, T., & Gollwitzer, P. (2015). Implementation Intentions. In M. Conner & P. Norman (Eds.), *Predicting and changing health behaviour Research and Practice with Social Cognition Models: Third edition* (pp. 321-357). Maidenhead, UK: McGraw-Hill Education.

Radloff, L. S. (1977). The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement, 1*(3), 385-401. doi:10.1177/014662167700100306

Ramanuj, P., Ferenchick, E. K., & Pincus, H. A. (2019). Depression in primary care: part 2-management. *BMJ, 365*, l835. doi:10.1136/bmj.l835

Randall, E. M., & Bewick, B. M. (2015). Exploration of counsellors' perceptions of the redesigned service pathways: a qualitative study of a UK university student counselling service. *British Journal of Guidance & Counselling, 44*(1), 86-98. doi:10.1080/03069885.2015.1017801

RCPsych. (2019). *The NHS Long Term Plan in England: RCPsych Briefing*. Retrieved from https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/policy/nhs-long-term-plan-briefing.pdf.

Reinherz, H. Z., Paradis, A. D., Giaconia, R. M., Stashwick, C. K., & Fitzmaurice, G. (2003). Childhood and adolescent predictors of major depression in the transition to adulthood. *American Journal of Psychiatry, 160*(12), 2141-2147. doi:10.1176/appi.ajp.160.12.2141

Rice, F., Harold, G., & Thapar, A. (2002). The genetic aetiology of childhood depression: a review. *Journal of Child Psychology and Psychiatry, 43*(1), 65-79. doi:10.1111/1469-7610.00004

Richards, D., Murphy, T., Vigano, N., Timulak, L., Doherty, G., Sharry, J., & Hayes, C. (2016). Acceptability, satisfaction and perceived efficacy of "Space from Depression" an internet-delivered treatment for depression. *Internet Interventions, 5*, 12-22. doi:10.1016/j.invent.2016.06.007

Richards, D., & Richardson, T. (2012). Computer-based psychological treatments for depression: a systematic review and meta-analysis.

Clinical Psychology Review, 32(4), 329-342. doi:10.1016/j.cpr.2012.02.004

Richards, D., & Timulak, L. (2012). Client-identified helpful and hindering events in therapist-delivered vs. self-administered online cognitive-behavioural treatments for depression in college students. *Counselling Psychology Quarterly, 25*(3), 251-262. doi:10.1080/09515070.2012.703129

Richards, D. A., & Farrand, P. (2010). Choosing self-help books wisely: sorting the wheat from the chaff. In J. Bennett-Levy, D. Richards, P. Farrand, H. Christensen, K. Griffiths, D. Kavanagh, B. Klein, M. A. Lau, J. Proudfoot, L. Ritterband, J. White, & C. Williams (Eds.), *Oxford Guide to Low Intensity CBT Interventions* (pp. 201-208). Oxford, UK: Oxford University Press.

Richardson, R., Richards, D. A., & Barkham, M. (2010a). Self-help books for people with depression: the role of the therapeutic relationship. *Behavioural and Cognitive Psychotherapy, 38*(1), 67-81. doi:10.1017/s1352465809990452

Richardson, T., Stallard, P., & Velleman, S. (2010b). Computerised cognitive behavioural therapy for the prevention and treatment of depression and anxiety in children and adolescents: a systematic review. *Clinical Child and Family Psychology Review, 13*(3), 275-290. doi:10.1007/s10567-010-0069-9

Riso, L. P., du Toit, P. L., Blandino, J. A., Penna, S., Dacey, S., Duin, J. S., . . . Ulmer, C. S. (2003). Cognitive aspects of chronic depression. *Journal of Abnormal Psychology, 112*(1), 72-80.

Ritchie, J., & Spencer, L. (1994). Qualitative data analysis for applied policy research. In A. Bryman & R. Burgess (Eds.), *Analyzing Qualitative Data* (pp. 173-194). London: Routledge.

Roberts, J. E., Gilboa, E., & Gotlib, I. H. (1998). Ruminative Response Style and Vulnerability to Episodes of Dysphoria: Gender, Neuroticism, and Episode Duration. *Cognitive Therapy and Research, 22*(4), 401-423. doi:10.1023/a:1018713313894

Robichaud, M., Dugas, M. J., & Conway, M. (2003). Gender differences in worry and associated cognitive-behavioral variables. *Journal of Anxiety Disorders, 17*(5), 501-516. doi:10.1016/s0887-6185(02)00237-2

Robinson, M. S., & Alloy, L. B. (2003). Negative Cognitive Styles and Stress-Reactive Rumination Interact to Predict Depression: A Prospective Study. *Cognitive Therapy and Research, 27*(3), 275-291.

Ruscio, A. M., Gentes, E. L., Jones, J. D., Hallion, L. S., Coleman, E. S., & Swendsen, J. (2015). Rumination predicts heightened responding to stressful life events in major depressive disorder and generalized anxiety disorder. *Journal of Abnormal Psychology, 124*(1), 17-26. doi:10.1037/abn0000025

Ryan, M. L., Shochet, I. M., & Stallman, H. M. (2010). Universal online interventions might engage psychologically distressed university students who are unlikely to seek formal help. *Advances in Mental Health, 9*(1), 73-83. doi:10.5172/jamh.9.1.73

Sander, L., Rausch, L., & Baumeister, H. (2016). Effectiveness of Internet-Based Interventions for the Prevention of Mental Disorders: A Systematic Review and Meta-Analysis. *JMIR Mental Health, 3*(3), e38. doi:10.2196/mental.6061

Santucci, L. C., McHugh, R. K., Elkins, R. M., Schechter, B., Ross, M. S., Landa, C. E., . . . Barlow, D. H. (2014). Pilot Implementation of Computerized Cognitive Behavioral Therapy in a University Health Setting. *Administration and Policy in Mental Health and Mental Health Services Research, 41*(4), 514-521. doi:10.1007/s10488-013-0488-2

Schmaling, K. B., Dimidjian, S., Katon, W., & Sullivan, M. (2002). Response styles among patients with minor depression and dysthymia in primary care. *Journal of Abnormal Psychology, 111*(2), 350-356.

Schoenfeld, D. A. (1983). Sample-Size Formula for the Proportional-Hazards Regression Model. *Biometrics, 39*(2), 499-503. doi:10.2307/2531021

Schröder, J., Berger, T., Meyer, B., Lutz, W., Späth, C., Michel, P., . . . Moritz, S. (2018). Impact and change of attitudes toward Internet interventions within a randomized controlled trial on individuals with depression symptoms. *Depression and Anxiety, 35*(5), 421-430. doi:10.1002/da.22727

Schulz, K. F., Altman, D. G., Moher, D., & Group, C. (2010). CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ, 340*, c332. doi:10.1136/bmj.c332

Schwartz, J. A. J., & Koenig, L. J. (1996). Response styles and negative affect among adolescents. *Cognitive Therapy and Research, 20*(1), 13-36. doi:10.1007/bf02229241

Selby, E. A., Kranzler, A., Panza, E., & Fehling, K. B. (2016). Bidirectional-Compounding Effects of Rumination and Negative Emotion in Predicting Impulsive Behavior: Implications for Emotional Cascades. *Journal of Personality, 84*(2), 139-153. doi:10.1111/jopy.12147

Shansky, R. M., Glavis-Bloom, C., Lerman, D., McRae, P., Benson, C., Miller, K., . . . Arnsten, A. F. (2004). Estrogen mediates sex differences in stress-induced prefrontal cortex dysfunction. *Molecular Psychiatry, 9*(5), 531-538. doi:10.1038/sj.mp.4001435

Sharry, J., Davidson, R., McLoughlin, O., & Doherty, G. (2013). A Service-Based Evaluation of a Therapist-Supported Online Cognitive Behavioral Therapy Program for Depression. *Journal of Medical Internet Research, 15*(6), e121. doi:10.2196/jmir.2248

Shim, M., Mahaffey, B., Bleidistel, M., & Gonzalez, A. (2017). A scoping review of human-support factors in the context of Internet-based psychological interventions (IPIs) for depression and anxiety disorders. *Clinical Psychology Review, 57*, 129-140. doi:10.1016/j.cpr.2017.09.003

Smit, F., Beekman, A., Cuijpers, P., de Graaf, R., & Vollebergh, W. (2004). Selecting key variables for depression prevention: results from a population-based prospective epidemiological study. *Journal of Affective Disorders, 81*(3), 241-249. doi:10.1016/j.jad.2003.08.007

Smithson, J. (2008). Focus groups. In P. Alasuutari, L. Bickman, & J. Brannen (Eds.), The SAGE Handbook of Social Research Methods (pp. 357-370). London: SAGE Publications Ltd. Retrieved from http://methods.sagepub.com/book/the-sage-handbook-of-social-research-methods. doi:10.4135/9781446212165

So, M., Yamaguchi, S., Hashimoto, S., Sado, M., Furukawa, T. A., & McCrone, P. (2013). Is computerised CBT really helpful for adult depression?-A meta-analytic re-evaluation of CCBT for adult depression in terms of clinical implementation and methodological validity. *BMC Psychiatry, 13*(1), 113. doi:10.1186/1471-244X-13-113

Spasojević, J., & Alloy, L. B. (2001). Rumination as a common mechanism relating depressive risk factors to depression. *Emotion, 1*(1), 25-37. doi:10.1037/1528-3542.1.1.25

Spek, V., Cuijpers, P., Nyklicek, I., Riper, H., Keyzer, J., & Pop, V. (2007). Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. *Psychological Medicine, 37*(3), 319-328. doi:10.1017/S0033291706008944

Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of Internal Medicine, 166*(10), 1092-1097. doi:10.1001/archinte.166.10.1092

StataCorp. (2017). Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC.

Stawarz, K., Cox, A. L., & Blandford, A. (2015). *Beyond Self-Tracking and Reminders: Designing Smartphone Apps That Support Habit Formation*. Paper presented at the Proceedings of the 33rd Annual ACM Conference on Human Factors in Computing Systems, Seoul, Republic of Korea. Retrieved from https://doi.org/10.1145/2702123.2702230

Steinert, C., Hofmann, M., Kruse, J., & Leichsenring, F. (2014). Relapse rates after psychotherapy for depression - stable long-term effects? A meta-analysis. *Journal of Affective Disorders, 168*, 107-118. doi:10.1016/j.jad.2014.06.043

Stice, E., Shaw, H., Bohon, C., Marti, C. N., & Rohde, P. (2009). A meta-analytic review of depression prevention programs for children and adolescents: factors that predict magnitude of intervention effects. *Journal of Consulting and Clinical Psychology, 77*(3), 486-503. doi:10.1037/a0015168

Stockings, E. A., Degenhardt, L., Dobbins, T., Lee, Y. Y., Erskine, H. E., Whiteford, H. A., & Patton, G. (2016). Preventing depression and anxiety in young people: a review of the joint efficacy of universal, selective and indicated prevention. *Psychological Medicine, 46*(1), 11-26. doi:10.1017/S0033291715001725

Strauss, C., Cavanagh, K., Oliver, A., & Pettman, D. (2014). Mindfulness-based interventions for people diagnosed with a current episode of an anxiety or depressive disorder: a meta-analysis of randomised controlled trials. *PloS one, 9*(4), e96110. doi:10.1371/journal.pone.0096110

Student Minds. (2014). *Grand Challenges in Student Mental Health*. Oxford, UK: Student Minds Retrieved from https://www.studentminds.org.uk/uploads/3/7/8/4/3784584/grand_challenges_report_for_public.pdf.

Sugg, H. V. R., Frost, J., & Richards, D. A. (2020). Personalising psychotherapies for depression using a novel mixed methods approach: an example from Morita therapy. *Trials, 21*(1), 41. doi:10.1186/s13063-019-3788-3

Tabachnick, B. G., & Fidell, L. S. (2001). *Using multivariate statistics 4th edn*. Needham Heights, MA: Allyn & Bacon.

Takano, K., Sakamoto, S., & Tanno, Y. (2013). Ruminative self-focus in daily life: Associations with daily activities and depressive symptoms. *Emotion, 13*(4), 657-667. doi:10.1037/a0031867

Takano, K., Sakamoto, S., & Tanno, Y. (2014). Repetitive thought impairs sleep quality: an experience sampling study. *Behavior Therapy, 45*(1), 67-82. doi:10.1016/j.beth.2013.09.004

Teasdale, J. D., Segal, Z., & Williams, J. M. G. (1995). How does cognitive therapy prevent depressive relapse and why should attentional control (mindfulness) training help? *Behaviour research and therapy, 33*(1), 25-39. doi:https://doi.org/10.1016/0005-7967(94)E0011-7

Thapar, A., Collishaw, S., Pine, D. S., & Thapar, A. K. (2012). Depression in adolescence. *The Lancet, 379*(9820), 1056-1067. doi:10.1016/s0140-6736(11)60871-4

Thompson, N. J., Patel, A. H., Selwa, L. M., Stoll, S. C., Begley, C. E., Johnson, E. K., & Fraser, R. T. (2015). Expanding the efficacy of Project UPLIFT: Distance delivery of mindfulness-based depression prevention to people with epilepsy. *Journal of Consulting and Clinical Psychology, 83*(2), 304-313. doi:10.1037/a0038404

Thorley, C. (2017). *Not by degrees: Improving student mental health in the UK's universities*. London: IPPR Retrieved from http://www.ippr.org/research/publications/not-by-degrees.

Thornicroft, G., Chatterji, S., Evans-Lacko, S., Gruber, M., Sampson, N., Aguilar-Gaxiola, S., . . . Kessler, R. C. (2017). Undertreatment of people with major depressive disorder in 21 countries. *The British Journal of Psychiatry, 210*(2), 119-124. doi:10.1192/bjp.bp.116.188078

Tickell, A., Ball, S., Bernard, P., Kuyken, W., Marx, R., Pack, S., . . . Crane, C. (2020). The Effectiveness of Mindfulness-Based Cognitive Therapy (MBCT) in Real-World Healthcare Services. *Mindfulness, 11*(2), 279-290. doi:10.1007/s12671-018-1087-9

Titov, N., Andrews, G., Choi, I., Schwencke, G., & Johnston, L. (2009). Randomized Controlled Trial of Web-Based Treatment of Social Phobia

Without Clinician Guidance. *Australian & New Zealand Journal of Psychiatry, 43*(10), 913-919. doi:10.1080/00048670903179160

Titov, N., Andrews, G., Choi, I., Schwencke, G., & Mahoney, A. (2008). Shyness 3: Randomized Controlled Trial of Guided Versus Unguided Internet-Based CBT for Social Phobia. *Australian & New Zealand Journal of Psychiatry, 42*(12), 1030-1040. doi:10.1080/00048670802512107

Titov, N., Dear, B. F., Johnston, L., Lorian, C., Zou, J., Wootton, B., . . . Rapee, R. M. (2013). Improving adherence and clinical outcomes in self-guided internet treatment for anxiety and depression: randomised controlled trial. *PloS one, 8*(7), e62873. doi:10.1371/journal.pone.0062873

Topooco, N., Riper, H., Araya, R., Berking, M., Brunn, M., Chevreul, K., . . . consortium, E. C. (2017). Attitudes towards digital treatment for depression: A European stakeholder survey. *Internet Interventions, 8*, 1-9. doi:10.1016/j.invent.2017.01.001

Topper, M., Emmelkamp, P. M., Watkins, E., & Ehring, T. (2014). Development and assessment of brief versions of the Penn State Worry Questionnaire and the Ruminative Response Scale. *British Journal of Clinical Psychology, 53*(4), 402-421. doi:10.1111/bjc.12052

Topper, M., Emmelkamp, P. M., Watkins, E., & Ehring, T. (2017). Prevention of anxiety disorders and depression by targeting excessive worry and rumination in adolescents and young adults: A randomized controlled trial. *Behaviour Research and Therapy, 90*, 123-136. doi:10.1016/j.brat.2016.12.015

Topper, M., Emmelkamp, P. M. G., & Ehring, T. (2010). Improving prevention of depression and anxiety disorders: Repetitive negative thinking as a

promising target. *Applied and Preventive Psychology, 14*(1-4), 57-71. doi:10.1016/j.appsy.2012.03.001

Tucker, J. R., Hammer, J. H., Vogel, D. L., Bitman, R. L., Wade, N. G., & Maier, E. J. (2013). Disentangling self-stigma: are mental illness and help-seeking self-stigmas different? *Journal of Counseling Psychology, 60*(4), 520-531. doi:10.1037/a0033555

Unite Students. (2019). *The New Realists: Unite Students Insight Report 2019*. Retrieved from http://www.unite-group.co.uk/sites/default/files/2019-09/new-realists-insight-report-2019.pdf.

Universities UK. (2017). Stepchange Policy. Retrieved from https://www.universitiesuk.ac.uk/policy-and-analysis/stepchange/Pages/default.aspx

Universities UK. (2018). *Minding our future: starting a conversation about the support of student mental health*. London, UK: UUK Retrieved from https://www.universitiesuk.ac.uk/policy-and-analysis/reports/Pages/minding-our-future-starting-a-conversation-support-student-mental-health.aspx.

van Ballegooijen, W., Cuijpers, P., van Straten, A., Karyotaki, E., Andersson, G., Smit, J. H., & Riper, H. (2014). Adherence to Internet-based and face-to-face cognitive behavioural therapy for depression: a meta-analysis. *PloS one, 9*(7), e100674. doi:10.1371/journal.pone.0100674

van der Zanden, R., Kramer, J., Gerrits, R., & Cuijpers, P. (2012). Effectiveness of an Online Group Course for Depression in Adolescents and Young Adults: A Randomized Trial. *Journal of Medical Internet Research, 14*(3), e86. doi:10.2196/jmir.2033

Van Voorhees, B. W., Mahoney, N., Mazo, R., Barrera, A. Z., Siemer, C. P., Gladstone, T. R., & Muñoz, R. F. (2011). Internet-based depression prevention over the life course: a call for behavioral vaccines. *Psychiatric Clinics of North America, 34*(1), 167-183. doi:10.1016/j.psc.2010.11.002

Van Voorhees, B. W., Vanderplough-Booth, K., Fogel, J., Gladstone, T., Bell, C., Stuart, S., . . . Reinecke, M. A. (2008). Integrative internet-based depression prevention for adolescents: a randomized clinical trial in primary care for vulnerability and protective factors. *Journal of the Canadian Academy of Child and Adolescent Psychiatry = Journal de l'Academie canadienne de psychiatrie de l'enfant et de l'adolescent, 17*(4), 184-196.

van Zoonen, K., Buntrock, C., Ebert, D. D., Smit, F., Reynolds, C. F., 3rd, Beekman, A. T., & Cuijpers, P. (2014). Preventing the onset of major depressive disorder: a meta-analytic review of psychological interventions. *International Journal of Epidemiology, 43*(2), 318-329. doi:10.1093/ije/dyt175

Vanderhasselt, M. A., Brose, A., Koster, E. H. W., & De Raedt, R. (2016). Co-variation between stressful events and rumination predicts depressive symptoms: An eighteen months prospective design in undergraduates. *Behaviour Research and Therapy, 87*, 128-133. doi:10.1016/j.brat.2016.09.003

Verplanken, B., Friborg, O., Wang, C. E., Trafimow, D., & Woolf, K. (2007). Mental habits: metacognitive reflection on negative self-thinking. *Journal of Personality and Social Psychology, 92*(3), 526-541. doi:10.1037/0022-3514.92.3.526

Verplanken, B., & Orbell, S. (2003). Reflections on Past Behavior: A Self-Report Index of Habit Strength. *Journal of Applied Social Psychology, 33*(6), 1313-1330. doi:10.1111/j.1559-1816.2003.tb01951.x

Verplanken, B., & Wood, W. (2006). Interventions to break and create consumer habits. *Journal of Public Policy and Marketing, 25*(1), 90-103. doi:10.1509/jppm.25.1.90

Voelker, R. (2004). Stress, Sleep Loss, and Substance Abuse Create Potent Recipe for College Depression. *JAMA: Journal of the American Medical Association, 291*(18), 2177-2179. doi:10.1001/jama.291.18.2177

Wada, M., Suto, M. J., Lee, M., Sanders, D., Sun, C., Le, T. N., . . . Chauhan, S. (2019). University students' perspectives on mental illness stigma. *Mental Health & Prevention, 14*. doi:10.1016/j.mph.2019.200159

Waller, R., & Gilbody, S. (2009). Barriers to the uptake of computerized cognitive behavioural therapy: a systematic review of the quantitative and qualitative evidence. *Psychological Medicine, 39*(5), 705-712. doi:10.1017/S0033291708004224

Walsh, A., & Richards, D. (2016). Experiences and engagement with the design features and strategies of an internet-delivered treatment programme for generalised anxiety disorder: a service-based evaluation. *British Journal of Guidance & Counselling, 45*(1), 16-31. doi:10.1080/03069885.2016.1153039

Wang, P. S., Aguilar-Gaxiola, S., Alonso, J., Angermeyer, M. C., Borges, G., Bromet, E. J., . . . Wells, J. E. (2007). Use of mental health services for anxiety, mood, and substance disorders in 17 countries in the WHO world mental health surveys. *Lancet, 370*(9590), 841-850. doi:10.1016/s0140-6736(07)61414-7

Watkins, E., Newbold, A., Tester-Jones, M., Javaid, M., Cadman, J., Collins, L. M., . . . Mostazir, M. (2016). Implementing multifactorial psychotherapy research in online virtual environments (IMPROVE-2): study protocol for a phase III trial of the MOST randomized component selection method for internet cognitive-behavioural therapy for depression. *BMC Psychiatry, 16*(1), 345. doi:10.1186/s12888-016-1054-8

Watkins, E. R. (2008). Constructive and unconstructive repetitive thought. *Psychological Bulletin, 134*(2), 163-206. doi:10.1037/0033-2909.134.2.163

Watkins, E. R. (2016). *Rumination-focused Cognitive Behavioural Therapy for Depression*. New York: Guilford Press.

Watkins, E. R., Baeyens, C. B., & Read, R. (2009). Concreteness training reduces dysphoria: proof-of-principle for repeated cognitive bias modification in depression. *Journal of Abnormal Psychology, 118*(1), 55-64. doi:10.1037/a0013642

Watkins, E. R., & Baracaia, S. (2002). Rumination and social problem-solving in depression. *Behaviour Research and Therapy, 40*(10), 1179-1189. doi:10.1016/s0005-7967(01)00098-5

Watkins, E. R., & Moberly, N. J. (2009). Concreteness training reduces dysphoria: a pilot proof-of-principle study. *Behaviour Research and Therapy, 47*(1), 48-53. doi:10.1016/j.brat.2008.10.014

Watkins, E. R., Moberly, N. J., & Moulds, M. L. (2008). Processing mode causally influences emotional reactivity: distinct effects of abstract versus concrete construal on emotional response. *Emotion, 8*(3), 364-378. doi:10.1037/1528-3542.8.3.364

Watkins, E. R., & Moulds, M. (2005). Distinct modes of ruminative self-focus: impact of abstract versus concrete rumination on problem solving in depression. *Emotion, 5*(3), 319-328. doi:10.1037/1528-3542.5.3.319

Watkins, E. R., Mullan, E., Wingrove, J., Rimes, K., Steiner, H., Bathurst, N., . . . Scott, J. (2011). Rumination-focused cognitive-behavioural therapy for residual depression: phase II randomised controlled trial. *The British Journal of Psychiatry, 199*(4), 317-322. doi:10.1192/bjp.bp.110.090282

Watkins, E. R., & Nolen-Hoeksema, S. (2014). A habit-goal framework of depressive rumination. *Journal of Abnormal Psychology, 123*(1), 24-34. doi:10.1037/a0035540

Watkins, E. R., Scott, J., Wingrove, J., Rimes, K., Bathurst, N., Steiner, H., . . . Malliaris, Y. (2007). Rumination-focused cognitive behaviour therapy for residual depression: a case series. *Behaviour Research and Therapy, 45*(9), 2144-2154. doi:10.1016/j.brat.2006.09.018

Watkins, E. R., Taylor, R. S., Byng, R., Baeyens, C., Read, R., Pearson, K., & Watson, L. (2012). Guided self-help concreteness training as an intervention for major depression in primary care: a Phase II randomized controlled trial. *Psychological Medicine, 42*(7), 1359-1371. doi:10.1017/S0033291711002480

Webb, T., & Sheeran, P. (2007). How do implementation intentions promote goal attainment? A test of component processes. *Journal of Experimental and Social Psychology, 43(2)*, 295-302. doi:10.1016/j.jesp.2006.02.001

Weisel, K. K., Zarski, A. C., Berger, T., Krieger, T., Schaub, M. P., Moser, C. T., . . . Ebert, D. D. (2019). Efficacy and cost-effectiveness of guided and unguided internet- and mobile-based indicated transdiagnostic

prevention of depression and anxiety (ICare Prevent): A three-armed randomized controlled trial in four European countries. *Internet Interventions, 16*, 52-64. doi:10.1016/j.invent.2018.04.002

WHO. (2004). *Prevention of Mental Disorders: Effective Interventions and Policy Options. Summary Report*. Switzerland: WHO Press.

WHO. (2008). *The Global Burden of Disease 2004 Update*. Switzerland: WHO Press.

WHO. (2017). *Depression and other common mental disorders: global health estimates*. Geneva, Switzerland: WHO Press.

WHO. (2019). *Suicide in the World: Global Health Estimates*. Geneva, Switzerland: WHO Press.

Wieber, F., Sezer, L. A., & Gollwitzer, P. M. (2013). Asking “why” helps action control by goals but not plans. *Motivation and Emotion, 38*(1), 65-78. doi:10.1007/s11031-013-9364-3

Williams, C., & Morrison, J. (2010). A new language for cognitive behavioural therapy: new ways of working require new thinking, as well as new words. In J. Bennett-Levy, D. Richards, P. Farrand, H. Christensen, K. Griffiths, D. Kavanagh, B. Klein, M. A. Lau, J. Proudfoot, L. Ritterband, J. White, & C. Williams (Eds.), *Oxford Guide to Low Intensity CBT Interventions.* (pp. 69-86). Oxford: Oxford University Press.

Williams, M., Coare, P., Marvell, R., Pollard, E., Houghton, A.-M., & Anderson, J. (2015). *Understanding provision for students with mental health problems and intensive support needs*. (IES project code: 00099-3782). Brighton, UK: IES Retrieved from http://www.hefce.ac.uk/pubs/rereports/year/2015/mh/.

Williams, S., Clausen, M. G., Robertson, A., Peacock, S., & McPherson, K. (2012). Methodological Reflections on the Use of Asynchronous Online Focus Groups in Health Research. *International Journal of Qualitative Methods, 11*(4), 368-383. doi:10.1177/160940691201100405

Wood, W., & Neal, D. T. (2007). A new look at habits and the habit-goal interface. *Psychological Review, 114*(4), 843-863. doi:10.1037/0033-295x.114.4.843

Wörfel, F., Gusy, B., Lohmann, K., Töpritz, K., & Kleiber, D. (2015). Mental health problems among university students and the impact of structural conditions. *Journal of Public Health, 24*(2), 125-133. doi:10.1007/s10389-015-0703-6

Ziegelmann, J. P., Lippke, S., & Schwarzer, R. (2006). Adoption and maintenance of physical activity: Planning interventions in young, middle-aged, and older adults. *Psychology & Health, 21*(2), 145-163. doi:10.1080/1476832050018891

Appendix 1: Declaration of Candidate's Contribution to Co-Authored Papers

Chapter 3

The candidate designed the study, obtained ethical approval, collected and analysed the data, and wrote the paper with supervisory support from Prof. Edward Watkins.

Chapters 5 and 6

The candidate designed the study, obtained ethical approval, recruited participants and conducted the baseline and follow-up interviews. The candidate compiled the data and conducted some of the analyses. The advanced analyses were conducted by Mohammod Mostazir (Research Fellow in Medical Statistics). The candidate wrote the papers, with supervisory support from Prof. Edward Watkins.

Supervisor's Declaration

The undersigned certifies that:

1. The above declarations correctly reflect the nature and extent of the candidate's contribution to the work and the nature of the contribution of each of the co-authors

2. The candidate meets the criteria for first author on each paper in that they have participated in the conception, execution, and interpretation of the manuscript.

3. There are no other authors of the publications according to these criteria.

4. There were no conflicts of interest.

Signed:  Date: 28th January 2020

Professor Edward Watkins

Appendix 2: Text for online focus group

Note: Headings in bold will be added as categories and each question relating to that heading will be set as a separate discussion thread within that category

1. Information about the research topic and aims

Thank you for participating in this online forum.

We asked you to look at an internet-based intervention targeting stress, worry, and rumination in young adults. As explained in the information that was sent to you, the ultimate aim of this research is to assess whether this particular intervention is effective in reducing stress and worry and preventing depression. The underlying theory is that by targeting a specific risk factor, namely rumination and worry, people's risk of developing depression in the future can be reduced. The intervention will therefore be offered to people who have no current or past diagnosis of depression, but who show high levels of rumination, and is focused on helping people find better ways of handling day-to-day stress.

There are several internet-based treatments for depression available, but there is little evidence about what would be important to users of an internet-based preventive intervention. This particular internet-based intervention was translated directly from Dutch. The Dutch version is currently being trialled in the Netherlands as a preventive intervention, with encouraging preliminary results. We are aiming to build on that study by assessing its effectiveness in an English-speaking population.

Given that there is little evidence on what people would value in terms of an internet-based preventive intervention, and we also don't know whether the Dutch version translates well to an English-speaking population, we are keen to gather your opinions on the platform and to determine whether you think any changes should be made. We are particularly interested in hearing about those aspects of the treatment that you found engaging, useful, and personally meaningful, as well as those aspects that you found less relevant, less helpful, or less motivating. In this way, we can try to make the treatment as engaging and personally relevant for users as possible. We'd like to stress that there are no right or wrong answers to any of the questions. We are planning to make changes based on what you say so we welcome any suggestions, both positive and negative.

2. Information about confidentiality

What will happen with the information gathered from today's group?

Information gathered from today's group will be used to inform potential changes to the platform. Data will also be analysed and written up as part of Lorna's PhD thesis and potentially published in a journal article. This will involve quoting excerpts of the discussion but all data will be fully anonymised (the usernames you use here will be changed) to ensure confidentiality.

Confidentiality

Your personal details and anything you say on the forum will be completely confidential. Your chosen usernames will not be included in the transcript so anything you say on the forum cannot be linked to your personal details. You have the right to refuse to answer any particular question or to withdraw your participation from the study at any point, without giving a reason for doing so.

We ask that you also respect each other's confidentiality and do not discuss anything written on the forum with third parties.

3. Forum rules

We welcome debate and disagreements as we want to obtain a wide range of opinions. However you will be expected to abide by the following ground rules:

1. Respect each other's views – we don't expect you to agree with each other on everything but it is important that people are allowed to express their own views.
2. Posts will be moderated by Lorna Cook. Any posts deemed to be inappropriate or offensive will be edited or removed (including offensive language and any posts likely to cause upset or distress to other participants)
3. The moderator will log in regularly to monitor posts but if you see any content that is unsuitable, please flag it either through the forum, or by direct email to Lorna (lzc204@exeter.ac.uk) and it will be dealt with as soon as possible.
4. Participants who post an offensive or inappropriate post will be issued with a warning. If they repeat this behaviour, they will be asked to leave the study and their log-in will be deactivated.

4. Give your opinion on internet-based interventions in general

The intervention you have looked at uses an adapted form of cognitive-behavioural therapy (CBT), focusing on rumination as a key factor in stress and worry. CBT is most commonly delivered face-to-face by a therapist

but internet-based interventions using CBT are becoming more widespread.

- What do you consider to be the benefits of an internet-based intervention?
- What do you consider to be the barriers to using an internet-based intervention?

5. **Give your opinion on what you think is important in an internet-based preventive intervention**

   This intervention is aimed at preventing depression by targeting a known risk factor, rather than treating depression in those who have already been diagnosed. The target user group is therefore different to those who use internet-based CBT as a treatment for depression, in that they will be healthy individuals (albeit with high levels of rumination and possibly mild symptoms of depression). The intervention is aimed at people experiencing worry and stress and is focused on helping people find better ways of handling day-to-day stress, to reduce future problems.

   - What elements would be important to you in a preventive internet-based intervention?

6. **Give your opinion on the content of the platform**

   - What did you like about the platform?
   - What didn't you like about the platform?
   - Which elements were particularly relevant to you and which were less relevant?

- Which elements did you think might be helpful in reducing stress and worry?
- Which elements did you think might be less helpful?

7. Give your opinion on the language and tone

- Was there anything in particular you found difficult to understand or felt could be explained more clearly?
- How did you feel about the tone of the language used?
  (Did you find the language supportive? Did you find it motivating?)

8. Give your opinion on the visuals and interactive features

- What are your opinions on the visual appearance of the site?
- What are your opinions on the range of interactive features?

9. Give your opinion on the ease of navigation

- How easy did you find it to navigate through the platform?
- Is there anything in terms of layout that could be changed to make it easier to access the different features?

10. Safety/trustworthiness of site

There will be two versions of the therapy, one where clients are supported by a coach (guided therapy) and another that is purely self-help (unguided therapy).

In the guided therapy, each client will be assigned a named coach who they can contact with any questions while they are working through the exercises. At the end of each module, the user will be asked to submit their

responses to the exercises to their assigned coach. The coach will view these responses and provide the user with feedback and guidance via on-line responses within the internet treatment.

In the unguided therapy, clients' responses will be saved by the platform and will only be viewed by the research team after the client has completed the full programme.

Responses from both groups will only be shared within the research team and will not be shared with third parties.

- How safe or secure would you feel using this website?
- Is there anything that would make it feel more secure?

11. Motivation

The full intervention is expected to take 6-12 weeks, which would allow clients one to two weeks to complete each module. In the unguided group, clients will receive automated feedback on their responses and can work through all modules at their own pace.

In the guided group, the client will be supported by a coach and will be required to submit their responses to their coach at the end of each module, before they can proceed to the next. The coach will provide feedback on progress and highlight areas to focus on in the coming week. Clients in the guided group will also able to send direct messages and questions to their coach at any time.

- How would you feel about completing each module to a specific deadline?

- How might the coach encourage an individual to meet the deadline without making them feel under pressure?
- How might the unguided group be encouraged to complete the modules without using direct communication from a coach?
- What do you think might be a reasonable and realistic time to work through all the modules?
- Would you structure the modules any differently (for example, in terms of order, dividing them into shorter sections)?
- Which modules were more/less relevant to you?
- What might increase your motivation to complete the programme?

12. Changes to the platform

If you were going to adapt the site, what changes would you make?

Appendix 3 Screening, Baseline and Risk measures for the RESPOND Trial

Note: A subset of the same set of questionnaires was administered at each follow-up (Past treatment, SCID-I, Stressful events interview, RRS, PSWQ, PHQ-9, GAD-7)

Questions from IMPROVE Mood Screener (to be used during the telephone screening)

A yes answer to the <u>current</u> drug, <u>current</u> alcohol, bipolar disorder or schizophrenia or positive responses to screening questionnaires below would exclude someone from the internet therapy - explain outcome of their responses, offer them sources of information, recommend talking to doctor/medical professional

- *Has your alcohol use ever caused any problems for you? Yes or No*
- *Does your alcohol use currently cause problems for you? Yes or No*
- *Has your drug use ever caused any problems for you? Yes or No*
- *Does your drug use currently cause problems for you? Yes or No*
- *Have you ever been diagnosed with manic-depression / bipolar disorder? Yes or No*
- *Have you ever been diagnosed with psychosis or schizophrenia? Yes or No*
- *Have you ever been diagnosed with any other mental health problems? Yes or No*
- *What was the problem?*

The next set of screening questions need to follow a sequential and contingent structure such that different questions follow depending if the previous questions are answered Yes or No – i.e., a tailored if-then structure, as indicated by the arrows:

- *In this section, I will ask about a whole range of experiences. Some of these experiences are quite rare. However, we would be very obliged if you would bear with us and answer the following questions.*
-

[Q1]. Over the past year, have there been times when you felt very happy indeed without a break for days on end ?	*Yes*	*1*	*→*	*(a)*
	Unsure	*2*	*}→*	*Q2*
	No	*3*		

-

(a) Was there an obvious reason for this ?	*Yes*	*1*	*}→*	*Q2*
	Unsure	*2*		
	No	*3*	*→*	*(b)*

-

(b) Did your relatives or friends think it was strange or complain about it ?	*Yes*	*1*	*→*	*Screen positive*
	Unsure	*2*	*}→*	*Q2*
	No	*3*		

-

Q2. Over the past year, have you ever felt that your thoughts were directly interfered with or controlled by some outside force or person ?	*Yes*	*1*	*→*	*(a)*
	Unsure	*2*	*}→*	*Q3*
	No	*3*		

-

(a) Did this come about in a way that many people would find hard to believe, for instance, through telepathy ?	*Yes*	*1*	*→*	*Screen positive*
	Unsure	*2*	*}→*	*Q3*
	No	*3*		

-

Q3. Over the past year, have there been times when you felt that people were against you ?	*Yes*	*1*	*→*	*(a)*
	Unsure	*2*	*}→*	*Q4*
	No	*3*		

-

(a) Have there been times when you felt people were deliberately trying to harm you or your interests ?	*Yes*	*1*	*→*	*(b)*
	Unsure	*2*	*}→*	*Q4*
	No	*3*		

-

	Yes	*1*	*→*	*Screen positive*

(b) Have there been times when you felt a group of people was plotting to cause you serious harm or injury ?	*Unsure* *No*	*2* *3*	*}→*	*Q4*

-

Q4. Over the past year, have there been times when you felt that something strange was going on ?	*Yes* *Unsure* *No*	*1* *2* *3*	*→* *}→*	*(a)* *Q5*

-

(a) Did you feel it was so strange that other people would find it hard to believe ?	*Yes* *Unsure* *No*	*1* *2* *3*	*→* *}→*	*Screen positive* *Q5*

-

Q5. Over the past year, have there been times when you heard or saw things other people couldn't ?	*Yes* *Unsure* *No*	*1* *2* *3*	*→* *}→*	*(a)* *End Schedule*

-

(a) Did you at times hear voices saying quite a few words or	*Yes*	*1*	*→*	*Screen positive*

sentences when there was no one around that might account for it ?	*Unsure*	*2*	*End Schedule*
	No	*3*	

Treatment history

1. Have you ever received any mental health treatment in the past?

If, yes – please provide some details:

2. Are you currently receiving any mental health treatment?

If, yes – please provide some details:

3. Are you taking any medication related to mental health?

If yes – please provide:

a. Name of the medicine:

b. Dosage:

c. Has the dosage been changed in the past 4 weeks?

SCID-I screening questions to determine which modules to assess further

SCID SCREENING MODULE (OPTIONAL)

Now I want to ask you some more specific questions about problems you may have had. We'll go into more detail about them later.

RESPOND TO POSITIVE RESPONSES WITH: We'll talk more about that later.

1.	Has there been any time in your life when you had five or more drinks (beer, wine, or liquor) on one occasion?	CIRCLE 'NO' ON **E 1**	CIRCLE 'YES' ON **E 1**	S1
2.	Have you ever used street drugs?	CIRCLE 'NO' ON **E 10**	CIRCLE 'YES' ON **E 10**	S2
3.	Have you ever gotten "hooked" on a prescribed medicine or taken a lot more of it than you were supposed to?	CIRCLE 'NO' ON **E 10**	CIRCLE 'YES' ON **E 10**	S3
4.	Have you ever had a panic attack, when you suddenly felt frightened or anxious or suddenly developed a lot of physical symptoms?	CIRCLE 'NO' ON **F 1**	CIRCLE 'YES' ON **F 1**	S4
5.	Were you ever afraid of going out of the house alone, being in crowds, standing in a line, or traveling on buses or trains?	CIRCLE 'NO' ON **F 7**	CIRCLE 'YES' ON **F 7**	S5
6.	Is there anything that you have been afraid to do or felt uncomfortable doing in front of other people, like speaking, eating or writing?	CIRCLE 'NO' ON **F 11**	CIRCLE 'YES' ON **F 11**	S6
7.	Are there any other things that you have been especially afraid of, like flying, seeing blood, getting a shot, heights, closed places, or certain kinds of animals or insects?	CIRCLE 'NO' ON **F 16**	CIRCLE 'YES' ON **F 16**	S7

1=NOT PRESENT 2=UNSURE OR EQUIVOCAL 3=PRESENT

Example scoresheet for SCID-I: Current MDE

r: _____ Date: __/__/___ Patient ID):_____

SCID BASELINE TEMPLATE SCORE SHEET

A. MOOD EPISODES

***CURRENT MAJOR DEPRESSIVE EPISODE* in Past month**

1.	Depressed or down (2 wks+)	?	1	2	3
	and / or				
2.	Loss interest/ pleasure (most activities/day).	?	1	2	3

**IF NEITHER IS CODED "3" SKIP TO A12 (PAST MDE)

3.	Weight change (increased / decreased)	?	1	2	3
4.	Sleep change (insomnia / hypersomnia)	?	1	2	3
5.	Psychomotor agitation/retardation	?	1	2	3
6.	Fatigue/low energy	?	1	2	3
7.	Worthlessness/Guilt (NB excessive or inappropriate)	?	1	2	3
8.	Concentration (thinking/indecisiveness)	?	1	2	3
9.	Suicide	?	1	2	3

Thought of own death __ Suicidal ideation __ Specific Plan __ Suicide attempt__

Five sxs coded "3", and at least one of these is item 1 or 2. **1** **3**

(CRITERION B HAS BEEN OMITED FROM SCID)

C. Functional Impairment **? 1 2 3**

**IF CODED 1 GO TO A12 (PAST MDE)

D. Not Due to General Medical Condition/ Substance abuse **? 1 3**

**GO TO A43 TO CHECK IF NECESSARY

E. Recent Bereavement **? 1 3**

**IF EITHER D or E 1 GO TO A12 (PAST MDE)

=>MDE IF A, C, D, AND E ARE CODED "3" **1** **3**

Total No of MDEs (including current) _____ (CODE 99 if too many or indistinct)

CURRENT MDE SPECIFIERS

WITH POSTPARTUM ONSET (A6)	1	3
WITH CATATONIC FEATURES (A6-A7)	1	3
WITH MELANCHOLIC FEATURES (A8-A9)	1	3
WITH ATYPICAL FEATURES (A10-A11)	1	3

**IF Past Major Depressive Episode/s GO TO A12 otherwise GO TO A18

Modified Paykel List of Life Events (used to probe the number and severity of stressful events)

Work

- Start working for the first time ever.
- Change to a new line of work, or get a new job.
- Substantial change in work conditions e.g. transfer, new boss/colleagues, change in duties or responsibilities.
- Substantial change in work hours.
- Onset of troubles or disagreement with boss or co-workers.
- Promotion.
- Demotion.
- Fired or laid off.
- Unemployed for one month or more.
- Failure of business.
- Quit job.

Education

- Begin full time or half time education.
- Change schools.
- Ceases full time education (graduation or drop out).
- Important academic failure.
- Trouble with professor.
- Prepare for, or take important exam.
- Graduation.

Financial

- Moderate financial difficulties (needing second job or more income).
- Major financial difficulties (e.g. bankruptcy, very heavy debts, defaulting on bills, loans).
- Substantial improvement in finances (unconditional improvements, not loans).

Health

- Minor physical illness, injury or accident.
- Major physical illness, operation, injury or accident.
- Physical or emotional illness, injury or accident to close family member, friend, romantic partner (not leading to death).
- Wanted pregnancy.
- Unwanted pregnancy.
- Miscarriage, stillbirth or abortion.
- Birth of child.
- Assault, rape (including date rape).

Bereavement

- Death of a close friend or family member.

- Death of an acquaintance or distant family member.
- Death of own child.
- Death of spouse or romantic partner.
- Loss or robbery of objects of personal or actual value.
- Termination of therapy.

Migration

- Move out of home for first time.
- Move within same city.
- Move to another city or state.
- Move to another country.
- Move back home with parents.

Courtship and cohabitation

- Become engaged.
- Break engagement.
- Begin new dating relationship.
- End dating relationship.
- Serious argument or difficulties with romantic partner.
- Begin cohabiting.
- Resume dating relationship.
- Affair with married person or with person in a relationship.
- Problems related to affair.

Legal

- Minor violation not leading to court appearance (e.g. traffic ticket, academic violations).
- More important violation leading to court appearance.
- Jail sentence.
- Law suit with legal action.
- Legal problems of close family member.
- Traffic accident.

Family and Social

- Birth of child to family member or close friend.
- Adoption of child by family member or close friend.
- New person (other than new baby) moves into the household.
- Serious argument or problem with family member.
- Marked improvement in relationship with family member.
- Serious argument or problem with friend.
- Marked improvement in relationship with friend (not meeting a new friend).
- Start new friendship.
- End friendship.
- Separation from significant person (e.g. family member, close friend, romantic partner, therapist).
- Marital problems of close family members.

Marital

- Marriage.
- Serious argument or problem with spouse.
- Marital separation not due to argument (e.g. in hospital, out of town, any circumstance where couple is separated and does not want to be).
- Marital separation due to argument.
- Extramarital affair by either partner or extra-relationship affair.
- Marked improvement in relationship with spouse.
- Marital reconciliation after separation.
- Divorce.

Other

- Generic other.
- Natural disaster.
- Victim of crime.

Baseline Questionnaires (RRS, PSWQ, PHQ-9, GAD-7, EPQ-R)

Thank you for completing the telephone screening interview. Please complete the following questionnaires and return to Lorna Cook by email (lzc204@exeter.ac.uk) or by post: Sir Henry Wellcome Building for Mood Disorders Research, University of Exeter, Perry Road, EX4 4QG. **If completing on screen, please make sure you save the document regularly to avoid losing your responses.**

1. **Here are some questions about what you generally think and do when you are feeling down**

For each of the following statements, please mark an **x** in the box that best represents how often you feel this way.

People think and do many different things when they feel down, sad or depressed. Please read each of the items below and indicate whether you never, sometimes, often, or always think or do each one when you feel down, sad or depressed. Please indicate what you *generally* do, not what you think you should do.

	Almost never	**Sometimes**	**Often**	**Almost always**
1. Think about how alone you feel.				
2. Think "I won't be able to do my job/work because I feel so bad"				
3. Think about your feelings of fatigue and achiness.				
4. Think about how hard it is to concentrate.				
5. Think about how passive and unmotivated you feel.				
6. Analyse recent events to try and understand why you are depressed.				
7. Think about how you don't seem to feel anything anymore				
8. Think "Why can't I get going?"				

9. Think “Why do I always react this way?”				
10. Go away by yourself and think about why you feel this way.				
11. Write down what you are thinking about and analyse it				
12. Think about a recent situation, wishing it would have gone better				
13. Think ““Why do I have problems other people don’t have?”				
14. Think about how sad you feel.				
15. Think about all your shortcomings, failings, faults and mistakes				
16. Think about how you don’t feel up to doing anything				
17. Analyse your personality to try and understand why you are depressed				
18. Go someplace alone to think about your feelings.				
19. Think about how angry you are with yourself.				
20. Listen to sad music.				
21. Isolate yourself and think about the reasons why you feel sad				
22. Try to understand yourself by focusing on your depressed mood				
23. Think “What am I doing to deserve this?”				
24. Think “I won’t be able to concentrate if I keep feeling this way”.				
25. Think “Why can’t I handle things better?”				

2. Here are some questions about worry

Please rate how much each of the following statements is typical of you by placing an **x** in the appropriate box.

	Not at all typical of me	**Slightly typical of me**	**Moderately typical of me**	**Mainly typical of me**	**Very typical of me**
1. If I don't have enough time to do everything, I don't worry about it					
2. My worries overwhelm me.					
3. I don't tend to worry about things.					
4. Many situations make me worry.					
5. I know I shouldn't worry about things, but I just can't help it.					
6. When I am under pressure I worry a lot.					
7. I am always worrying about something.					
8. I find it easy to dismiss worrisome thoughts.					
9. As soon as I finish one task, I start to worry about everything else I have to do.					
10. I never worry about anything.					
11. When there is nothing more I can do about a concern, I don't worry about it anymore.					
12. I've been a worrier all my life.					
13. I notice that I have been worrying about things.					
14. Once I start worrying, I can't stop.					
15. I worry all the time					
16. I worry about projects until they are all done.					

3. **Here are some questions about your mood:**

For each question, please place an **x** in the box that best represents how often you have felt that way over the last two weeks.

When you think about **the last two weeks**, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things				
2. Feeling down, depressed, or hopeless				
3. Trouble falling or staying asleep or sleeping too much				
4. Feeling tired or having little energy				
5. Poor appetite or overeating				
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down				
7. Trouble concentrating on things, such as reading the newspaper or watching television				
8. Moving or speaking so slowly that other people could have noticed. Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual				
9. Thoughts that you would be better off dead, or of hurting yourself in some way				

4. Here are some questions about how stress may affect you:

To answer each question, please type an x in the box under the answer that best represents how often you feel this way. Place one x in one box in each row.

Over the last two weeks, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
1) Feeling nervous, anxious or on edge				
2) Not being able to stop or control worrying				
3) Worrying too much about different things				
4) Trouble relaxing				
5) Being so restless that it is hard to sit still				
6) Becoming easily annoyed or irritable				
7) Feeling afraid as if something awful might happen				

5. Here are some more questions about how stress might affect you:

INSTRUCTIONS: Please answer each questions by putting a circle around the 'YES' or NO following the question. There are no right or wrong answers, and no trick questions. Work quickly and do not think too long about the exact meaning of the questions**.**

PLEASE REMEMBER TO ANSWER EACH QUESTION

1. Does your mood often go up and down?	Yes	No
2. Do you ever feel "just miserable" for no reason?	Yes	No
3. Are you an irritable person?	Yes	No
4. Are your feelings easily hurt?	Yes	No
5. Do you often feel "fed up"?	Yes	No
6. Are you often troubled about feelings of guilt?	Yes	No
7. Would you call yourself a nervous person?	Yes	No
8. Are you a worrier?	Yes	No
9. Would you call yourself tense or "highly-strung"?	Yes	No
10. Do you worry too long after an embarrassing experience?	Yes	No
11. Do you suffer from ‘nerves’?	Yes	No
12. Do you often feel lonely?	Yes	No

6.Here are some questions about your background:

- Is there a history of depression in your family? **(Yes/No)**
- Have either of your parents experienced depression? **(Yes/No)**
- **If YES:**
    - Which parent?
    - How long ago was their last episode of depression?
    - How many episodes have they experienced since you were born?

- Did you experience any physical abuse before the age of 16? **(Yes/No)**
- Did you experience any emotional abuse before the age of 16? **(Yes/No)**
- Did you experience any sexual abuse before the age of 16? **(Yes/No)**

Thank you for completing these questionnaires.

MOOD DISORDERS CENTRE

PROTOCOL FOR ASSESSING AND REPORTING RISK

The following principles and procedures govern risk assessment and reporting in the Mood Disorders Centre (MDC). The MDC does not manage risk.

General principles

MDC clinical academic faculty are responsible for risk assessment in their research programmes. This includes ensuring that staff, students and interns working with them receive adequate induction and training prior to participant contact in which risk could be disclosed and ongoing supervision during their research work.

Many of the research projects in the MDC will include supplementary and more detailed protocols for risk assessment.

The AccEPT Clinic has its own risk protocol.

General procedures

Background training materials are available on the shared directory. All staff should attend training in the use of this protocol as soon as is reasonably possible and attend training normally at least biennially. If they undertake any work where risk may be an issue prior to receiving formal training, it is the PI's responsibility to ensure that they have reviewed all the materials and have received bespoke training.

Whenever any significant risk is identified a risk assessment should be completed and (counter-) signed by the responsible member of staff. If at all possible this should be done at the time of the assessment, or as soon afterwards as possible. This record should be kept on file in line with the Centre's or study's data storage procedures.

Any significant, but not imminent risk should be reported to the person's GP and, if appropriate, other health care professionals, as soon as is reasonably possible.

For research outside of the local area, PIs / supervisors should familiarise themselves with the local providers' risk procedures, and researchers should hold the relevant contact details needed in the case of immediate risk.

When clinical academic staff are away from the Centre they should ensure appropriate cover is arranged for any risk issues that might arise in their absence.

When conducting telephone interviews in which risk may be disclosed, the interviewer should establish the telephone number and location of the participant at the start of the call, and clarify the boundaries of confidentiality (as per trial / clinic protocol).

Exeter emergency contact numbers

- Crisis Resolution Home Treatment Team (East and Mid Devon)
  07968 845048
  Please note, this number is to make an urgent referral to the Crisis Team and <u>should not</u> be given out to participants / clients / members of the public under any circumstances. The participant's / client's GP can also make an urgent referral to the Crisis Team and should be the first port of call.

- Exeter Accident and Emergency Department
  This is located at the Royal Devon and Exeter Hospital (Wonford), Barrack Road, Exeter, EX2 5DW

- Student Health Services – The Streatham Campus Student Health Centre is located in Reed Mews and is run solely for students. Phone: 01392 676606 (Streatham) or, 01392 211511 (St Luke's)

  If you need a doctor urgently out of Student Health Centre opening hours, phone the Devon Doctors on Call Patient line: 0845 6710 270

THOUGHTS

"I see that you've said / you mentioned that…….. These are thoughts / feelings that people suffering from depression often have, but it's important to make sure you are receiving the right kind of support. So I would now like to ask you some more questions that will explore these feelings in a little more depth."

PLANS

1 Do you know how you would kill yourself? Yes / No
If **yes –** details

---

2 Have you made any actual plans to end your life? Yes / No
If **yes –** details

ACTIONS

3 Have you made any actual preparations to kill yourself? Yes / No
If **yes –** details

---

4 Have you ever attempted suicide in the past? Yes / No
If **yes –** details

PREVENTION

5 Is there anything stopping you killing or harming yourself at the moment? Yes / No

If **yes –** details

---

6 Do you feel that there is any immediate danger that you will harm or kill yourself? Yes / No

Details:

FOLLOW-UP FROM PREVIOUS CONTACT

7 **If Action B was enacted at previous assessment and level B risk is identified at current assessment**: Last time we met I suggested that you spoke to your GP about these thoughts, and I also wrote to your GP about this. Have you been able to speak with your GP about these thoughts since we last met? Yes / No

See risk table overleaf for appropriate actions

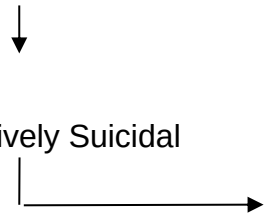
Researcher Risk Protocol

To be used following any indication of risk from questionnaire items, responses to interview questions or any other sources. Look at answers from the sheet to determine the level of risk, A B or C:

Actions by Researcher	***Tell Participant***
All answers 'no' apart from Q5 'yes': ↓ **A** →	*I can see that things have been very difficult for you, but it seems to me these thoughts about death are not ones you would act on – would this be how you see things? (if they say yes) I would advise you to make an appointment to see your GP to talk about these feelings* ***(as per trial protocol)****.*
'Yes' for any **one** of Qs 1-4; plus 'yes' for Q5 and 'no' for Q6 ↓ **B1** →	*Things seem to be very hard for you right now and I think it would help if you were to speak to your GP about these feelings. I will be writing to your GP to tell them that you have been here today and have been having some troubling thoughts. I would also advise you to make an appointment to see your GP to talk about these feelings. (****as per trial protocol).***
'Yes' for any **one** of Qs 1-4; plus 'yes' for Q5 and 'no' for Q6 **and** 'no' to Q7 ↓ B2 →	*I think it's important that your GP knows how difficult things are for you right now. I will be telephoning your GP to speak with him/her and suggest that you meet with one another. I also advise that you make an appointment to see your GP to talk about these feelings.* ***(as per trial protocol****).N.B: telephone call to GP to be followed up by letter. The letter should include the statement "*the clinical management of this patient remains your responsibility, but it is part of our protocol to inform you of any risks disclosed to

ourselves so that you can take account of them in your care plan.”

Scoring ‘no’ to Q5 or ‘yes’ to Q6



C Actively Suicidal

I am very concerned about your safety at this moment, I am not a clinician but I would like you to talk to one right now. I am going to make some telephone calls now to your GP Care Co-ordinator / Crisis Management team/the emergency services to let them know how you are feeling and to arrange for you to receive immediate help.

Action to take in the case of immediate risk:

Participant needs immediate help – **do not leave them alone, or if on telephone, do not hang up**. Follow your trial’s chain of supervisory clinical contact in order to involve supervisory clinician right away. Then either yourself or the supervisory clinician* should follow the chain of contact below:

1. GP / out of hours GP; if not

2.Crisis team; if not

3. Call ambulance; if this does not result in ambulance attending

4..Clinician accompanies to A&E (by taxi rather than private car)

**Individual projects should determine in advance whether clinician or researcher (with clinician support) enacts steps 1-4*

Risk Report

Patient name: _____ DOB: _____

Suicide risk information:

Include whether the participant has reported any of the following:

- *History of previous suicide attempts*
- *Current suicidal ideation*
- *Relevant inventory scores (e.g., BDI item 9)*
- *Suicide plans / preparations*
- *Protective factors*
- *Regular contact with GP?*

Date reported: ___/___/___

Additional notes / actions taken:

*As part of the MDC risk protocol, suicide risk is **managed** by the patient's GP.*

Date action taken: ___/___/___

Researcher / assessor: _____ Signed: _____ Date: ___/___/___

Supervisor: _____ Signed: _____ Date: ___/___/___

Sources of Help Sheet: sent by email to all participants meeting criteria for current MDE and/or reporting risk

Sources of Help

National

Your GP

If you are experiencing depressive symptoms or suicidal thoughts and are not currently receiving treatment, we strongly recommend you speak to your GP about your symptoms. Your GP will be able to support you and discuss any treatment options with you.

Samaritans

Samaritans provides confidential emotional support, 24 hours a day for people who are experiencing feelings of distress or despair. Samaritans are there if you're worried about something, feel upset or confused, or you just want to talk to someone.

24 hour telephone helpline: 116 123 (UK)
Email help service: jo@samaritans.org
Website: http://www.samaritans.org/

Befrienders Worldwide

Befrienders is an international network of 169 emotional support centres in 29 countries, offering confidential and impartial emotional support to people who are in distress. International email and helpline details are available on the website.
Website: http://www.befrienders.org

SANEline

SANEline operates an out-of-hours helpline and an email service providing emotional support and information for people experiencing mental health issues.
Helpline: (6pm-11pm daily): 08457 678000
Email: http://www.sane.org.uk/what_we_do/support/email/
Website: http://www.sane.org.uk/what_we_do

Nightline

Nightline is a listening and information service run by students for students. It runs through the night during term-time. Specially trained volunteers are willing to listen if you want to talk about any problems you may be experiencing. Calls are confidential, anonymous and listened to in a non-judgmental, non-advisory manner.
Website: http://www.nightline.ac.uk/home
Find your University's Nightline: http://www.nightline.ac.uk/find-my-nightline

Depression Alliance

Depression Alliance is a charity working to relieve and to prevent depression by providing information, support and understanding. Depression Alliance offers a range of publications, self-help groups and an information telephone line.

Depression Alliance
20 Great Dover Street
London
SE1 4LX
Tel: 0845 123 23 20
Website: http://www.depressionalliance.org/

Students Against Depression
A website run by students for students offering information, resources and real student stories.
Website: http://www.studentsagainstdepression.org/

University of Exeter

Student Health Centre
Reed Mews
Streatham Drive
University Campus
Exeter
EX4 4QP
Tel: 01392 676606
Email: studenthealth@ex.ac.uk
Website: http://www.exeterstudenthealthcentre.co.uk

Wellbeing Services
The Wellbeing Services team is made up of counsellors and mental health practitioners who are able to offer confidential advice and therapeutic and practical support. Student Counselling is available free of charge to all students, full-time, part-time, undergraduate and postgraduate.

Reed Mews Wellbeing Centre
University of Exeter
Streatham Drive
Exeter
EX4 4QP

Tel: 01392 724381
Email: wellbeing@exeter.ac.uk
Website: http://www.exeter.ac.uk/wellbeing/
To book an appointment:
http://www.exeter.ac.uk/wellbeing/appointments/#d.en.223005

Voice
Exeter Voice is a confidential listening and information service run by students for students. It is confidential, anonymous and non-judgmental so you can contact them to discuss any problems you may be experiencing. It is available from 8pm-8am every night during term-time.

Internal number (free from halls): 724000
External number: 01392 724000
Email and online chat options also available. See website for details:
http://www.exetervoice.co.uk/

Samaritans Local Branch
Exeter, Mid and East Devon Branch
10 Richmond Road
Exeter
Devon
EX4 4JA
Tel: 01392 411711
Drop-in: 10.30am - 9.30pm Mon – Sat, 4.30pm – 9.30pm Sun