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Sexual health promotion and contraceptive services in local authorities

A systematic review of economic evaluations 2010-2015

Ginny Brunton, Christine Michaels-Igbokwe, Andreia Santos, Jenny Caird, Mariana Sipka, Noemia Teixeira-Filha, Helen Burchett, Gillian Stokes, James Thomas

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The authors of this report are:

G Brunton,[1] C Michaels-Igbokwe,[2] A Santos,[2] J Caird,[1] M Siapka,[2] N Teixeira-Filha,[3] H Burchett,[3] G Stokes, [1] J Thomas [1]

[1] EPPI-Centre, Social Science Research Unit, UCL Institute of Education, University College London
[2] Department of Global Health and Development, Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine
[3] PhD student, London School of Hygiene and Tropical Medicine

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Contents

Glossary

This is taken in part from the NICE (2014) NICE Guideline Development Manual online, https://www.nice.org.uk/article/pmg20/chapter/glossary

Anti-retroviral treatment (ART): a specific type of treatment for HIV.

Cost-benefit analysis (CBA): The costs and benefits are measured using the same monetary units (for example, pounds sterling) to see whether the benefits exceed the costs. A cost-benefit ratio of greater than 1 suggests that an intervention is worthwhile, while a ratio of less than 1 suggests that the costs outweigh the benefits.

Cost-consequences analysis (CCA): The costs (e.g. treatment and hospital care) and consequences (e.g. health outcomes) of an intervention, test or treatment are compared with those for a suitable alternative. Unlike cost–benefit analysis or cost-effectiveness analysis, it does not attempt to summarise outcomes in a single measure (such as the quality-adjusted life year) or in financial terms. Instead, outcomes are shown in their natural units (some of which may be monetary) and it is left to decision makers to determine whether, overall, the intervention is worth carrying out.

Cost-effectiveness analysis (CEA): The additional costs and benefits of a new intervention are compared with those of the current standard intervention over a time period which is deemed long enough to capture these differences, in similar units of outcome. These are compared in terms of 'cost per unit of effect'. In a cost-effectiveness analysis, the benefits are expressed in non-monetary terms related to health, such as symptom-free days, heart attacks avoided, deaths avoided or life years gained (that is, the number of years by which the intervention extends life). Cost-effectiveness analysis assesses the cost of achieving the same benefit by different means. Where an intervention is less costly and provides more positive units of effect compared to the next best alternative, it is considered more cost-effective.

Cost-savings/cost-minimisation analysis (CSA): Alternative interventions are determined to be equally effective and a comparison of costs is made to see which is cheaper.

Cost-utility analysis (CUA): When alternative interventions produce different levels of effect in terms of quantity and quality of life (or different effects), the effects may be expressed in utilities. Utilities are measures which comprise both length of life and subjective levels of well-being. The best known utility measure is the quality-adjusted life year, or QALY. Alternative interventions are compared in terms of cost per unit of utility gained (e.g. cost per QALY gained), with lower costs per QALY considered more cost-effective.

Disability-adjusted life year (DALY): A measurement of the gap between current health status and an ideal health situation where one lives to an advanced age, free from disease and disability.

Emergency contraception (EC): Oral 'morning after' pill or IUD usually administered subject to license up to five days after unprotected sex.

Health promotion: The art and science of helping people discover the synergies between their core passions and optimal health, enhancing their motivation to strive for optimal health, and supporting them in changing their lifestyle to move toward a state of optimal health. Optimal health is a dynamic balance of physical, emotional, social, spiritual and intellectual health. Lifestyle change can be facilitated through a combination of learning experiences that enhance awareness, increase motivation and build skills, together with, most importantly, through the creation of opportunities that open access to environments that make positive health practices the easiest choice (O'Donnell 2009).

Incremental cost-effectiveness ratio (ICER): A ratio of the cost of the intervention less the cost of the comparison divided by the outcomes of the intervention less the outcomes of the comparison. When comparing two interventions, the one with the lowest ICER will be most cost-effective.

Long-acting reversible contraceptive (LARC): Contraceptive methods with a long period of action which are not reliant on users, e.g. intrauterine devices and subdermal implants.

National Institute for Health and Care Excellence (NICE): a government-funded but operationally independent standards organisation which provides advice and guidance to improve health and social care in the UK.

Organisation for Economic Co-operation and Development (OECD): An established consortium of (currently) 34 democratic countries with market economies which work together to ensure economic growth, development and prosperity.

Quality-adjusted life year (QALY): A measure of burden of disease in which both the quantity of life expectancy and quality of life are taken into account. A year of perfect health is worth 1 and death is equivalent to 0.

Sensitivity analysis: In economic evaluations, a sensitivity analysis examines the differences that would result from varying any important assumptions in the model that would alter the results, both for better and worse. Sensitivity analyses may address methodological uncertainty, parameter uncertainty or uncertainty around the structure of the model used to combine costs and outcomes. Conducting a sensitivity analysis may involve adding or removing parameters (such as including or removing societal costs), changing the value of key parameters (such as the discount rate) or allowing parameters to vary over a specified distribution rather than utilising a point estimate. Threshold analysis may also be conducted whereby a willingness to pay for a unit of outcome is specified and the analyst is then able to determine how effective an intervention would have to be, or how low the associated cost would need to be, in order for the cost per unit of outcome to fall below the threshold.

Sexually transmitted infection (STI): Can include human immunodeficiency virus, syphilis, chlamydia, gonorrhoea, herpes and hepatitis C.

User-dependent contraceptive (UDC): Contraceptive methods that are self-administered by individuals, i.e. their efficacy is dependent on the users. They can include condoms and oral hormonal contraceptives.

Abstract

Background

Since 2013, health commissioners in England's local authorities have been responsible for sexual health services, including contraception, HIV testing, STI testing and treatment, health education and specialist sexual health services. Effective commissioning requires information to indicate which interventions may, or may not, be cost-effective. However, current UK guidance and recent research on the cost-effectiveness of sexual health services provides patchy and fragmented evidence. This study aims systematically to review the evidence available on the cost-effectiveness of OECD-based interventions relevant to UK local authority-commissioned sexual health services.

Methods

Key informants, bibliographic database searches and reference lists of guidance documents and included studies were searched for potentially relevant research. Guided by key stakeholders, we sought economic evaluations of sexual health interventions within the responsibility of local authorities, and focused in the UK, on contraception and on health promotion, published between 2010 and 2015 in English. Eligible studies were full economic evaluations based in an OECD country. Studies were classified using a specifically developed tool and assessed for methodological risk of bias using one of three design-specific assessment tools. Descriptive frequencies of codes were analysed to provide a 'map' of research that informed stakeholder discussions to focus the subsequent synthesis. The characteristics of studies, quality ratings and cost outcomes from each included study were extracted into tables and findings summarised narratively. Studies were assessed for their relative cost-saving or cost-effectiveness according to NICE guidance.

Results

In total, 17,705 references were screened; of these, 29 met our inclusion criteria and were included in the synthesis. Nine studies were undertaken in the UK; the remainder were US-based. Fifteen studies examined the economics of contraception and 14 evaluated health promotion. Overall, studies were of medium methodological quality.

In general, economic evaluations of contraception reported cost-effectiveness or cost-savings for ulipristal acetate (UPA) as emergency contraception, long-acting reversible contraceptives (LARCs) for regular, post-natal and post-abortion contraception, and targeting to high risk groups; none, however, reported costs per quality-adjusted life year (QALY) within NICE thresholds.

Economic evaluations of sexual health promotion interventions indicated more mixed results. Only three interventions were found to be cost-effective according to the NICE thresholds for HIV or sexually transmitted infection (STI) outcomes: nurse-led rapid testing and tailored counselling; condom negotiations skills training for female sex workers; and a teacher-led STI prevention and skills training intervention.

UK studies focused on health promotion and contraception, and supported the above findings. In general, there has been a reasonable amount of economic research into sexual health interventions since 2010, and these support current NICE sexual health guidance.

Conclusions

The broad nature of the research question posed in this systematic review resulted in the inclusion of a dataset very diverse in terms of populations, interventions, outcomes and types of economic evaluation designs. In considering the cost-effectiveness of these strategies in relation to their own commissioning climate, policy and decision makers should consider carefully the fit between their context and that of individual studies. Use of longer-term outcomes in trials used in economic evaluations would strengthen estimates of effects such as QALYs, as would the routine use of longitudinal cohort data.

How to read this report

This report has been designed so that key messages appear early in the document, condensed into an Executive Summary for quick reference. More detailed methodological information appears in the Appendices, including methods of searching (Appendix 1), discussion of the types of economic evaluation (Appendix 2), the flow of studies through the review (Appendix 3), quality assessment and data extraction tools (Appendix 5), and details of the studies, including quality assessment ratings (Appendices 6 and 7), characteristics of the included studies (Appendices 4, 8, 9 and 10), structured summaries (Appendix 11) and the costs and outcomes of each study (Appendices 12 to 14).

Readers are encouraged to reference the specific appendices while reading the report.

Executive summary

Background

Since 2013, health commissioners in England's local authorities have been responsible for putting in place a wide range of sexual health services, including contraception, HIV testing, sexually transmitted infection (STI) testing and treatment, health education and specialist sexual health services. Provision of these services must be negotiated alongside the wider commissioning of multiple statutory and non-statutory local authority services, including transport, planning, fire and public safety, housing, social services, libraries, waste management and trading standards.

In order to commission sexual health services, local authorities require information regarding the interventions that are clinically effective or effective compared to current practice. However, the perceived benefits of these interventions may be outweighed by the costs; alternatively, other services may achieve the same (or better) outcomes for less money. Data in relation to cost-effectiveness is therefore crucial for informing local authority commissioning decisions. However, current UK guidance and recent research on the cost-effectiveness of sexual health services provides patchy and fragmented evidence. A systematic review was undertaken to bring together this research. The aims of the review were to answer the following research questions:

> What evidence is available on cost-effectiveness for local authority commissioned sexual health services concerning studies of health promotion and in relation to studies of contraception, and what is the evidence specific to the UK?

Methods

Guidance from key stakeholders was sought in order to focus on relevant topics for synthesis. Stakeholders formed an Advisory Group of sexual health policy makers, charity representatives, academics and local commissioners.

Studies published between 2010 and 2015 were sought through key informants, bibliographic database searches, and reference lists of guidance documents and included studies. Located references were screened on the basis of title and abstract, and the full-text reports and papers of potentially relevant references were retrieved and assessed. To be included in the review, studies had to: be published during or after 2010, in English; evaluate sexual health interventions within local authority responsibility; present economic or cost data; be a full economic evaluation; and be conducted in an OECD country. At full report screening, potentially relevant studies also had to be focused on either contraception or health promotion activities. UK studies were also grouped separately for analysis.

Studies were coded for characteristics of interest, using a data extraction tool developed and tested by the research team. Codes included: publication year; targeted population, health issue, behaviour; type of economic evaluation; intervention characteristics and outcomes measured. Included economic evaluations could be derived from trials, systematic reviews of effectiveness or mathematical modelling; for this reason, three types of risk of bias assessment tools were used. These were the NICE intervention study checklist

(NICE 2012), the AMSTAR tool for systematic reviews (Shea et al. 2009), and a combined health and economic evaluation checklist developed from three tools currently in common use (Evers et al. 2005; NICE 2012; Phillips et al. 2004).

Descriptive frequencies of codes extracted from studies were calculated and findings narratively summarised across all sexual health services offered by local authorities, providing a 'map' of literature relevant to the review question. The findings from this map informed the identification and synthesis of a more focused set of studies, grouped first by their specific focus (UK-based, contraception or health promotion). Where possible, studies within each of these were grouped according to the type of economic evaluation in order to make comparisons of cost outcomes as similar as possible. Cost outcomes for each group of studies were then compared and contrasted in terms of their populations, interventions, health outcomes, costs and magnitudes. Studies were also assessed for their relative cost-saving or cost-effectiveness according to NICE guidance (2012): below GBP £20,000; £20,000 to £30,000; and above £30,000. All costs were converted to GBP using the relevant exchange rate for the year in which they were originally reported. The findings are presented narratively and in tabular format.

To assure review quality, several steps were taken, including: developing searches in conjunction with an information scientist using free text and thesaurus terms; manual screening on title and abstract and then full reports with two reviewers until good agreement was reached, then single screening; assessing for risk of bias and conducting synthesis with at least two researchers; and use of EPPI-Reviewer© specialist software (Thomas et al. 2010) to manage data, allow rating comparisons and structure the synthesis.

Results and discussion

A total of 17,705 potentially relevant references were located; of these, 108 titles and abstracts met our inclusion criteria and were retrieved and assessed on the basis of their full report. Descriptive 'map' findings from a subset of 86 available at the time were presented to the Advisory Group, where the decision was made to focus on UK studies meeting the initial criteria, plus studies of contraception and health promotion (from any OECD country). Reports describing 29 studies meeting these additional criteria were available for analysis. Twenty of these were US-based and nine were UK-based. A total of 15 studies focused on contraception and 14 on health promotion interventions, with some overlap between all three groups.

Contraception studies

Findings from 15 contraception studies indicated a wide range of interventions considered to be cost-effective, although few met NICE thresholds. Studies suggested that:

- oral ulipristal acetate (UPA) is more cost-effective than oral levonorgestrel (LNG) as a method of emergency contraception.
- advance and on-demand emergency contraception offered in clinics or community pharmacies are cost-saving compared to no access, for both high- and low-use groups.
- long-acting reversible contraceptives (LARCs) could be more cost-effective to use than user-dependent contraceptive methods in terms of the pregnancies they would avert and the resultant costs potentially borne by health and social services.

- provision of LARC methods post-natally or post-abortion could generate cost savings, particularly beyond one year, though it should be noted that this is based on US studies undertaken in a different healthcare system and focusing on a specific population of Latina immigrant women. It is open to debate whether they would be appropriate in a UK context.
- expanded contraceptive provision targeted to low- and high-risk groups such as sexually active teens, adolescent mothers and new immigrants could result in cost savings resulting from services not needing to provide health and social care for unintended pregnancy, maternal benefits and early childhood care.

Of the studies that reported cost per QALY gained as an outcome, none showed a cost of less than £20,000 per QALY gained, a nationally recognised threshold for cost-effectiveness.

Health promotion studies

Health promotion studies which evaluated HIV prevention interventions indicated that many different interventions were cost-effective or cost-saving. For example:

- studies found that condom distribution or condom negotiation skills programmes were cost-effective or cost-saving in comparison to standard care or no intervention respectively.
- clinical provider assessment and counselling was more cost-effective than provision by peer or mixed peer and clinical providers.
- nurse-led rapid HIV testing and tailored counselling was more cost-effective than routine screening and counselling, and on-site rapid testing and tailored counselling dominated (i.e. was less costly and more effective) off-site testing and referral or on-site testing and information only.
- four educational sessions to reduce onward HIV infections was suggested to be cost-saving in relation to well-woman examinations for intravenous drug users.
- offering housing rental assistance to unstably housed HIV-infected persons as part of locally provided sexual health services was described as cost-effective in comparison to no provision. Multiple HIV prevention strategies evaluated in order to determine the 'optimum package' of interventions reported cost-savings for 10 different interventions over current HIV testing and counselling provision or no service provision.

However, of these interventions reported to be cost-effective, only two nurse-led rapid HIV testing and tailored counselling (£6,876-£23,472 per QALY gained) and condom negotiations skills training for female sex workers (£121-£713 per QALY) were shown to be cost-effective within NICE thresholds.

Health promotion studies evaluating the cost-effectiveness of STI prevention presented more mixed findings. Some evaluations suggested clear cost-effectiveness:

- an analysis of school-based condom distribution compared to a standard school nurse intervention was suggested to be cost-effective for STI prevention.
- a cost-benefit analysis of mass media STI prevention messaging targeted to unmarried male adults was deemed to be cost-saving.

However, other findings were mixed:

- while a teacher-led STI prevention and skills training for school-age youth was found to be cost-effective in comparison to standard sex and relationships education (and cost-effective by NICE standards – £18,041 per QALY gained), the peer-led STI prevention and skills training in the same study was not found to be cost-effective compared to the teacher-led intervention (£72,062 per QALY gained).
- an STI screening uptake campaign led by sexual health advisers targeted to football club members was found to have similar costs and outcomes to a poster-only campaign; the same campaign led by football captains was found to be more costly and less effective in terms of testing uptake.

Other findings suggested differential cost-effectiveness:

- for hepatitis C and gonorrhoea outcomes, well-woman examinations provided to women using intravenous drugs in addition to standard drug treatment were found to be cost-effective compared to a standard intervention; however, a four-education session added to standard drug treatment was found to be more cost-effective for chlamydia outcomes than the standard intervention alone.

Other economic evaluations found that interventions were not cost-effective, including brief risk reduction counselling that included sexual risk behaviour amongst adults presenting at substance abuse clinics.

UK-based studies

The nine UK-based studies of largely high and medium methodological quality contributed to the syntheses of contraception and health promotion studies, indicating that there has been a reasonable amount of research into the economics of sexual health services in the UK since 2010. Findings from these suggested that:

- interventions to promote STI screening indicated that point-of-care tests, and interventions offered to high-risk groups in more accessible locations such as clinics, pharmacy, by phone, or at schools, could potentially be more cost-effective than their relevant alternatives.
- interventions that targeted annual HIV testing to high-risk adults were found to be cost-effective by NICE standards, with (£17,500 per QALY gained) and without anti-retroviral treatment (ART) (£26,800 per QALY gained).
- UPA could be more cost-effective than LARCs for emergency hormonal contraception.
- LARC methods could be more cost-effective to use than user-dependent contraceptive methods in terms of the pregnancies they would avert and the resultant costs potentially borne by health and social services.
- school contraceptive services such as condom distribution, hormonal contraceptive provision and advance contraceptive provision could be cost-effective.

Limitations

Several limitations to the set of studies included in this review should be considered. Sexual health services encompass a broad range of potential interventions, provided to diverse populations in mixed settings. The effectiveness of such interventions is often evaluated by measuring different outcomes, also often using comparison conditions that differ across studies. For these reasons, it proved difficult to synthesise results across studies other than by narrative comparison. The methodological quality of included studies was varied, with studies evenly split between low, medium and high methodological quality, suggesting that some caution is needed in interpreting the findings. In addition, the inclusion of a majority of US-based studies raises questions about the applicability of cost-effectiveness judgements to the UK context, given the differences in healthcare system funding, access, reimbursement and impact on health inequalities. Different categorisations of some LARCs were noted, and some studies of cost consequences may have gone beyond their ability to claim cost-effectiveness.

This review sought to answer a broad research question. While it provided a considerable range of information on different interventions and different ways in which they were cost-effective (or not), the small number of studies across contraception, health promotion and UK-based areas meant that limited depth of information on cost-effectiveness was available. The assessment of multiple types of studies necessitated the use of several different types of risk of bias tools, and the wide range of cost-outcome types also necessitated the development of a cost-outcome findings table, showing all results within a range of cost-effectiveness (please see Appendices 12 to 14 for more detail).

Conclusions and recommendations

The findings from this systematic review suggest that a large amount of research on the cost-effectiveness of sexual health services has been undertaken in the past five years, and that, while the study findings do not always measure costs per QALY or achieve NICE thresholds for cost-effectiveness, this evidence base generally suggests the cost-effectiveness of interventions that meet current NICE guidance, particularly for sexual health services aimed towards young people and those at high risk. However, some interventions may be equivocal in terms of their cost-effectiveness, and others show cost-effectiveness for some STIs but not others. The methodological quality of the included studies also warrants caution in interpretation of the findings, and the disparity of interventions, outcomes and study designs suggests that policy and decision makers should consider carefully the fit between their context and the population that they wish to reach, and those of individual studies.

The differences in methods between economic evaluations make drawing comparisons across such studies difficult. Future economic evaluations of sexual health interventions which are based on internal trials could be strengthened by designing for longer-term outcomes that would allow for more robust modelling. In addition, use of large cohort study datasets measuring such long-term outcomes should be routinely used to strengthen model estimates.

1 Background

1.1 Rationale for the review

As of April 2013, following the government's public health reforms, England's local authorities assumed responsibilities for commissioning comprehensive sexual health services (Heath 2014; Hind 2013). These include:

- contraception;
- chlamydia testing as part of the National Chlamydia Screening Programme;
- HIV testing;
- STI testing and treatment;
- sexual health aspects of psychosexual counselling;
- sexual health specialist services such as young people's sexual health and teenage pregnancy services, outreach, HIV prevention and sexual health promotion work, and services in schools, colleges and pharmacies.

In order to commission sexual health services, local authorities require information regarding the interventions that are effective. The perceived benefits of these interventions may be outweighed by their costs; alternatively, other services may achieve the same (or better) outcomes for less money. Data in relation to cost-effectiveness are therefore critical in informing local authority commissioning decisions, in order to ensure value for money and a return on investment for any public health interventions undertaken (Local Government Association 2013). Current National Institute of Health and Care Excellence (NICE) guidance suggests that cost-effectiveness ratios of less than £20,000 per Quality-adjusted Life Year (QALY) may be considered cost-effective and good value (NICE 2013a,b).

Cost-utility analysis is of broad applicability in public health decision making because, as in cost-effectiveness analysis, it can explore single or multiple outcomes. However, cost-utility analysis adds in a notion of value (utilities, measured as QALYs or disability-adjusted life years – DALYs). These utilities can be assessed for a range of interventions and facilitate comparisons between different health interventions using a common metric. However, some limitations for these metrics should be considered, such as their lack of compensation for socio-economic and demographic differences.

Current UK guidance and recent research on the cost-effectiveness of sexual health services provides somewhat patchy evidence. In terms of recent research activity, a brief review on the economics of sexual health produced by the UK Department of Health to aid commissioning and planning for sexual health services was originally published in 2005 (Payne and O'Brien 2005). This provided a useful, succinct summary of the relative cost-effectiveness of sexual health services in the areas of health promotion, screening, treatment, fertility control and service delivery and organisation. While this report was compiled using evidence from a relatively limited number of sources and is in need of update, it did provide a basis for examining local authority sexual health provision.

Currently there are five existing UK guidelines concerning sexual health, focused on specific high-risk groups. Most of these guidelines provide very limited data in relation to the cost implications of sexual health services (NICE 2007, 2011a,b, 2014a,b). The cost-implications of these sexual health services are summarised below.

NICE public health guidance 3: prevention of sexually transmitted infections (STI) and under-18 conceptions

In 2007, NICE published guidance examining the effectiveness of interventions for the prevention of STI and conceptions in those aged less than 18 years. The authors concluded that most brief STI counselling interventions were cost-effective when compared with 'usual treatment', but since no costs were attributed to 'usual treatment', the incremental cost of adding a new programme on to existing programming would be overestimated. This would result in a higher estimate of cost per outcome compared to an analysis that did consider the cost of usual care or existing programming (NICE 2007).

NICE public health guidance on increasing the uptake of HIV testing

Two NICE guidelines examining the uptake of HIV testing were published in 2011. Both guidelines concluded that finding, testing and treating people with HIV before they became symptomatic was likely to reduce onward transmission and be cost-effective (NICE 2011a, NICE 2011b).

In NICE public health guideline 33 on increasing the uptake of HIV testing among black Africans in England, no studies were available to be included in a review of cost-effectiveness. An economic model was constructed incorporating data from reviews of effectiveness and data on infectivity and the impact of treatment on life expectancy and disease progression (NICE 2011a).

In NICE public health guideline 34 on increasing the uptake of HIV testing among men who have sex with men, one US study evaluating a peer education and testing recruitment programme was included in a review of cost-effectiveness. Again, an economic model was constructed incorporating data from reviews of effectiveness and data on infectivity and the impact of treatment on life expectancy and disease progression (NICE 2011b).

NICE guidance costing report: contraceptive services with a focus on young people up to the age of 25.

This costing report, produced in conjunction with key clinicians and commissioners and reviewed by clinical, public health and financial professionals, examined the potential resource impact of implementing NICE's guidance, *Contraceptive services focusing on young people up to the age of 25* in England (NICE 2014a). A local costing template was produced alongside the costing report to help users calculate the local cost impact of implementing the guidance. The authors anticipated savings due to a reduction in costs associated with unintended pregnancy and birth in young people and subsequent socio-economic deprivation, mental health difficulties and lower levels of educational attainment. Savings were also estimated in relation to reduced costs for abortion and the treatment of STI (NICE 2014a).

NICE guidance: Long-acting reversible contraception

NICE guidance on long-acting reversible contraception (LARC) suggests that: all currently available LARC methods (intrauterine devices, the intrauterine system, injectable contraceptives and implants) are more cost-effective than the combined oral contraceptive pill; intrauterine devices, the intrauterine system and implants are more cost-effective than injectable contraceptives; and increasing the uptake of LARC methods will reduce costs associated with unintended pregnancies (NICE 2014b).

The findings from current national guidance and recent systematic reviews provide a somewhat limited and potentially out-of-date picture of the cost-effectiveness of sexual health services in relation to local authority needs, focusing on specific interventions and/or particular populations.

1.2 Aims and research question

This review was undertaken in order to provide local authorities with current, rigorously assessed research evidence on the cost-effectiveness of sexual health interventions. The objective of the review was to classify sexual health interventions according to their relative cost-saving or cost-effectiveness as defined by current NICE public health guidelines (NICE 2013a, NICE 2013b). The following research question was developed following consultation with the funders and our Advisory Group:

> What evidence is available from OECD economic evaluations published in the last five years in relation to those sexual health services for which local authorities are responsible?

Studies identified through searching constituted a 'map' of research, which provided information on the breadth of economic evaluations undertaken in local authority sexual health service provision. Further consultation with funders and our advisory group while presenting these findings resulted in a second question, which drove more in-depth analysis:

> From the relevant identified studies, what evidence is available on cost-effectiveness for local authority commissioned sexual health services concerning studies of health promotion and in relation to studies of contraception, and what is the evidence specific to the UK?

2 Methods

2.1 Stakeholder consultation

It is beneficial to involve those who will ultimately be affected by the findings of a study, for several reasons. Stakeholders provide: expertise on an issue; perspectives on relevant areas in which to focus the work; suggestions for presenting findings in an accessible way; and the potential to communicate research findings to their networks (Rees and Oliver 2012).

Consultation with the Department of Health's Sexual Health Policy team and key commissioning stakeholders in November 2014 resulted in a preliminary research synthesis comprising a systematic review of systematic reviews. This was presented to an Advisory Group comprised of specialist academics, commissioners, sexual health charity members and the funder in April 2015. The Advisory Group members' role in the project was to identify potentially relevant research, to provide feedback on the scope of the review, and to comment upon the draft report. Members of sexual health charities were sought in order to represent, to some extent, the views of service users.

The findings from the analysis of data extractions were presented and group members were asked to provide their thoughts on how to usefully focus the research. They noted that, while this informed their thinking on the scope of research available, it did not provide clear answers for local commissioning. A request was made subsequently by the Advisory Group for the research team to conduct a similar preliminary research synthesis 'map' on primary economic evaluations in sexual health. The Advisory Group met once again with researchers in July 2015, to consider the findings from this preliminary map and to agree upon the focus of the review for the in-depth synthesis presented here.

2.2 Searching for studies

Potentially relevant citations were located through three sources: key informants, bibliographic database searches and reference lists of included studies. Advisory Group members were asked for any relevant reviews of cost-effectiveness. Economic evaluations from all NICE guidelines relevant to sexual health services were identified for screening assessment. Bibliographic database sources of economic and sexual health literature were searched, including EconLIT, NHS Economic Evaluations Database (NHS EED), POPLINE (reproductive health literature database) and PubMed.

Database searches were limited to citations published between 2010 and 2015. Search strings based on a combination of free-text and database-specific terms were developed in collaboration with our information scientist. The concepts to be combined included: (sexual health terms) AND (cost terms). An example showing the PubMed search string is provided in Appendix 1. The located citations were uploaded into EPPI-Reviewer software, for management of retrieval, coding and synthesis (Thomas et al. 2010). Reference lists of all included studies were searched for potentially relevant research.

2.3 Inclusion/exclusion screening

All located citations were assessed first for eligibility on the basis of their titles and abstracts. After consultation with our Advisory Group to determine the scope of the in-depth analysis, the full text of those citations meeting the inclusion criteria were retrieved and assessed again for inclusion. At the title and abstract stage of screening, in order to be included for further analysis, studies had to:

- be published during or after 2010
- be published in the English language
- evaluate sexual health interventions for which local authorities are responsible
- present economic or cost data
- be a full economic evaluation (i.e. cost-effectiveness, cost-benefit, cost-utility, cost-minimisation or cost-consequence studies).
- be conducted in an OECD country.

Studies published since 2010 were sought in order to reflect current local authority sexual health service provision. Only English language studies were included because the time and resources available did not permit the translation of foreign language material. However, relevant international references were grouped for later translation and could be used where resources and need permit.

Studies which examine cost-effectiveness, cost-utility, cost-benefit, cost-saving and cost-consequence are considered 'full economic evaluations' (Shemilt et al. 2008). Each of these types is defined in the Glossary. Full economic evaluations compare both the outcomes and costs of an intervention against the outcomes and costs of an alternative condition, which may be either standard care, the next best alternative, or a 'do nothing' scenario. Full economic evaluations were selected for inclusion because they are considered more robust than burden of cost or cost of illness studies, which do not have a comparator (Drummond 2015; Shemilt et al. 2008).

Finally, only primary studies from OECD countries were sought in order to limit the scope of the review, promote relevance for policy makers and avoid the difficulties of comparing economic data across different health service commissioning contexts.

Citations were coded on the basis of their titles and abstracts according to the data extraction methods described below. These findings were presented to the Advisory Group in July 2015, and the group recommended that further synthesis should focus on specific areas of sexual health service delivery. For this reason, full-text reports were retrieved and screened according to the above criteria and also according to whether they were:

- UK-based
- or about contraception
- or focused on health promotion activities.

2.4 Data extraction/coding

Studies were coded according to characteristics of interest, including:

- year of publication
- targeted population
- targeted health issue or condition
- targeted behaviour
- type of economic evaluation
- intervention characteristics
- outcomes measured

To code the studies, data on the above characteristics were extracted from each study, using a tool developed and tested by the research team.

2.5 Risk of bias assessments

Two types of risk of bias/methodological quality assessment were undertaken in this review. Full economic evaluations can be conducted based on a trial of effectiveness (internal economic evaluation), or based on findings from a review of effectiveness (external economic evaluation). Such economic evaluations will provide an estimate of *actual* costs and outcomes. Full economic evaluations can also be developed as a hypothetical model of costs and outcomes within a given context; in this case, the model will draw on multiple sources of effectiveness evidence to justify the parameters used. These can include prevalence studies or findings from several effectiveness studies. These economic evaluations provide an estimate of *potential* costs and outcomes, given a similar context.

Because these two types of full economic evaluation contain different sources of effectiveness evidence, we utilised different risk of bias/methodological quality assessment tools to consider the studies. Where internal economic evaluations were undertaken, a previously tested risk of bias tool was used (NICE 2012). If effectiveness evidence arose from systematic reviews, AMSTAR criteria were used to assess review quality (Shea et al. 2009). In addition, where an economic evaluation was built on modelled costs and outcomes, a tool combining relevant criteria from recognised risk of bias and methodological quality assessment tools for economic evaluations was developed by three health economists, tested for face validity and applied (Evers et al. 2005, NICE 2012, Phillips et al. 2004).

2.6 Synthesis

Citations determined to be potentially relevant to the review question were coded based on their title, abstract and citation information, using codes developed from the data extraction items described above. Descriptive frequencies of these codes were calculated and findings narratively summarised, providing a 'map' of literature relevant to the review question. The findings from this map informed the identification and synthesis of a more focused set of studies. These were grouped first by their specific focus (UK-based; contraception; health promotion). Within each group, studies were organised first by whether they were based on an 'internal' or 'external' trial or whether they were derived from a model. Where the number of studies allowed, each of these were then grouped by the type of full economic evaluation (i.e. CBA, CUA, CEA, cost saving) in order to make

comparison of cost outcomes as similar as possible. Costs were converted according to the following rates listed in Table 2.1.

Table 2.1: Cost-conversion rates

Year	USD to GBP	Euro to GBP
2002	0.658	-
2003	0.659	-
2004	0.655	-
2005	0.649	-
2006	0.648	-
2007	0.645	-
2008	0.653	-
2009	0.663	-
2010	0.675	-
2011	0.677	-
2012	0.675	0.74
2013	0.679	-

Source: http://eppi.ioe.ac.uk/costconversion/default.aspx (accessed 8 March 2016).

Costs and outcomes for each group of studies were then compared and contrasted in terms of their populations, interventions, health outcomes, costs and cost-effectiveness. Studies were also arranged according to their relative cost-saving or cost-effectiveness (NICE 2013a,b):

- Below GBP £20,000 per QALY gained (cost-effective)
- £20,000 - £30,000 per QALY gained (potentially cost-effective)
- Above £30,000 per QALY gained (not cost-effective).

2.7 Quality assurance

Several steps were taken to assure the review's quality. Searches were developed in consultation with our information scientist, using a combination of free-text and thesaurus terms to ensure sensitivity of searching. At each stage of screening (i.e. title/abstract stage and full report stage), risk of bias/methodological quality assessment and data extraction and synthesis were initially undertaken by at least two researchers with expertise in either health research methods or health economics. Once inter-rater reliability for screening was established (kappa=0.9), individual screening was subsequently undertaken. All references were manually screened. Two researchers independently assessed risk of bias/

methodological quality and extracted data from all studies, meeting to compare and agree ratings. For each stage of the review, EPPI-Reviewer specialist systematic review software was used to manage data, allow rating comparisons and structure the synthesis (Thomas et al. 2010).

2.8 Presentation of findings

The findings were synthesised narratively and also presented in tabular format; these are presented in the Appendices at the end of this report. In addition, consultations with Advisory Group commissioners suggested that the development of structured summaries for each included study would help readers to interpret and generalise the study descriptions and results to their own context.

3 Results

3.1 Flow of studies through the review

In total, 17,705 potentially relevant references were identified on the basis of title and abstract. Of these, 108 were retrieved and assessed for inclusion again based on the full report. A subset of 86 of these available for analysis were included in a descriptive map of research, which is described in further detail below. After consultation with our Advisory Group, further screening according to revised criteria, and removal of linked and duplicate studies, a total of 29 studies were included for further analysis. The reasons for exclusion at each stage of the inclusion screening process is documented in Appendix 3.

3.2 Map of studies

Findings from 86 available reports meeting our inclusion criteria were descriptively analysed by country, topic, setting, population, intervention focus, targeted behaviour and type of economic evaluation. The map was intended to serve as a method of illustrating the breadth of research available in order to facilitate discussion and decision making by the Advisory Group and research team as to which areas would be most appropriate for in-depth analysis. Tables and charts illustrating these characteristics of included studies are provided in Appendix 4.

The majority of reports included in the map described economic evaluations which took place in the US (n=56). A total of nine UK economic evaluations were located, the next highest number by country, followed by Australia (n=4), Canada (n=2), and one each for France, Italy, the Netherlands, Mexico and Portugal. Ten reports did not specify the country of origin.

Sexual health topics under study varied considerably, and many reports examined multiple topics. HIV was studied most often (n=45), followed by contraception (n=23) and STIs (n=18). Related to these were the relevant interventions which were evaluated. These included: screening (n=39), sexual health promotion (n=16), contraception (n=15), treatment (n=14) service delivery and organisation (n=8) and other (n=3).

The reports did not describe well the settings in which interventions took place: only 33 of the 86 reports provided this information. Sexual health or genitourinary medicine (GUM) clinics were the setting in the largest group of studies (n=13), followed by clinic settings of unspecified type and family planning clinics (n=3 each).

There was considerable variation in the populations studied by the economic evaluations. These included women (n=21) most often, followed by men who have sex with men (n=14), and then studies with the general population (n=11). A total of 24 reports did not describe the populations under study.

Targeted behaviour most often focused on service provision (n=63), followed by uptake of screening (n=15) and unspecified behaviour (n=10).

Finally, studies were mapped according to the type of economic evaluation design employed. A total of 48 reports described cost-effectiveness design, followed by 31 reports

estimating cost-utility. Cost-benefit designs were used in seven reports and two reported using cost-minimisation designs.

3.3 Stakeholder consultation on map and in-depth topics

The descriptive map findings above were presented to Advisory Group members in July 2015. Various combinations of topics, setting, populations and designs were discussed, as was the overlap of the current review with other work taking place on pre-exposure prophylaxis for HIV, and on hepatitis, and wider screening functions shared with national screening programmes. Advisory Group members considered that it was important to focus the review in three ways, in order to provide the most relevant information for local authority decision making. They advised a focus on UK economic evaluations, and economic evaluations of contraception and of health promotion.

The reports included in the map were re-screened according to these topics and, once linked studies and duplicates were identified, a final set of 29 studies was included in further analysis. Of the modelling studies, the majority utilised decision-analytic or Markov modelling (n=7), followed by cost-effectiveness modelling (n=4). Two studies each utilised Bernoulli, compartmental or state transition modelling. The remainder described cost-utility (n=1), cost-benefit (n=1), cost-consequence (n=1), progression (n=1), cost-sequence analysis (n=1) and general modelling (n=3). Eight models were based on internal randomised controlled trials; five models were based on observational studies. The studies are described by topic below: UK-based, contraception and health promotion.

3.4 UK-based economic evaluations

A total of nine UK-based economic evaluations published since 2010 were located (Cooper et al. 2012; Crawford et al. 2015; Jackson et al. 2015; Long et al. 2014; National Collaborating Centre (NCC) 2013; Pilgrim et al. 2010; Roberts et al. 2012; Thomas and Cameron 2013; Turner et al. 2014). Of these, four were cost-effectiveness analyses (Cooper et al. 2012; NCC 2013; Pilgrim et al. 2010; Thomas and Cameron 2013). Two were cost-consequence analyses (Jackson et al. 2015; Roberts et al. 2012). Long et al. (2014) and Crawford et al. (2015) undertook cost-utility analyses and Turner et al. (2014) conducted both cost-effectiveness and cost-utility analyses. These studies focused on STI screening and treatment, contraception and health promotion interventions. They are summarised below, with their main findings. Full details of these studies are provided in the Evidence Tables in Appendix 8, and relative costs and outcomes are shown in the Costs and Outcomes Tables in Appendix 12.

3.4.1 STI screening

Four of the nine included studies undertaken in the UK examined the costs and outcomes of STI screening (Long et al. 2014; Jackson et al. 2015; Roberts et al. 2012; Turner et al. 2014). Two of these focused on methods of testing and treatment (Long et al. 2014; Turner et al. 2014); the other two examined specific health promotion interventions (Jackson et al. 2015; Roberts et al. 2012).

The findings from two studies undertaking cost-utility analyses suggested that, compared to standard care, annual HIV testing and treatment targeted to high risk groups and point-of-care testing for chlamydia and gonorrhoea provided to GUM clinic patients met NICE threshold criteria for cost-effectiveness. No cost benefit analyses were conducted. In order to test potential expanded HIV testing in the UK, **Long et al. (2014)** modelled different HIV

epidemic scenarios based on different interventions in a hypothetical UK population aged 15 to 64 years, categorised by country of origin and risk states (men who sleep with men - MSM, injecting drug users - IDU, men and women from HIV-endemic countries with high disease prevalence) and further subdivided by HIV infection and diagnosis status, ART status and male circumcision status. The interventions under study were: universal HIV testing, targeted HIV testing and expanded ART, each compared to current HIV testing and treatment levels. The findings indicated that annual HIV testing of all adults could avert 5% of new infections, even with no behaviour change after diagnosis, due to the earlier initiation of ART treatment. However, this could rise to 18% if risky behaviour were reduced by half. The authors reported that this strategy cost £67,000-106,000 per QALY gained (2012 GBP), not cost-effective according to the NICE threshold for cost-effectiveness (NICE 2013a,b). However, annual testing targeted to high-risk groups compared to universal one-time testing resulted in averting 4–5% of new infections, with a cost outcome of £17,500 per QALY gained. Targeted annual testing with ART treatment compared to universal one-time testing resulted in 145,000 QALYs added to the population over ten years, with a cost outcome of £17,500 per QALY gained. This falls below the £20,000 per QALY gained NICE threshold for cost-effectiveness.

The study rated as 'medium' in terms of its methodological quality. It was one of the first to combine epidemiological, behaviour and CD4 bands into a complex HIV disease progress assessment for a cost-effectiveness analysis of HIV screening in the UK, using different sources of data. Although some limitations can be identified, the presented results are robust and informative for policies on interventions for HIV. The reviewers (i.e. the research team undertaking this review) noted that in addition to the limitations identified by the authors, HIV treatment was not explicitly modelled; instead, upon diagnosis it was assumed that individuals were estimated to have a longer life expectancy that was (implicitly) due to ART, and that the assumed reductions in HIV infectiousness were due to reductions in viral load due to ART. Additional attempts can be made to better explore the implications of early HIV screening and treatment to better understand the impact of the costs of ART in the long term for the control of HIV transmission. The reviewers also suggested that, rather than the 3% used for both costs and outcomes, a 3% discount rate could be applied for costs and 1.5% for health effects in line with NICE recommendations for treatment effects that are substantial in restoring health and are sustained over a very long period (at least 30 years). Using a lower discount rate to value QALYS gained in the future will result in more QALYs gained and is therefore likely to result in a more favourable cost-effectiveness ratio.

Turner et al. (2014) estimated the costs and consequences of providing a point of care (POC) chlamydia and gonorrhoea test to a hypothetical sample of 1.2 million GUM clinic patients, compared to the standard practice of off-site testing. The model estimated that 189 cases of pelvic inflammatory disease (PID) would be prevented per year, with 17,561 onward transmissions prevented per year, saving £11.7 million (2012 GBP) and adding 46 QALYs compared with the standard off-site testing. The authors suggested that this was a cost-saving intervention. This study was determined to be of high methodological quality by the reviewers, however limitations were noted associated with the availability of quality data to model the implications of POC nucleic acid amplification test (NAAT) testing on STIs.

Two studies utilised other methods to evaluate costs and outcomes. **Roberts et al. (2012)** aimed to examine the costs and consequences of accelerated partner therapy (APT) offered by telephone or in community pharmacies, compared to routine patient referral partner notification for sex partners of people with chlamydia, gonorrhoea or non-gonococcal urethritis. Accelerated partner therapy is a form of partner notification in which identification and treatment of potentially affected partners is expedited more by professionals. The authors suggested that both interventions were more cost-effective than the control condition, but because this was a cost-comparison analysis, neither intervention was better than the other. In comparison to routine patient referral partner notification, which cost £46 per partner treated (2008 GBP) and identified 11% of partners, the phone APT intervention identified 35% more partners for treatment, and cost £54 per partner treated. The community pharmacy APT intervention identified 34% of partners for treatment at a cost of £53 per partner treated. This study rated medium on methods for its economic evaluation. The main limitations are associated with the fact that, as an exploratory analysis, emphasis should have been given to the assessment of key parameters used in the model to better understand sources of uncertainties.

Jackson et al. (2015) aimed to compare the costs and outcomes of two STI screening interventions targeting men aged 18 years and older in six England football clubs, by undertaking a randomised controlled trial (RCT) in which cost data were also collected. Two interventions were evaluated. A STI screening health promotion campaign led by team captains and one led by sexual health advisers were each compared with a poster-only campaign control condition. The results indicated that all three interventions cost similar amounts, but the sexual health-adviser-led intervention was most cost-effective in terms of screening uptake, as it led to 67% screening at a cost of £88.33 per person screened (2012-2013 GBP), compared to the poster-only campaign, which cost £81.87 but resulted in only 61% screening uptake. The team captain-led intervention was least cost-effective, resulting in 50% screening uptake at a cost of £88.89 per person. The economic evaluation conducted alongside the trial also aimed to assess the cost per case of gonorrhoea and chlamydia detected; however, no cases were identified as part of the trial. The trial was judged to be of medium methodological quality, with many uncertainties around the parameters used in the analysis. It was unclear whether costs were annuitised, and the time horizon was unclear. Seemingly, the analysis was undertaken for a time horizon of one year and the costs with posters were considered for three years. If this was the case, the costs may be slightly underestimated.

In summary, UK-based HIV/STI economic evaluations suggested that the following strategies could potentially be cost-effective: (1) targeted annual HIV testing and ART to high risk groups (compared to universal testing and no treatment); (2) point-of-care chlamydia and gonorrhoea testing to people presenting at GUM clinics (compared to off-site testing); and (3) accelerated partner therapy either by phone or through community pharmacy notification (compared to routine referral); and (4) sexual health adviser-led screening promotion (compared to poster-only screening promotion). Two strategies were found to not be cost-effective. Universal HIV testing of whole populations was estimated to cost more than accepted NICE thresholds for cost-effectiveness; and football team captain-led STI screening uptake promotion was found to be more costly and less effective than sexual health adviser-led or poster-only alternatives. Only targeted annual testing (Long et al. 2014) and point of care testing (Turner et al. 2014) were found to fall below NICE thresholds for cost-effectiveness. Methodological quality of this set of studies varied from

low to high, limiting somewhat the confidence readers can place in the findings. All STI screening studies are summarised in Appendix 11.

3.4.2 Contraception

Three of the UK economic evaluations that were included examined contraception. One focused on methods of emergency contraception, one on long-acting reversible contraceptives (LARCs), and one on promoting uptake of contraceptive services among disadvantaged youth.

Thomas and Cameron (2013) modelled the cost-effectiveness of ulipristal acetate (UPA) versus levonorgestrel (LNG) as emergency hormonal contraception (EC) among women in England presenting for contraception within 24 to 72 hours of unprotected intercourse. The authors estimated that 'almost one-quarter' of pregnancies in England were unintended, and UPA was shown to cost between £194 and £1,453 less per avoided pregnancy than LNG (2011 GBP), depending on whether social care costs were included or not. This led the authors to conclude that it was a cost-saving intervention. The methodological quality of this economic modelling study was rated as low due to limitations in: outcome measurement, model cycle, baseline estimates of health effect and resource use, sensitivity analyses, model calibration and unclear reporting of the time horizon and adverse events.

The **National Collaborating Centre for Women and Children's Health (NCC-WCH) (2013)** aimed to evaluate the cost-effectiveness of LARCs (IUD, IUS, injectable or implant) compared with user-dependent methods (combined oral contraceptives (COC), the male condom), and non-reversible contraceptive methods (i.e. male and female sterilisation). The number of unintended pregnancies averted and costs for care and contraception were calculated. The economic outcome was the cost per pregnancy averted. Costs and effectiveness were modelled from an NHS (i.e. direct costs) in a hypothetical cohort of 1,000 UK women using contraception. The results suggested that over one year of use, LARC methods would be associated with a smaller number of unintended pregnancies due to contraceptive failure compared to combined oral contraceptives and male condoms. Over 15 years of use, all LARCs would dominate user-dependent methods (i.e. would be less costly and more effective). Comparing LARCs to each other, the IUD and implant were found to dominate the IUS; and all three dominated the injectable method. However, which LARC dominates is also dependent on how long each method is used. For example, implants had a lower cost per pregnancy than all other LARCs over the first three years of use, potentially costing £14,730-17,866 per pregnancy averted (2004-2005 GBP). The methodological quality of this economic modelling study was rated as medium because many uncertainties were not fully described relating to the parameters and structure of the model. Sensitivity analyses were undertaken to examine variation in: the duration of use, combined use with condoms, changes in ingredients and costs of health service comparisons, ideal use of condom and combined oral contraceptives, and discount rates. Key parameters should be assessed in a sensitivity analysis to account for uncertainties related to them. In addition, the model was adapted from previous studies, but no validation and/or calibration was reported.

Pilgrim et al. (2010) also focused on health promotion topics, by testing three different school-based contraceptive models to determine their cost-effectiveness. In the first, two strategies were tested amongst a hypothetical cohort of 100,000 young people aged 14 to

16 years: condom provision was compared to a routine school nurse role only; and hormonal contraceptive provision was compared to condom provision. Condom provision was estimated to cost £38 for each pregnancy averted and to cost £822 for each abortion avoided (2007-2008 GBP). In comparison to condom provision only, contraceptive provision was estimated to cost £443 for each averted pregnancy and £1,453 for each abortion avoided. In the second model, school-based peer education and social work case management to prevent repeat pregnancy was examined amongst teen mothers under 19 years of age who were attending school, compared to no follow-up after the first pregnancy. The authors suggested that this resulted in an estimated £4,031-15,155 cost for each repeat pregnancy averted. The third model estimated the costs per pregnancy averted and abortion avoided when providing advanced hormonal contraception to a hypothetical cohort of 100,000 young people aged 15 to 19 years, compared to no advance provision. The findings estimated that advanced provision cost £310 for each repeat pregnancy averted, and cost £2,795 for each abortion avoided. The methodological quality of this economic modelling study was rated as medium due to limitations in outcome measures, baseline and treatment effect estimates, missing costs, conflict of interest reporting and model validation.

In summary, the findings from UK-based contraception economic evaluations suggest: (1) UPA could be more cost-effective than LNG; (2) LARCs are potentially more cost-effective than user-dependent contraceptive methods, and implants more cost-effective than other LARCs by three years of use; (3) school-based contraceptive provision could be more cost-effective than condom provision, which itself is more cost-effective than school nurse services; and (4) school-based advance provision of contraception was more cost-effective than costs related to pregnancy. The mixed methodological quality of these studies suggests some caution in applying the findings. These cost and outcome findings are presented in Appendix 12.

3.4.3 Health promotion

Four economic evaluations focused on health promotion topics (Cooper et al. 2012; Crawford et al. 2015; Jackson et al. 2015; Pilgrim et al. 2010). Using a cost-effectiveness analysis design, **Cooper et al. (2012)** compared teacher- or peer-led sexual health education interventions to standard school sexual health education. The authors suggested that compared to standard sexual health education, the teacher-led intervention was cost-effective at £18,041 per QALY gained (2011-2012 GBP); this demonstrates cost-effectiveness as it is below the £20,000 NICE threshold. However, in comparison to the teacher-led intervention, the peer-led intervention exceeded the NICE upper limit for cost-effectiveness at £72,062 per QALY gained. This economic evaluation was rated as high in terms of its methodological quality.

As noted above, **Jackson et al. (2015)** focused on a cost comparison of screening and health promotion (as described above). A STI screening health promotion campaign led by team captains and one led by sexual health advisers were each compared with a poster-only campaign control condition. The results indicated that all three interventions cost similar amounts, but the sexual health-adviser-led intervention was most cost-effective, as it led to 67% screening at a cost of £88.33 per person screened (2012-2013 GBP), compared to the poster-only campaign which cost £81.87 but resulted in only a 61% screening uptake. The team captain-led intervention was the least cost-effective, resulting in 50% screening uptake at a cost of £88.89 per person. The trial was judged to be of medium

methodological quality, with many uncertainties around the parameters used in the analysis. It was unclear whether costs were annuitised, and the time horizon was unclear. Seemingly, the analysis was undertaken for a time horizon of one year and the costs with posters were considered for three years. If this was the case, the costs may be slightly underestimated.

As described above, **Pilgrim et al. (2010)** examined contraception and health promotion strategies by testing three different school-based contraceptive models for cost per unit of health effect, where health effects were expressed as pregnancies averted and abortions avoided. Condom provision was estimated to cost £38 for each pregnancy averted and to cost £822 for each abortion avoided (2007-2008 GBP), compared to routine school nurse utilisation. In comparison to condom provision only, contraceptive provision was estimated to cost £443 for each averted pregnancy and £1,453 for each abortion avoided. In the second model, school-based peer education and social work case management to prevent repeat pregnancy was compared to no follow-up after the first pregnancy. The authors suggested that this resulted in an estimated £4,031-15,155 cost for each repeat pregnancy averted. The third model estimated the costs per pregnancy averted and abortion avoided when providing advanced hormonal contraception compared to no advance provision. The findings estimated that advanced provision cost £310 for each repeat pregnancy averted, and cost £2,795 for each abortion avoided. The methodological quality of this economic modelling study was rated as medium due to the limitations described above.

One other economic evaluation was identified which took a health promotion focus. **Crawford et al. (2015)** aimed to investigate the clinical and cost-effectiveness of brief advice for excessive alcohol consumption, which included sexual health education amongst people aged 19 years and older attending one of three sexual health clinics in London, England. The researchers used an RCT design in which costs were collected and analysed and a cost-utility analysis undertaken. Comparison group participants received a health education leaflet only. While costs to provide intervention or control conditions were similar in both groups (intervention £311 per person v. control £319 per person) (2010-2011 GBP) and the average additional cost of the intervention was modest at £12.57 (SD £6.59), no significant differences in either 90-day alcohol consumption or reported unprotected sex were found. The authors concluded that the intervention was not cost-effective as it was more costly than not providing any intervention and did not provide any additional benefit. The methodological quality of the integral trial was rated to be high, as study design and parameters seemed to be appropriately explored, also in a sensitivity analysis, where the authors tested the strength of the findings: 'bootstrap' techniques and non-hierarchical linear models were undertaken to assess missing data. The quality of the economic evaluation was also rated as high.

In summary, UK-based health promotion studies evaluated a diverse range of interventions, most of which were found to be potentially cost-effective. A sexual health adviser-led screening promotion campaign amongst football clubs had a lower cost per case detected compared to the poster-only comparison. In school settings, hormonal contraceptive provision could be more cost-effective than condom provision, which itself was predicted to be more cost-effective than school nurse services; and school-based advance provision of contraception was estimated to be more cost-effective than no provision. Teacher-led sexual health education was found to be cost-effective according to NICE thresholds, but peer-led interventions were less cost-effective in comparison to those which were teacher-

led. In contrast, brief alcohol advice and referral provided in STI clinics was found to be less costly but also less effective than health information leaflet provision, and football team captain-led STI screening uptake promotion amongst football club members was found to be more costly and less effective than a poster-only campaign. Again, it should be noted that the findings were derived from economic evaluations of mixed quality, suggesting that some caution is needed in the interpretation. The costs and outcome findings are described in more detail in Appendix 12.

3.5 Economic evaluations of contraception

A total of fifteen studies were economic evaluations of contraception. Three of these examined emergency hormonal contraception (Bayer et al. 2013; Foster et al. 2010; Thomas and Cameron 2013); nine assessed long-acting versus user-dependent contraception methods (Foster et al. 2013; Han et al. 2014; NCC 2013; Rodriguez et al. 2010a,b; Salcedo et al. 2013; Trussell et al. 2013, 2014, 2015); and two studies examined different contraceptive services provision (NCC 2013; Pilgrim et al. 2010). Full details of these studies are provided in the Evidence Tables in Appendix 10; and relative costs and outcomes are shown in the Costs and Outcomes Tables in Appendix 13.

3.5.1 Emergency hormonal contraception

Three economic evaluations modelled different scenarios of the provision of emergency hormonal contraception (EC): one cost-benefit analysis (Foster et al. 2010) and two cost-effectiveness studies (Bayer et al. 2013; Thomas and Cameron 2013).

The cost-benefit analysis by **Foster et al. (2010)** modelled two scenarios: (1) advance emergency contraception (EC) provision and (2) on-demand community or pharmacy provision of an unspecified contraceptive drug in comparison to no access within three hypothetical cohorts of one million sexually active US women using a public payer perspective. For both high and low frequency of use, both scenarios were estimated to produce a lower pregnancy rate than no access. The authors estimated that the cost savings ratio for both types of provision was greater than 1.00, meaning that the money saved by averting pregnancies was less than the cost of providing the EC, and the advance provision was slightly more cost-saving than on-demand provision. This economic evaluation was judged to be of medium methodological quality. Some limitations were noted, for example, that the authors only looked at savings from pregnancies averted for one year, potentially underestimating cost savings of advance provision if an EC supply was kept for longer. Also, the authors assumed that unprotected acts of intercourse occurred randomly throughout the menstrual cycle, but costs savings would be higher if women were more likely to use emergency contraceptive for acts that occurred in the week before ovulation. The authors only modelled intercourse where no contraception was used; in this case cost-effectiveness would be lower if EC were used in situations where the likelihood of conception was lower than with no contraception (e.g. missed pill). In addition, the authors only considered the medical costs of unintended pregnancy for up to two years after a birth, but social, welfare and private costs were likely to be much higher. The reviewers suggest that the authors model scenarios assessing the identified limitations for a longer period, and that they should include complications such as STIs in a long-term assessment of health benefits and costs.

Two cost-effectiveness studies examined the use of oral UPA compared to oral LNG. **Bayer et al. (2013)** modelled the use of UPA 30 mg compared to oral LNG 1.5 mg administered

within 120 hours of unprotected sex. This was examined in a hypothetical US national cohort of reproductive-aged women. Over an unstated but assumed 10-month time horizon, use of UPA was estimated to result in 54,295 unintended pregnancies at a cost of £270.25 million (2011 GBP) ($399.19 million 2011 USD), compared to 91,884 unintended pregnancies with use of LNG at a cost of £348.96 ($515.45) million. Cost-effectiveness was estimated to be £78.73 million ($116 million) per 8,053 QALYs, leading the authors to conclude that UPA was cost saving. This economic evaluation was rated low in terms of its methodological quality. The reviewers noted that the analysis was limited by a number of issues, including the fact that the authors did not state the perspective of analysis, so the reviewers were unsure whether results could be extrapolated to the entire society or not, or whether they should be interpreted only from the perspective of Medicaid users. The reviewers also noticed that complications such as STIs were not included.

Thomas and Cameron (2013) modelled the provision of UPA 30 mg within 120 hours of unprotected intercourse versus LNG 1.5 mg taken within 72 hours of unprotected sexual intercourse, using a healthcare and societal perspective in a hypothetical cohort of sexually active UK women. The authors suggested that the associated costs of unintended pregnancy would be £1,663-2,922 (2011 GBP), depending on the perspective used, and the model suggested that UPA would cost £194-1,453 less per avoided pregnancy than LNG. The methodological quality of this economic modelling study was rated as low due to limitations in outcome measurement, model cycle, baseline estimates of health effect and resource use, and sensitivity analyses and model calibration, and unclear reporting of the time horizon and adverse events.

Taken together, these three economic evaluations suggest that advance and on-demand EC are cost-saving in relation to no access for both high- and low-use groups, and that oral UPA is more cost-effective than LNG as a method of emergency contraception. However, these findings are based on studies that are rated low and medium in terms of their methodological quality.

3.5.2 Long-acting versus user-dependent methods

Nine studies assessed the economics of long-acting reversible contraception (LARCs). Five of these looked specifically at how different contraceptive methods compared with each other or with no contraception.

Foster et al. (2013) examined all contraceptive methods in comparison to no contraception using a cost-benefit model. Data were assessed from over 1 million low-income US women using contraceptive services offered through the American Family PACT medical health insurance programme over a two-year period. Findings suggest that all forms of contraception are effective in reducing unintended pregnancies, and all would potentially save more money than they cost to provide. Contraceptive implants and copper and hormonal intrauterine systems (IUS) were estimated to provide the largest cost savings, ranging from £3.24 to £3.32 (2009 GBP) ($4.89 to $5.00 2009 USD) in costs averted for each $1.00 spent. This economic evaluation was judged to be of medium methodological quality. The main limitations associated with the study were identified by the authors, but the reviewers also suggest that future research incorporates the long-term benefits, in terms of costs and health outcomes, of the impact on complications such as HIV and other STIs.

Similarly, **Trussell et al. (2015)** assessed the cost-effectiveness of all contraceptive methods versus no method, and LARCs versus UDC, using a hypothetical cohort of US women aged 20 to 29 years and a public payer perspective. Modelling predicted that 2.1 years of any type of LARC use (IUD, IUS or implants) would result in cost savings in comparison to user-dependent contraceptive methods (injectables, oral contraceptives - OC, ring, patch, condoms). This study was rated medium in terms of methodological quality. The reviewers suggested the inclusion of long-term complications into the analysis to better understand the benefits of the interventions; they also noticed that costs of interventions might be underestimated because only the price of wholesale acquisition seemed to be taken into account.

Three economic evaluations compared the use of LARCs directly against UDC methods. The **National Collaborating Centre (NCC) study (2013)** evaluated the cost-effectiveness of LARC methods (IUD, IUS, implant, injectable) in comparison to user-dependent methods (combined oral contraceptive - COC, male condom)[1]. Costs and effectiveness were modelled in a hypothetical cohort of UK men and women of reproductive age. The results estimated that over 15 years of use, LARCs would dominate user-dependent methods (i.e. were less costly and more effective), and implants would dominate all other LARCs over the first three years of use, potentially costing £14,730-17,866 (2004-2005 GBP) per pregnancy averted. The methodological quality of this economic modelling study was rated as medium because many uncertainties were not fully described relating to the parameters and structure of the model; in addition, no validation or calibration of the previous model adapted for use in this study was reported.

Trussell et al. (2013) undertook a US-based cost analysis of LARCs (implant, IUD, IUS) versus user-dependent reversible contraceptives (UDCs) (COC, condoms, patch, injectables, vaginal ring). The authors suggested that higher LARC uptake from OC or from no contraception would result in cost savings, and that cost neutrality would be achieved at just over two years of use. **Trussell et al. (2014)** further examined the costs of LNG-IUS against all other types of contraception (OC, ring, patch, injectables, implant, condoms). Using a hypothetical cohort of US women aged 20 to 29 years requiring contraception and a third-party healthcare payer perspective, the authors estimated that LARC use over three years would result in 64 unintended pregnancies, compared to 276 potentially occurring with use of UDC. The costs for each intervention were estimated at LNG-IUS £866,348 (2012 GBP) ($1,283,479 2012 USD) v. UDCs £1,257,277 ($1,862,633), suggesting that LNG-IUS dominates UDC methods. The reliability/quality rating of these two economic evaluations using our assessment tool was low. The reviewers noted that a limited age group was explored in the analysis and that future results should assess whether this could influence the final outcome. In addition, the reviewers suggested the modelling of complications associated with unintended pregnancies (including HIV and STIs) in order to better capture the long-term potential benefits of the interventions.

In sum, these economic evaluations suggest that LARC methods could be more cost-effective to use than user-dependent contraceptive methods in terms of the pregnancies

[1]Note that in some studies, injectable contraception was classified as a LARC; in other studies it was classified as a UDC.

they would avert and the resultant costs potentially borne by health and social services. This is based on findings from studies of medium and low methodological quality.

The remaining four studies examined the costs and effects of different configurations of contraceptive services. **Han et al. (2014)** conducted a cost-effectiveness and cost-savings analysis to estimate the potential savings from post-natal implant insertion offered to adolescent mothers, compared to standard contraceptive initiation over three years. A cohort of adolescents aged 13-22 years enrolled in a pre-natal/post-natal programme. This provided clinical data and a healthcare payer perspective was taken to estimate costs. The authors reported that in the first year of provision, £0.53 (2013 GBP) ($0.79 2013 USD) would be saved for each $1.00 spent; however, the estimated cost savings rose in each subsequent year to £2.40 ($3.54) at two years and £4.41 ($6.50) saved for each $1.00 spent in comparison to standard contraceptive provision. This economic evaluation was judged to be of low methodological quality, because the reviewers considered that the robustness of the results might be compromised because only one parameter was assessed in the sensitivity analysis (rather than all). The reviewers also reported that the benefits - in terms of repeat pregnancy rates by type of complications - were not reported, so the full benefits generated by each outcome were not captured.

Rodriguez et al. (2010a) undertook a cost-benefit analysis to assess potential cost savings over five years if post-natal IUD insertion was offered to recently immigrated low-income women compared to no IUD insertion, using a hospital and societal perspective. The authors estimated that over five years, £1.93 (2002 GBP) ($2.94 2002 USD) would be saved for every $1.00 spent on post-natal IUD provision. This study was rated low in terms of its methodological quality. The reviewers suggested that further research was necessary into interstate migratory patterns and their probabilities in order to better interpret the results. In a related publication (**Rodriguez et al. 2010b**), the authors evaluated the cost-effectiveness of this expansion of Medicaid provision of post-natal IUD insertion for the same population, concluding that, from a hospital perspective, expanded provision would result in hospitals losing £0.46 per £0.66 GBP ($1 2002 USD) spent on expanded provision. However, from a state perspective, £1.92 ($2.92 2002 USD) would be saved for every £0.66 ($1) spent. The study was rated low in terms of its methodological quality and the reviewers suggested that further research into interstate migratory patterns and probabilities should be conducted to assess the economic value of a federal mandate for preventive coverage of new immigrants.

Finally, **Salcedo et al. (2013)** used cost-benefit analysis to assess whether post-abortion IUD insertion for low-income women was more cost-effective compared to IUD insertion at a first post-abortion follow-up visit. The authors reported that post-abortion IUD insertion would potentially save $111 in direct hospital costs per woman at one year, rising to a potential £548 (2011 GBP) ($810 2011 USD) in savings over five years. With societal costs included, this increases to savings of £1,324-2,908 ($1,956-4,296) per woman compared to insertion at follow-up visit. The methodological quality of this study was determined to be medium. The reviewers noted that the model was heavily based on administrative data and the authors should have discussed the applicability of the parameters and the implications of extension of the conclusions to the general population; the implications were only partly included in the model (no STIs for example).

These economic evaluations of earlier provision of LARC methods post-natally or post-abortion suggest that long-acting contraception could generate cost savings, particularly beyond one year. However, these findings should be tempered by the low to medium methodological quality of the studies and further by the challenges of interpreting their results for use outside the specific health system context within which they were situated.

3.5.3 Contraceptive services

Two studies assessed the costs and effects of different contraceptive services provision. A cost-effectiveness study by **Pilgrim et al. (2010)** modelled two different scenarios: (1) school-based condom provision compared to school nurse services only; and (2) hormonal contraception provision versus condom distribution in secondary schools. This was modelled in three hypothetical cohorts of: young people aged 14 to 16 years in school; young mothers in school; and sexually active young people aged 15 to 19 years, taking a societal perspective. The authors asserted that both scenarios were cost-effective: school-based condom provision cost £38 (2007-2008 GBP) for each pregnancy avoided and £822 for each abortion avoided compared to school nurse only; and contraceptive provision cost £443 for each avoided pregnancy and £1,453 for each abortion avoided compared to condom distribution. The methodological quality of this economic modelling study was rated as medium because the parameters used in the model were not validated and calibrated using empirical data.

Thomas (2012) conducted a cost-benefit analysis to model three scenarios of service provision, compared to no such programme: (1) a mass media campaign targeted to unmarried men aged 15 to 44 years; (2) a teenage pregnancy prevention programme targeted to unmarried low socio-economic status (SES) youth; and (3) expanded Medicaid coverage for contraception provision to low-income unmarried youth. A hypothetical cohort of 10,000 nationally representative individuals aged 15 to 44 years was assembled, and a social and public sector (government) perspective was taken. The mass media campaign would potentially save £2.81 (2008 GBP) ($4.31 2008 USD) for each $1 spent, with the teenage pregnancy prevention programme estimated to save £1.61 ($2.46) for each $1 spent. The expanded contraception coverage was predicted to save £3.67 ($5.62) for each $1 spent. The study was rated as medium by the reviewers. The main limitations were discussed by the authors; however, the reviewers suggest that short- and long-term complications associated with unintended pregnancies (and unprotected sex) be taken into account to further understand the benefits, in terms of health outcomes and costs, of the interventions. For example, not all studies explored the role of STIs, such as congenital syphilis, associated with unintended pregnancies in the short- and long-term. Adverse outcomes associated with STIs and unintended pregnancies are still a challenge in high-income settings.

In summary, these economic studies of medium methodological quality suggest that expanded contraceptive provision targeted to high-risk groups could result in cost savings resulting from health and social care services not needing to be provided for unintended pregnancy, maternal benefits and early childhood care.

3.6 Economic evaluations of health promotion interventions

Overall, fourteen studies were identified which conducted economic evaluations of sexual health promotion or HIV/STI prevention. Of these, nine evaluated the costs and outcomes of HIV health promotion/prevention and six evaluated STI health promotion/prevention

interventions (one study examined both HIV and STIs). These are summarised below; full details of these studies are provided in the Evidence Tables in Appendix 9 and relative cost outcomes are shown in the Costs and Outcomes Tables in Appendix 14.

3.6.1 HIV health promotion/prevention interventions

Cost-effectiveness was evaluated for HIV prevention interventions in nine included studies (Burgos et al. 2010; Holtgrave et al. 2012, 2013; Kessler et al. 2013; Lasry et al. 2012; Marseille et al. 2011; Ruger et al. 2014; Sanders et al. 2010; Schackman et al. 2013). Seven of these addressed particular HIV/STI prevention programmes, while two sought to identify the 'optimised' group of interventions to deliver from a range of those currently delivered.

Burgos et al. (2010) reported a cost-effectiveness analysis of a brief condom negotiation skills intervention designed to improve HIV and STI incidence amongst female sex workers, compared to an information-only session on HIV and STI prevention. Using an NHS perspective, the authors reported HIV cost outcomes only, suggesting that without universal Highly Active Anti-Retroviral Treatment (HAART) access, providing a once-only session could result in 33 HIV-averted infections for 151 days of quality-adjusted life expectancy (QALE), costing £121 (2009 GBP) ($183 2009 USD) per QALY and £1,571 ($2,370) to prevent each HIV case. The authors suggested that this intervention was cost-effective; and it is cost-effective according to the NICE threshold for cost-effectiveness. An annually provided session could result in an additional 29 new HIV cases prevented, at a cost per QALY gained of between £713 and £8,893 ($1,075 and $13,413) per HIV case averted. These would also be cost-effective according to the NICE threshold criteria (i.e., less than £20,000 per QALY). This economic evaluation rated medium in terms of its methodological quality. The reviewers suggested that that HIV complications be explicitly modelled into the analysis, in addition to implicitly through the use or non-use HAART by CD4 levels, in order to better understand the implications on costs and health outcomes in the long term.

Holtgrave et al. (2012) examined the cost-effectiveness and cost-utility of a female condom distribution and HIV prevention education programme targeted universally to men and women. At a cost of £2.15 (2012 GBP) ($3.19 2012 USD) per product used (including the education component), the intervention was estimated to be cost saving from a societal perspective when 1.13 new infections were averted, and from a payer perspective when 1.50 new infections were averted. The methodological quality of this study was determined to be high. When the model allows use of male condoms by women, at a specific level, the cost-utility analysis is still costing-saving, as well as when female use of male and female condoms were dropped as low as 7.04%; these results were demonstrated in a sensitivity analysis.

Marseille et al. (2011) conducted a cost-effectiveness modelling of three interventions to reduce onward HIV transmissions amongst HIV-infected individuals in a clinic setting. Primary care clinical provider-led brief computer-based risk assessment and individual counselling, peer educator-based individual or group counselling and mixed primary care provider and peer-educator based counselling were compared with a standard care condition of provider-based risk assessment without specific counselling. Primary provider assessment and counselling was found to dominate the other two conditions; in comparison to no intervention, its cost-effectiveness was estimated at £72,668 (2010 GBP) ($107,656 2010 USD) per HIV case averted. The study was rated as high for its methodological quality. The reviewers suggested that future research explore complications associated with HIV

infections in the long term to better capture the potential health and costs benefits of the intervention.

Ruger et al. (2014) undertook at cost-effectiveness and cost-utility analysis of two health promotion interventions compared to standard assessment and treatment of women who inject drugs. Findings from a trial and a modelling study were reported. One condition tested well-woman examination with standard care; the second condition evaluated four HIV prevention education sessions in addition to the well-woman examination and standard care. A healthcare and societal perspective was taken. Findings from the trial suggested that the well-woman examinations were more costly and less effective than the standard intervention for HIV, and that for the modelled outcomes (relative to the standard intervention), the well-woman examination cost £137,280 (2003 GBP) ($208,316 2003 USD) per primary HIV infection averted. This economic evaluation rated high in terms of its methodological quality. The reviewers suggested that complications regarding HIV complications by CD4 level be assessed for a full understanding of the long-term benefits of the intervention.

Sanders et al. (2010) conducted a cost-effectiveness and cost-benefit analysis of primary care patients who received either nurse-initiated routine screening with traditional HIV testing and counselling or nurse-initiated rapid HIV testing and streamlined counselling in comparison to traditional HIV testing and counselling, taking a healthcare payer and patient perspective. Uptake of screening and receipt of results were the health outcomes. The results estimated that traditional HIV testing and counselling offered a per-patient lifetime discounted cost of £31,379 (2007 GBP) ($48,650 2007 USD) and benefits of 16.271 QALYs, which could be potentially cost-effective according to the NICE cost-effectiveness threshold criteria (i.e. £20,000-30,000 per QALY). Likewise, both nurse-initiated routine screening and traditional HIV testing and counselling and nurse-initiated routine screening with rapid testing and streamlined counselling conditions were found to be cost-effective according to the NICE threshold (respectively adding £34 ($53) and 0.0013 more QALYs and £42 ($66) and 0.66 more QALYs above those estimated by the traditional condition). The nurse-initiated routine screening with rapid testing and streamlined counselling remained cost-effective whether benefit of reduced HIV transmission was incorporated into the model or not. This economic evaluation was rated medium in terms of its methodological quality. The reviewers noted that costs were modelled based on reimbursement costs not economic costs, which may have an influence on the final results (costs maybe either be under- or over-estimated). They suggested that a cost estimation based on the use of resources be conducted and taken into account in the model, and that complications associated with HIV by CD4 levels be assessed to capture the long-term benefits of the intervention.

Schackman et al. (2013) undertook a cost-effectiveness and cost-utility analysis by modelling the findings from an intervention study targeting high-risk groups presenting at a substance use treatment clinic using a societal perspective. Here, on-site rapid HIV testing with information only or on-site rapid HIV testing with risk reduction counselling were compared with off-site HIV testing and referral in terms of costs and sexual risk behaviour. On-site rapid testing and information only was found to dominate the other conditions, resulting in a cost-effectiveness ratio of £39,979 (2009 GBP) ($60,300 2009 USD) per QALY. This is not cost-effective according to the NICE cost-effectiveness threshold criteria (i.e. it exceeds £30,000 per QALY). The on-site rapid testing with counselling cost £7 ($11) more per person but did not provide additional benefit. This economic evaluation was rated high

in terms of its methodological quality. The authors acknowledged the main limitations of their model and analysis and the reviewers did not have further suggestions.

A later study by **Holtgrave et al. (2013)** assessed the cost-utility of a rental assistance programme for homeless and unstably-housed persons living with HIV, using an unstated perspective. The authors suggested that the cost per QALY saved by the intervention was £40,558 (2005 GBP) ($62,493 2005 USD). This also exceeds the NICE criteria for determining cost-effectiveness. This economic evaluation was rated low in terms of its methodological quality. The trial on which the economic evaluation was based was considered to have significant potential for bias, because the findings were based on as-treated analyses rather than intention to treat. Further, the model did not capture any complications associated with HIV, thus none of the long-term benefits in terms of costs and health outcomes could be captured. In addition, the reviewers were unable to judge if the time horizon for the analysis was satisfactory to capture changes in HIV transmission or behaviour, as this information was not presented.

Taken together, each of these seven studies evaluated one intervention (or combination of interventions) delivered in one setting. All reported cost-effectiveness or cost-savings, and the majority of studies were of medium to high methodological quality. Two studies were targeted to universal populations, i.e. a mix of low- and high-risk individuals (Holtgrave et al. 2012; Sanders et al. 2010). The remaining studies focused on different risk groups, such as HIV-infected individuals (Marseille et al. 2011; Holtgrave et al. 2013) and individuals either at risk of HIV or of abusing substances (Burgos et al. 2010; Ruger et al. 2014; Schackman et al. 2013). Likewise, these studies addressed disparate interventions, including condom distribution, condom negotiation skills and rental assistance to influence HIV outcomes. Four studies did focus on various forms of risk assessment, testing and counselling (Marseille et al. 2011; Ruger et al. 2014; Sanders et al. 2010; Schackman et al. 2013). Only two of these were found to be cost-effective or potentially cost-effective according to NICE threshold criteria, or were cost saving (Ruger et al. 2014; Sanders et al. 2010). However, even the Ruger et al. study was cost-effective for hepatitis C outcomes rather than HIV. Only the condom distribution intervention reported by Holtgrave et al. (2012) was deemed to be cost saving. Thus limited cost-effectiveness relative to the UK standards is found within these studies.

Two further included studies examined multiple widely-delivered HIV prevention programmes. **Kessler et al. (2013)** conducted a cost-saving analysis to model the cost-effectiveness of all programmes, and then to model the optimum configuration of cost-effective interventions within an annual budget for each intervention of £242,999 (2010 GBP) ($360,000 2010 USD). A total of 16 single interventions were estimated to be cost-effective in preventing HIV infection or transmission over 20 years. The ten most cost-effective were: condom distribution (£126,368 ($187,212) per infection averted), social marketing (£55,709 ($82,532)) or community-based prevention (£4,482 ($7,173)) to all risk groups; prioritised use of surveillance data in HIV infected individuals (£18,673 ($27,663)); co-factor risk reduction in HIV-infected, high risk individuals (£21,130 ($31,304)); a brief intervention and referral for alcohol use in HIV-infected, high risk individuals (£24,821 ($36,772)); linkage to care for HIV-infected individuals (£257,112 ($380,906)); HIV-infected individuals' linkage to support services (£83,896 ($124,291)); partner services for HIV-infected individuals (£133,821 ($198,253)); and STI screening of HIV-infected, high-risk individuals (£228,843 ($339,026)). Interventions estimated not to be cost-effective included

STD screening (£322,639 ($477,984)) or risk reduction (£518,016 ($767,431)) of HIV-infected individuals; social services for HIV-uninfected, high-risk groups (£706,311 ($1,046,387)); care coordination for HIV-infected individuals on ART (£781,784 ($1,158,199)); clinical (£1,190,066 ($1,763,061)) or non-clinical (£2,099,507 ($3,110,381)) testing in people uninfected with HIV; and co-factor screening (£2,451,098 ($3,631,257)), brief alcohol interventions (£2,629,434 ($3,895,458)), pre-exposure prophylaxis (£6.075 million ($9,803,449)) or STD screening (£7,698,044 ($11,404,509)) in any HIV-uninfected, high-risk individuals. The most optimum hypothetical package (of seven modelled in total) was a combination of community-level interventions, linkage to support HIV positive individuals and STD screening of high-risk individuals (estimating 20,211 HIV infections averted at a cost of £71,805 ($106,378) per infection averted). This economic evaluation rated high in terms of its methodological quality. The authors had calibrated their model by using empirical figures, and had identified the main limitations of the study. The reviewers also suggested that in future analysis, the costs of ART and the treatment of complications associated with HIV be included in accordance with patient health status (defined by the patient's level of CD4 cell counts). In addition, the time horizon should be extended to a lifetime analysis. This approach would better capture the full long-term costs and benefits of intervention strategies.

Finally**, Lasry et al. (2012)** used cost-utility analysis methods to model the cost-effectiveness of currently funded HIV testing and education interventions and an optimised model of the same interventions targeted to high risk groups (i.e. MSM, IVDU, HIV-infected and high risk individuals) delivered for the same cost (£216.8 million 2009 GBP ($327 million 2009 USD)). Over five years, the model predicted that, in comparison to no funding, currently funded interventions would avert 13% of the 252,000 new infections predicted with no funding, at a cost of £37,332 ($56,311 2012 USD) per infection averted. The optimised model would avert 31% of new infections predicted with no funding, and at a cost of £17,985 ($27,128) per infection averted. The study was rated low in its methodological quality. Reviewers noted that the time horizon for the analysis was too short to account for all the benefits generated by reductions in infection and recommended that a lifetime or other longer period for analysis be considered to capture the long-term benefits of the intervention, including an assessment of complications due to HIV.

In summary, both economic evaluations focused on nationally delivered interventions and examined a comprehensive range of services and strategies; however, they were mixed in terms of methodological quality. They modelled different interventions in low-risk as well as various high-risk groups (HIV-infected, high-risk behaviour, MSM, intravenous drug users etc.), which provide a wide-ranging look at cost-effective services and relevant populations. These two studies together suggested that optimised use of specific interventions targeting high-risk or HIV-infected individuals can make better use of existing budgets. However, it is not clear whether these combinations of intervention provision would work in different UK local authorities with such different populations and HIV incidence. Thus the information on single intervention cost-effectiveness is perhaps more generalisable to specific UK local authorities.

3.6.2 Sexually transmitted infection interventions

A total of six studies examined cost-effectiveness related to various STI prevention programmes (Cooper et al. 2012; Crawford et al. 2015; Jackson et al. 2015; Pilgrim et al. 2010; Ruger et al. 2014; Thomas 2012). Full details of these studies are provided in the

Evidence Tables in Appendix 9, and relative cost outcomes are shown in the Costs and Outcomes Tables in Appendix 14.

Cooper et al. (2012) conducted a cost-effectiveness analysis of teacher- or peer-led STI prevention and skills training compared to standard sex education (which may or may not have had a skills training component). The authors suggested that compared to standard sexual health education, the teacher-led intervention was cost-effective at £18,041 per QALY gained (2011-2012 GBP): this is cost-effective as it is below the £20,000 per QALY NICE threshold for cost-effectiveness. However, in comparison to the teacher-led intervention, the peer-led intervention was not cost-effective as, at £72,062 per QALY gained, it exceeded the NICE threshold. This economic evaluation was rated as high in terms of its methodological quality. The reviewers suggested that the model be repeated using empirical data to better define interventions that are cost-effective.

Crawford et al. (2015) aimed to investigate the clinical and cost-effectiveness of brief advice for excessive alcohol consumption which included sexual health education amongst people aged 19 years and older attending one of three sexual health clinics in London, England. The researchers used an RCT design in which the costs were collected and analysed and a cost-utility analysis undertaken. Comparison group participants received a health education leaflet only. While costs to provide intervention or control conditions were similar in both groups (intervention £311 per person v. control £319 per person) (2010-2011 GBP) and the average additional cost of the intervention was modest at £12.57 (SD £6.59), no significant differences in either 90-day alcohol consumption or reported unprotected sex were found. Further, the ICER was calculated at −£1,200 per QALY, leading authors to conclude that the intervention was not cost-effective since it was more costly than not providing any intervention and did not provide any additional benefit. The methodological quality of the integral trial was rated to be high, as the study design and parameters seemed to be appropriately explored; also in a sensitivity analysis, where authors tested the strength of the findings; 'bootstrap' techniques and non-hierarchical linear models were undertaken to assess missing data.

Jackson et al. (2015) focused on a cost comparison of screening and health promotion (as described earlier). A STI screening health promotion campaign led by team captains and one led by sexual health advisers were each compared with a poster-only campaign control condition. The results indicated that all three interventions cost similar amounts, but the sexual health-adviser-led intervention was most cost-effective, as it led to 67% screening at a cost of £88.33 per person screened (2012-2013 GBP), compared to the poster-only campaign which cost £81.87 but resulted in only 61% screening uptake. The team captain-led intervention was least cost-effective, resulting in 50% screening uptake at a cost of £88.89 per person. The trial was judged to be of medium methodological quality, with many uncertainties around the parameters used in the analysis. Clarifications are necessary regarding the annuitisation of costs with posters and the time horizon for the analysis. It seems that the analysis was undertaken for a time horizon of one year and the costs with posters were considered for three years. If this was the case, the costs may be overestimated.

Also described earlier, **Pilgrim et al. (2010)** examined contraception and health promotion strategies by testing three different school-based contraceptive models to determine their cost-effectiveness. Condom provision was estimated to cost £38 for each pregnancy averted

and to cost £822 for each abortion avoided (2007-2008 GBP), compared to routine school nurse utilisation. In comparison to condom provision only, contraceptive provision was estimated to cost £443 for each averted pregnancy and £1,453 for each abortion avoided. In the second model, school-based peer education and social work case management to prevent repeat pregnancy was compared to no follow-up after the first pregnancy. The authors suggested that this resulted in an estimated £4,031-15,155 cost for each repeat pregnancy averted. The third model estimated the costs per pregnancy averted and abortion avoided when providing advanced hormonal contraception compared to no advance provision. The findings estimated that advanced provision cost £310 for each repeat pregnancy averted, and cost £2,795 for each abortion avoided. The methodological quality of this economic modelling study was rated as medium because the parameters used in the model were not validated and calibrated using empirical data.

Ruger et al. (2014) undertook a cost-effectiveness and cost-utility analysis of two health promotion interventions compared to standard assessment and treatment of women who inject drugs. The findings from a trial and a modelling study were reported. One condition tested well-woman examination with standard care; the second condition evaluated four HIV prevention education sessions in addition to the well-woman examination and standard care. A healthcare provider and societal perspective was taken. Results from modelling suggested that in terms of impact on hepatitis C infection rates, the well-woman examination, at £72,034 (2007-2008 GBP) ($109,308 2007-2008 USD) per additional infection averted, was less costly and more effective compared to the four education sessions. Similarly, the well-woman examination was less costly and more effective than the four education sessions intervention in reducing gonorrhoea rates (£706,949 ($1,072,760) per additional QALY). However, for chlamydia rates, the four education sessions intervention was less costly and more effective than the well-woman examination at £2,273,217 ($3,449,495) per additional QALY. This economic evaluation was rated high in terms of its methodological quality. Reviewers suggested assessing HIV complications by differences in CD4 level for a full understanding of the long-term benefits of the intervention.

Thomas (2012) conducted a cost-benefit analysis to model three scenarios of service provision, compared to no such programme: (1) a mass media campaign targeted at unmarried men aged 15 to 44 years; (2) a teenage pregnancy prevention programme targeted at unmarried low SES young people; and (3) expanded Medicaid coverage for contraception provision to low-income unmarried young people. A hypothetical cohort of 10,000 nationally representative individuals aged 15 to 44 years was assembled, and a social and public sector (government) perspective was taken. The mass media campaign would potentially save £2.81 ($4.31 (2008 USD)) for each $1 spent, with the teenage pregnancy prevention programme estimated to save £1.61 ($2.46) for each $1 spent. The expanded contraception coverage was predicted to save £3.67 ($5.62) for each $1 spent. The study was rated as of medium methodological quality by the reviewers. The main limitations were discussed by the authors. The reviewers suggested that short- and long-term complications associated with unintended pregnancies (and unprotected sex) be taken into account to further understand the benefits, in terms of health outcomes and costs, of the interventions.

In summary, this set of studies of mixed but mostly medium methodological quality examining the costs and outcomes of STI health promotion interventions provided equivocal results. All authors but one (Crawford et al. 2015) reported cost-effectiveness, cost savings

or positive costs and benefits for all interventions. After any relevant cost outcomes were compared to NICE thresholds for cost-effectiveness, three of these would still be deemed cost-effective or potentially cost-effective (Burgos et al. 2010; Pilgrim et al. 2010; Thomas 2012). Three studies were above the NICE criteria and thus not cost-effective (Cooper et al. 2012; Crawford et al. 2015; Ruger et al. 2014); and one study provided costs and outcomes similar to comparison conditions (Jackson et al. 2015). Three of the four studies examining the cost-effectiveness of interventions targeted to universal populations were not deemed cost-effective in a UK context or were equivocal (Cooper et al. 2012; Crawford et al. 2015; Jackson et al. 2015). Conversely, three of the four studies focusing on higher-risk groups were cost-effective relative to the UK context (Burgos et al. 2010; Pilgrim et al. 2010; Thomas 2012). Skills negotiation interventions provided equivocal results (Burgos et al. 2010; Cooper et al. 2012); however, this may have been because they targeted different (universal and high-risk) groups. Similarly, wide-ranging prevention campaigns provided mixed results and also targeted very different populations, which could explain the findings (Jackson et al. 2015; Thomas 2012).

4 Discussion

4.1 Main findings

This systematic review represents a comprehensive update examining the cost-effectiveness of economic evaluations of sexual health interventions undertaken since 2010, of specific interest to local authorities. In order to avoid duplicating review efforts being undertaken by Public Health England, and on the advice of our Advisory Group, we prioritised economic evaluations related to contraception and health promotion, and also assessed any UK-based economic studies of sexual health interventions. This resulted in the identification of 29 relevant economic evaluations.

4.1.1 Economic evaluations of contraception

Looking across the 15 identified economic evaluations focused on contraception, the findings from two cost-effectiveness studies suggested that oral UPA is more cost-effective than oral LNG as a method of emergency contraception (EC), based on one cost-benefit analysis and one cost-effectiveness analysis undertaken in the US and the UK respectively. One US cost-benefit analysis also reported that advance and on-demand EC offered in clinics or community pharmacies are cost-saving compared to no access, for both high- and low-use groups. This supports current NICE guidance (NICE 2014a).

In terms of longer-term contraceptive methods, the findings from one cost-benefit study, two cost-effectiveness studies, one cost-savings analysis and one costing study suggested that LARCs could be more cost-effective to use than user-dependent contraceptive methods in terms of the pregnancies they would avert and the resultant costs potentially borne by health and social services. Both US and UK studies reported findings with the same direction of effect. These findings support the most recent NICE recommendations (NICE 2014b).

Modelled findings from two cost-benefit studies and two cost-savings analyses suggested that earlier provision of LARC methods post-natally or post-abortion could generate cost savings, particularly beyond one year. While these findings were based on studies conducted in the US, with a different healthcare system funding structure, it could be argued that this is a potential strategy which could be cost-effective in the UK. Of course, its relative merit would require discussion by stakeholders.

Lastly, findings from one US cost-benefit study and one UK cost-effectiveness study suggested that expanded contraceptive provision targeted to low- and high-risk groups such as sexually active teens, adolescent mothers and new immigrants could result in cost savings resulting from services not needing to provide health and social care for unintended pregnancy, maternal benefits and early childhood care. These findings support the most recent NICE recommendations on contraceptive use in those under 25 (NICE 2014a).

4.1.2 Economic evaluations of HIV/STI health promotion/prevention

Fourteen health promotion studies focused on HIV or STI health promotion or prevention strategies. Of these, nine examined a range of HIV health promotion/prevention interventions and reported overall cost-savings or cost-effectiveness. The findings from one cost-effectiveness/cost-utility analysis and one cost-effectiveness analysis suggested that

condom distribution or condom negotiation skills programmes were cost-effective or cost-saving. Within interventions to assess risks and provide tailored testing or counselling to patients at risk of HIV, the findings from three cost-effectiveness analyses suggested that clinical provider assessment and counselling was more cost-effective than peer- or peer-provider counselling; that nurse-led rapid testing and tailored counselling was more cost-effective than routine screening and counselling; that on-site rapid testing and tailored counselling was better than either off-site testing and referral or than on-site testing and information only. A series of four educational sessions on HIV infections was suggested to be cost-saving in relation to well-woman examinations for intravenous drug users in one cost-effectiveness/cost-utility analysis; and one study of rental assistance to HIV-infected persons was described as cost-effective by the authors. In addition, two studies examining the cost-effectiveness of multiple HIV prevention strategies in order to determine the 'optimum package' of interventions reported cost-savings over current HIV testing and counselling provision or no service provision. While all of these studies reported cost-effectiveness or cost-savings for some or all evaluated interventions, only four studies reported costs per QALY; of these, only nurse-led rapid testing and tailored counselling and condom negotiations skills training for female sex workers were shown to be cost-effective or potentially cost-effective within NICE thresholds.

Six studies evaluated the costs and outcomes related to STI health promotion or prevention. These reported somewhat more mixed findings with respect to cost-effectiveness. Some findings were clear, for example, a cost-effectiveness analysis of school condom distribution was suggested to be cost-effective for STIs and a cost-benefit analysis of mass media STI prevention targeted to unmarried male adults was deemed to be cost-saving. Others provided more equivocal findings: teacher-led STI prevention and skills training for school-age youth was found to be cost-effective in comparison to standard sex and relationships education; however, peer-led STI prevention and skills training was not found to be cost-effective. An STI screening uptake campaign led by sexual health advisers targeted to football club members was found to have similar costs and outcomes to a poster-only campaign; the same campaign led by football captains was found to be more costly and less effective. For hepatitis C and gonorrhoea outcomes, well-woman examinations provided to women using intravenous drugs in addition to standard drug treatment was found to be cost-effective, but a four-education session added to standard drug treatment was found to be more cost-effective for chlamydia outcomes. And one evaluation of brief risk-reduction counselling that included sexual risk behaviour amongst adults presenting at substance abuse clinics was not found to be cost-effective. Of these six economic evaluations, only the teacher-led STI prevention and skills training intervention was found to be cost-effective by NICE standards.

Only four health promotion studies were UK-based (Cooper et al. 2012; Crawford et al. 2015; Jackson et al. 2015; Pilgrim et al. 2010). All were focused on STI prevention, and only Cooper et al. (2012) reported cost per QALY, allowing comparison against NICE thresholds. The remaining STI cost evaluation studies were all US-based, as were the entire subset of studies examining HIV health promotion/prevention. Thus there is limited information on cost-effectiveness relative to the UK.

4.1.3 UK economic evaluations

The findings from this systematic review of economic evaluations suggest that there has been a reasonable amount of research into the economics of sexual health services in the

UK since 2010: in total, nine full economic evaluations met the inclusion criteria for this review. UK-based cost-effectiveness and cost-consequence analyses focusing on interventions to promote STI screening indicated that those offered to high-risk groups, in more accessible locations such as clinics, pharmacy, by phone, or at community football clubs, could potentially be more cost-effective than their relevant alternatives. Cost-utility analyses of point-of-care testing for STIs was found to be cost-effective according to NICE thresholds, as were interventions that targeted annual HIV testing to high-risk adults, with or without ART. These findings support those of current Department of Health and NICE guidance, which recommend rapid access to testing in a variety of settings and for high-risk groups (Hind 2013; NICE 2011a,b, 2014a).

UK studies also indicated that UPA could be more cost-effective than LARCs for emergency hormonal contraception. Studies examining LARCs versus user-dependent methods suggested that LARC methods could be more cost-effective to use than user-dependent contraceptive methods in terms of the pregnancies they would avert and the resultant costs potentially borne by health and social services. These findings are consistent with current NICE guidance on long-acting contraceptives (NICE 2014b). In addition, it was suggested that school contraceptive services, such as condom distribution, hormonal contraceptive provision and advance contraceptive provision could be cost-effective compared to the alternatives; all of these are supported by current NICE guidance (NICE 2014a). Teacher-led sexual health education was also found to be cost-effective according to NICE thresholds; however, in comparison to teachers, peer-led education was not cost-effective.

4.2 Strength of evidence

There were more cost-benefit analyses undertaken on contraceptive topics (n=5) than on health promotion topics (n=1). It could be argued that cost and health outcome data for contraception studies (e.g. pregnancy/abortion rates, dispensing costs) are discrete, simple to access and have a more direct causal effect on outcomes than those of health promotion interventions. In addition, long-term outcomes of unintended pregnancy (e.g. future loss of earnings due to lower employability, need for childcare) may be easier to monetise than those outcomes resulting from health promotion (or a lack of it), including behaviour change, future ill health or infertility due to chronic STIs.

Only five of the included studies undertook cost-utility analyses, limiting our ability to judge intervention cost-effectiveness against NICE recommended thresholds. This further limited the comparability of interventions across the review.

The economic evaluations were evenly varied in their methodological and/or reporting quality: ten each were of low and medium methodological quality and nine were of high quality, according to the combined health economic evaluations checklist. While it is encouraging to see that over half of the included studies rated medium quality or higher, some caution in the interpretation of pooled findings is needed, particularly where there are few studies informing readers on the cost-effectiveness of an intervention and some of these are of low quality.

4.3 Evidence gaps

The majority of included economic evaluations were US-based and focused on interventions modelled in general populations or with those at low risk. Despite a call for locally-provided sexual health interventions to be provided to higher-risk groups such as those with learning

disabilities (Hind 2013), no relevant economic evaluations of such interventions were identified. In relation to other vulnerable groups relevant to the UK, only one US economic evaluation targeting sex workers was identified. In addition, no full economic evaluations of other popular sexual health interventions currently discussed in the literature were identified. For example, there are indications that internet-based STI screening and results provision are of increasing interest and may be acceptable to higher-risk groups (Gilbert et al. 2013; Greacen et al. 2013). While evaluations of such interventions have been published or are in process (Bailey et al. 2015b, Bracebridge et al. 2012; Wilson et al. 2015), no full economic evaluations were located. Systematic reviews of sexual health interventions offered population-wide and to vulnerable groups report limited or no data available on cost-effectiveness (Bailey et al. 2015a; Bonell et al. 2013; Gomez et al. 2013; O'Mara-Eves et al. 2013; Whitaker et al. 2014). This suggests a need for UK-based economic evaluations of sexual health interventions, as well as economic evaluations specific to vulnerable groups in the UK. It should also be noted that while economic evaluations of HIV pre-exposure prophylaxis were identified, they were not included in this review because of work currently being undertaken by Public Health England (McCormack et al. 2016).

4.4 Limitations of the dataset

In addition to issues previously identified in assessing the methodological rigour of the included studies, several other potential limitations of the dataset should be considered.

The research question posed by this systematic review asked a broad question of all sexual health services provided by local authorities. This resulted in the inclusion, assessment and synthesis of multiple intervention strategies, which (in concert with the review timelines) made synthesis of the findings amenable to only narrative discussion of the results. Similarly, challenges were identified in drawing comparisons across studies due to the use of different comparators (e.g. one economic evaluation comparing skills training to 'standard intervention' but another comparing skills training to 'no intervention'). Each economic comparison also differed (e.g. cost-effectiveness ICERs versus cost utility; cost per QALY versus costs per person intervened upon or per outcome for each group), which made further comparisons of effectiveness across common interventions difficult.

This review sought economic evaluations of sexual health promotion interventions provided in local authorities. It should be considered that while costs for these services are borne by local authorities, the benefits may be accrued elsewhere, as health promotion interventions often show results over a longer term and in different sectors than local authorities. An example is services relating to unintended teenage pregnancy. These are paid for by the local authority; however, most benefits, such as reduced unemployment/ better job prospects of mothers who delay childbearing until they have completed their education, and better health of infants in terms of reduced hospital or GP visits, are seen in cost savings experienced by other public sectors, and over a longer term. Research studies tend to report cost outcomes relevant to hospital services or welfare and education sectors rather than to local authorities per se. This requires stakeholders to take a much broader interdisciplinary approach when considering the costs and benefits of local authority sexual health service provision. Related to this, it should be noted that only some of the economic evaluations used a societal perspective, which is helpful in considering the wider social benefits. Decision making by local authorities requires a similarly broad consideration of these wider benefits to society.

The majority of economic evaluations included in this review were from the US (n=20), which has a different healthcare system from the UK. In particular, the US has a third-party payer (i.e. health insurance) system for reimbursing healthcare costs, and about 17% of the population is without any kind of protection in case of need. In contrast, the UK has universal healthcare free at the point of access (Berry 2015; Brown 2003; Centers for Disease Control and Prevention 2015). The context in which economic evaluations are undertaken is of critical importance when determining the cost-effectiveness of interventions (Anderson and Shemilt 2010). While differences in funding structures could raise some questions of applicability of economic evaluations between countries, we included US-based studies at the request of our Advisory Group in order to provide as much information as possible about the cost-effectiveness of relevant sexual health interventions. Several key differences between the US and UK healthcare systems exist that could impact on the findings and should thus be considered. These include: the use of insurer or reimbursement data whose costs do not cover the full range of benefits available in the NHS; the lack of US funding for abortion services; consideration that the drug costs in US studies would be limited to those provided in hospital whereas in the UK they are more likely to be covered; the potential for greater uptake of services in the UK due to the tendency of US analyses to look only at specific insured populations.

Related to the issue of context, the perspectives varied widely according to which economic evaluations were analysed in included studies. A total of five studies examined costs from a healthcare (i.e. hospital or clinic) perspective alone; at least 12 studies examined cost-effectiveness from a societal perspective and six used a third-party payer perspective only. Two studies did not report their perspective, and the remaining four utilised more than one perspective. This variation in perspectives alters the breadth of costs included in the analysis, potentially over- or underestimating cost-effectiveness where relevant costs are, and are not, taken into account. It has been suggested that employing a wider societal perspective provides a more realistic representation in terms of highlighting the costs and outcomes experienced beyond healthcare and over longer periods (Drummond et al. 2015); it is also argued that whichever perspective is selected, care should be taken to establish all reasonable costs and outcomes (Drummond and Sculpher 2005). However, within perspectives, it was not always clear if the same aspect was being examined. For example, US economic evaluations described their perspective as ‘third-party payer’, ‘health insurance company’, ‘state’, ‘government’. Without clear explanation from individual authors, it was not always possible to determine the extent to which these perspectives overlapped; presumably different costs could be derived from each.

Across the set of included studies, the costs and outcomes of interventions were assessed against different comparators in each case. For example, some studies compared interventions against ‘standard care’, others against ‘no intervention’, and others against a second intervention. The lack of standardised comparators across studies makes comparisons of cost-effectiveness difficult. For example, in some cases, it may be appropriate to compare an intervention to ‘no care’; however, in another context it may be more suitable to compare that same intervention to ‘standard care’. This is an issue also described in other systematic reviews of economic evaluations (Mangham-Jeffries et al. 2014).

It was also noted that some contraceptive methods (e.g. injectables) were labelled as LARCs in one study (NCC 2013) but as UDCs in another (Trussell et al. 2014). However, these

findings were not likely to have affected the overall conclusions, as analyses were undertaken separately for each method of contraception in each study, allowing readers to see direct costs and outcomes.

Finally, it should be noted that two cost-consequence analyses were included (Jackson et al. 2015; Roberts et al. 2012). While recognised by NICE as providing valid information on costs and outcomes (NICE 2012), cost-consequence studies can be challenging to interpret because often multiple outcomes are reported and it is difficult to know what proportion of costs should be attributed to which outcomes. Attributing the full cost to a single outcome may overestimate the cost of producing that outcome and does not take into account the synergies or externalities associated with additional benefits.

4.5 Limitations of review methods

Due to the broad nature of sexual health services commissioning in local authorities, the research question resulted in a wide range of relevant economic evaluations, but little depth due to the small number of studies evaluating each intervention. This limited our ability to build up a consistent picture of cost-effectiveness across a range of interventions; however, it did allow the illustration of the breadth of interventions that have been evaluated for cost-effectiveness as well as where gaps still remain. Such mapping of the range of economic evaluations available to inform a policy decision is considered useful (Anderson 2010; Anderson and Shemilt 2010; Gomersall et al. 2015). The findings from this review thus highlight priority areas for economic evaluation for researchers and policy makers to consider in the future.

Public engagement in reviews is important, to ensure that reviews are focused on questions and findings that are of use to those who are affected by the policies under study (Rees and Oliver 2012). To gain these perspectives, we consulted with sexual health charity members who provided input during Advisory Group meetings. Further discussions between local commissioners and patient groups would be recommended when the findings of this review are utilised to inform service commissioning.

For the purposes of this systematic review, economic evaluations of trials were presented alongside those based on modelling estimates. While it has been recommended that economic evaluations of RCTs and models be assessed separately (Anderson and Shemilt 2010), we opted to present both together in order to highlight the range of available research, clearly indicating where the findings arose from trials and from models. The incorporation of multiple economic evaluation designs also necessitated a much wider assessment of quality than any one quality assessment tool could provide, and our appraisal of relevant economic evaluations quality assessment tools indicated a large amount of overlap. This meant that quality assessment of the individual studies took considerably longer than anticipated, and necessitated the development and testing of an amalgamated tool to address all the study designs.

All cost outcomes were converted to current GBP according to good practice; however, no adjustments for inflation were made due to the potential for missing key costs due to limited reporting in studies. The potential impact of not adjusting for inflation means that costs are not directly comparable across studies. For example, those reported in 2002 GBP are not directly comparable to those reported in 2013 GBP.

In general, the findings supported recommendations made by the most current NICE guidance available related to contraceptive service provision and health promotion interventions. This may be the result of searching the current NICE guidelines for relevant economic evaluations. It should however be noted that local authorities may have a different willingness to pay than the NHS, and local judgements about whether an intervention is 'cost-effective' for that context may differ between local authorities.

Finally, we had intended to use the system of grading economic evaluations presented by Payne and O'Brien (2005) in this review, as a method of facilitating comparisons across different interventions. However, the complex nature of these studies and the need for transparent reporting of costs and outcomes required modification of the Payne and O'Brien framework, which resulted in the Cost Outcomes tables presented in Appendices 12 to 14.

5 Conclusions

This review sought to answer the research question:

> From the relevant identified studies, what evidence is available on the cost-effectiveness of local authority commissioned sexual health services from UK-based studies, concerning studies of health promotion and in relation to studies of contraception?

The findings from this systematic review suggest that a large amount of evidence on the cost-effectiveness of sexual health services has been undertaken in the past five years, and that, while the study findings do not always measure costs per QALY or report cost-effectiveness or potential cost-effectiveness according to NICE thresholds, this evidence base generally suggests the cost-effectiveness of interventions that support current NICE guidance, particularly for sexual health services aimed towards young people and those at high risk. However, some interventions may be equivocal in terms of the cost-effectiveness, and others show cost-effectiveness for some STIs but not others.

Asking broad questions about wide-ranging services amongst multiple populations inevitably created challenges. In order to present the findings from such diverse studies, we employed the use of structured summaries, evidence tables and cost-outcomes tables. These were designed with input from local commissioners, to assist readers in making comparisons between different interventions using standard formats. It is hoped that this will allow assessment of whether clear cost-effectiveness has been established and indicate to readers whether further consideration of costs and outcomes is required for their particular context.

5.1 Implications for future economic evaluations of sexual health research

As noted above, the methodological differences between economic evaluations make drawing comparisons across such studies difficult. While good practice for modelling studies has long been in place (Phillips et al. 2004), just under one-third of all included economic evaluations were rated highly in terms of their methodological quality. This suggests a need for economic evaluations to be designed and conducted according to recommended guidance (Anderson and Shemilt 2010; Drummond et al. 2015).

Future economic evaluations of sexual health interventions which are based on internal trials could be strengthened by designing for longer-term outcomes that would allow for more robust modelling. Similarly, modelling studies could be designed with longer-term costs and outcomes in mind. Such studies could also have more impact if they were designed and executed in a manner to show clearly the cross-sectoral benefits of investing in health services. In addition, the feasibility of complementary use of large cohort study datasets measuring such long-term outcomes could be investigated, in order to strengthen future model estimates.

6 References

A list of the included studies can be found, with summaries, in Appendix 11.

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Appendices

Appendix 1: Search strategy: PubMed

((Contraception[MH] OR Contraception, Postcoital[MH] OR Contraception, Immunologic[MH] OR Contraception, Barrier[MH] OR Contraception Behavior[MH] OR Contraceptive Agents[MH] OR Contraceptive Devices[MH] OR Contraceptive Agents, Male[MH] OR Contraceptive Agents, Female[MH] OR Contraceptive Devices, Male[MH] OR Contraceptive Devices, Female[MH] OR Vaccines, Contraceptive[MH] OR Spermatocidal Agents[MH] OR Contraceptives, Oral, Hormonal[MH] OR Contraceptives, Oral, Sequential[MH] OR Contraception, Immunologic[MH] OR Intrauterine Devices[MH] OR Condoms[MH] OR Condoms, Female[MH] OR Population Control[MH] OR Natural Family Planning Methods[MH] OR Family Planning Services[MH] OR Family Planning Policy[MH] OR Reproductive Health Services[MH] OR Sex Education[MH])

OR

(contraception[TIAB] OR contraceptive[TIAB] OR contraceptives[TIAB] OR family planning[TIAB] OR reproductive health service*[TIAB] OR sexual health service*[TIAB] OR fertility control[TIAB] OR condom[TIAB] OR condoms[TIAB]) OR sex education[TIAB] OR unplanned pregnancy[TIAB] OR unplanned pregnancies[TIAB] OR unwanted pregnancy[TIAB] OR unwanted pregnancies[TIAB]) OR ((HIV Infections[MH] OR HIV[TIAB] OR Human immunodeficiency virus[TIAB] OR Herpes Simplex[MH] OR Herpes Genitalis[MH] OR herpes simplex[TIAB] OR herpes genitalis[TIAB] OR genital herpes[TIAB] OR herpes virus[TIAB] OR Gonorrhea[MH] OR gonorrhea[TIAB] OR Syphilis[MH] OR syphilis[TIAB] OR Candida albicans[MH] OR candidiasis[TIAB] OR candida[TIAB] OR candidal[TIAB] OR candidosis[TIAB] OR vulvovaginitis[TIAB] OR vulvitis[TIAB] OR vulvodynia[TIAB] OR balanitis[TIAB] OR Chlamydia trachomatis[MH] OR chlamydia[TIAB] OR LGV[TIAB] OR Papillomavirus Infections[MH] OR human papillomavirus[TIAB] OR HPV[TIAB] OR genital wart*[TIAB] OR anogenital wart*[TIAB] OR anorectal wart*[TIAB] OR penile wart*[TIAB] OR Vaginosis, Bacterial[MH] OR Gardnerella[MH] OR Gardnerella vaginalis[MH] OR bacterial vaginosis[TIAB] OR gardnerella vaginalis[TIAB] OR vaginitis[TIAB] OR vaginosis[TIAB]) OR sexual health[TIAB]))

AND

((Economics[MH] OR Health care costs[MH] OR (costs and cost analysis[MH]) OR Cost allocation[MH] OR Cost-benefit analysis[MH] OR Cost control[MH] OR Cost savings[MH] OR Direct service costs[MH] OR Health expenditures[MH] OR economics, medical[MH] OR budgets[MH] OR Health Care Economics and Organizations[MH] OR cost-effective[TIAB] OR cost-effectiveness[TIAB]) OR economic analysis[TIAB] OR economic evaluation[TIAB]) OR ((effectiveness[TIAB] OR analysis[TIAB] OR savings[TIAB] OR minimisation[TIAB] OR minimization[TIAB] OR utility[TIAB] OR benefit[TIAB]) AND (cost)))

Appendix 2: Types of economic evaluation

Cost analysis and cost minimisation analysis

A key component of economic evaluation is understanding the costs associated with the delivery of an intervention. This can be done by performing a cost analysis; the aim is generally to identify, measure and value resources used to deliver an intervention. The results of a cost analysis may include an estimate of the total cost of an intervention and a breakdown of total costs by input or cost category. These data can be used to quantify and describe how resources are being used to deliver an intervention, identify who is using resources and understand how they are being used. A cost-minimisation analysis can be performed when the effectiveness of two or more alternatives is exactly equal and only costs vary (Drummond et al. 2005).

Cost-consequence analysis

A cost-consequence analysis goes one step beyond cost analysis by adding a description of the consequences associated with the intervention or programme being costed. This approach typically incorporates a range of consequences, which may vary across comparator interventions. This approach is considered a partial economic evaluation since the costs and consequences are reported separately and costs are not attached to a specific consequence in order to generate a cost per unit of consequence.

Cost-effectiveness analysis

Cost-effectiveness analysis is one of three approaches to conducting a full economic analysis. The defining feature is that health effects or outcomes are measured in natural units relative to programme objectives. In order to facilitate comparison between interventions, the consequences of the alternatives considered must be reported in the same units. Analyses focusing on interventions aimed at reducing mortality may use cost per life year gained or death averted as the main outcome, whereas interventions aiming to reduce unintended pregnancies may report the cost per unintended pregnancy averted.

Comparing the costs and effectiveness of two interventions, the ratio reflects the *incremental* cost and effect of one over the other and so is referred to as an Incremental Cost Effectiveness Ratio (ICER). An ICER is constructed as follows:

$$ICER = \frac{Cost_{\ Intervention\ A} - Cost_{Intervention\ B}}{Effect_{Intervention\ A} - Effect_{Intervention\ B}}$$

Using this approach, a lower cost-effectiveness ratio, or lower cost per unit of health effect, is considered desirable and an indication that the intervention being evaluated is more cost-effective than the comparator. Standard practice is to compare a new intervention with the standard of care, or next best alternative. Where no comparable intervention or service is currently available, one may compare an intervention to a 'do nothing' alternative, in which case the resulting ratio would simply be a CER (Morris et al. 2007).

While this approach is very useful for making comparisons between interventions with health effects that can be measured in the same units, this requirement can make it difficult to use cost-effectiveness analysis to conduct comparisons across different types of interventions. In this case, it is not possible to compare the relative cost-effectiveness of

the two different types of interventions because the measures of effect are reported in different units. In order to meaningfully compare interventions with different objectives and health effects, a composite measure of benefit is required.

Cost-utility analysis

A second approach to full economic evaluation is cost-utility analysis. Strictly speaking, this is a sub-type of cost-effectiveness analysis, since health effects are also measured in natural units. However, this approach is distinct in that it uses composite measures of benefit based on *utility*, which is a broad term used in economics to refer to the satisfaction that individuals gain from consumption. In terms of valuing health outcomes, utility-based measures refer to individual or societal preferences for different health outcomes or health states. These types of measures consider values placed on both quantity and quality of life and use weighting formulae to combine values into a single measure. A variety of direct and indirect methods for measuring utility are available. A commonly used indirect measure is the EQ-5D, a multi-attribute health status classification system which can be used along with weights derived from population surveys to value individual health states in terms of how they compare to either death or perfect health. The resulting score can be used to calculate the commonly used outcome measure, the Quality-adjusted Life Years (QALY) (Drummond et al. 2005).

For a given intervention, the number of QALYs gained is calculated by multiplying the utility score associated with a given condition or health state by the number of years of life gained as a result of the intervention. For example, consider a condition with a health utility score of 0.5 and an intervention which prolongs life for people with this condition by 2 years in this health state. The number of QALYs gained then would be 1 (0.5 utility score × 2 years). Other approaches to measurement that can be used to generate QALYs include the Health Utilities Index and the SF-36D (Drummond et al. 2005).

Cost-utility ratios are calculated in the same fashion as cost-effectiveness ratios, dividing differences in the cost of two or more interventions by the differences in outcomes. The incremental cost-utility ratio calculation is provided below. (Note that this is commonly referred to as an incremental cost-effectiveness ratio even when a utility-based outcome measure is used).

$$ICER = \frac{Cost_{\ Intervention\ A-}\ Cost_{Intervnetion\ B}}{QALYs\ Gained_{Intervention\ A} - \ QALYs\ Gained_{Intervention\ B}}$$

Cost-utility analysis is of broad applicability in public health decision making because, as in a cost-effectiveness analysis, it can explore single or multiple outcomes. However, cost-utility analysis adds in a notion of value (utilities, measured as QALYs or DALYs). These utilities can be assessed for a range of interventions and facilitate comparisons between different health interventions using a common metric. However, some limitations for these metrics should be considered, such as their lack of compensation for socio-economic and demographic differences.

Cost-benefit analysis

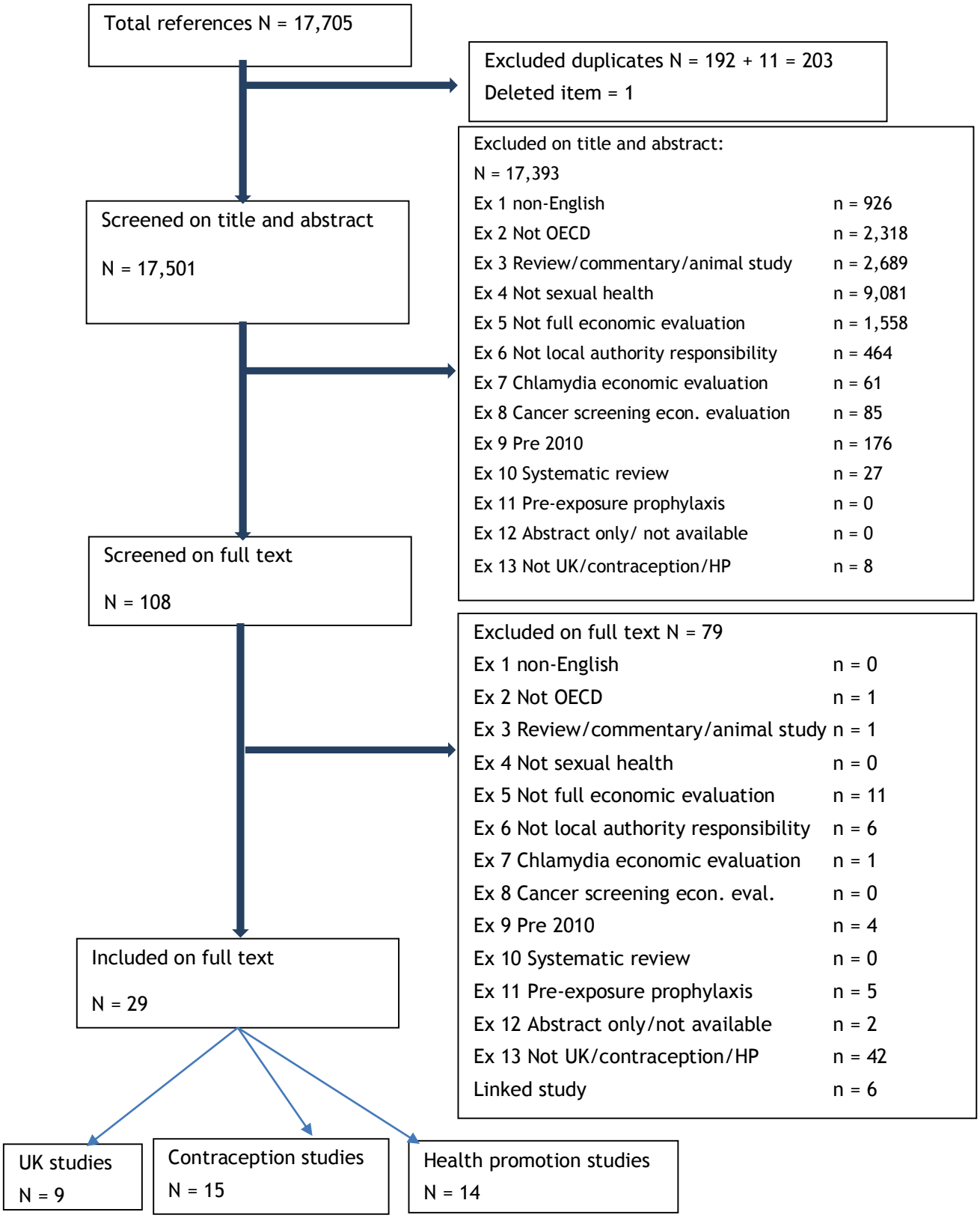
The final type of full economic analysis is a cost-benefit analysis. Its defining feature is that both the costs and health effects associated with an intervention are translated into monetary terms. This approach also typically seeks to include a broader range of social

benefits and costs beyond those that may accrue only to the health sector or patients themselves. The results are commonly expressed as a ratio of benefits to costs (where benefits are expressed as the monetary value of benefits), or in terms of money saved per unit of currency spent. Using this paradigm, interventions where social benefits outweigh the social costs associated with an intervention or programme are considered desirable.

An attractive feature of this approach to economic evaluation is that it is possible to incorporate costs and benefits occurring beyond the health sector. However, in practice, the process of converting benefits into monetary terms can be challenging. Beyond methodological challenges, the moral implications of placing a monetary value on life have led many researchers to steer away from this approach, particularly because there is potential for undervaluing health gains accrued to individuals with lower socio-economic status.

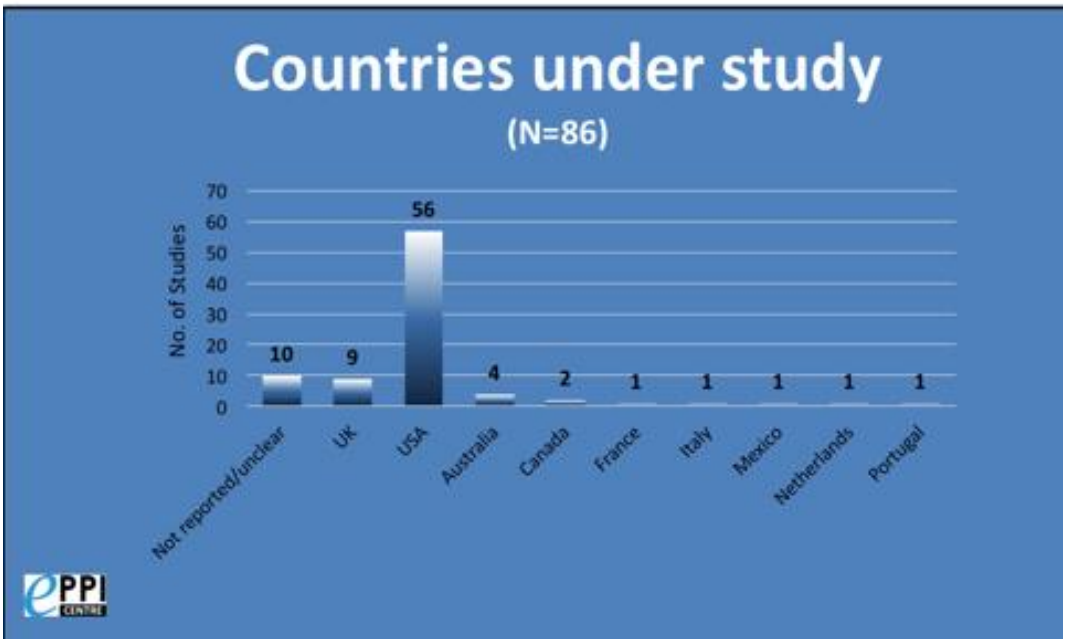
A key feature of the cost-benefit approach is that the analysis can be completed for a single intervention since the comparison is between costs and outcomes, not the difference between costs and outcomes as with cost-effectiveness and cost-utility analysis.

Appendix 3: Flow of studies through review

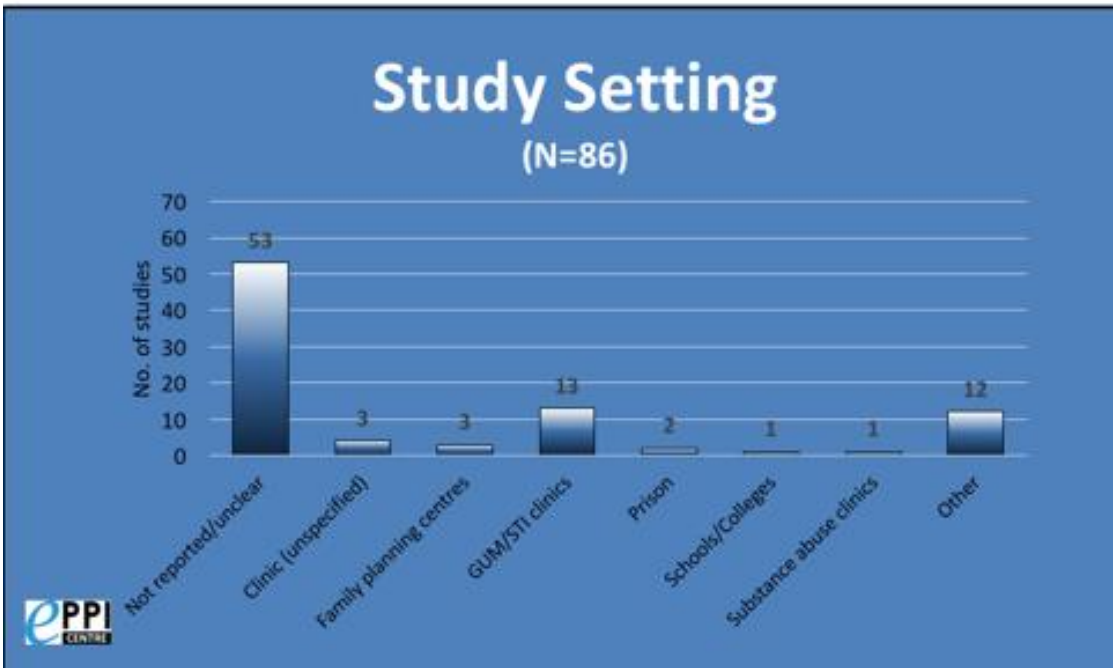


Appendix 4: Characteristics of included studies: Descriptive map

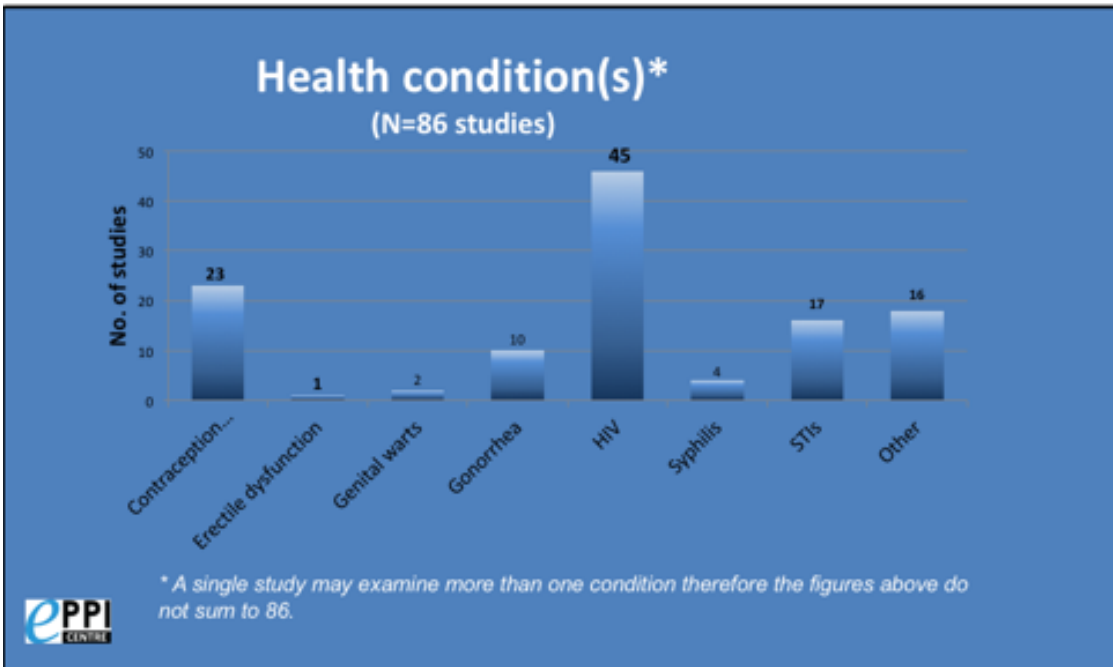
Characteristics of included economic evaluations



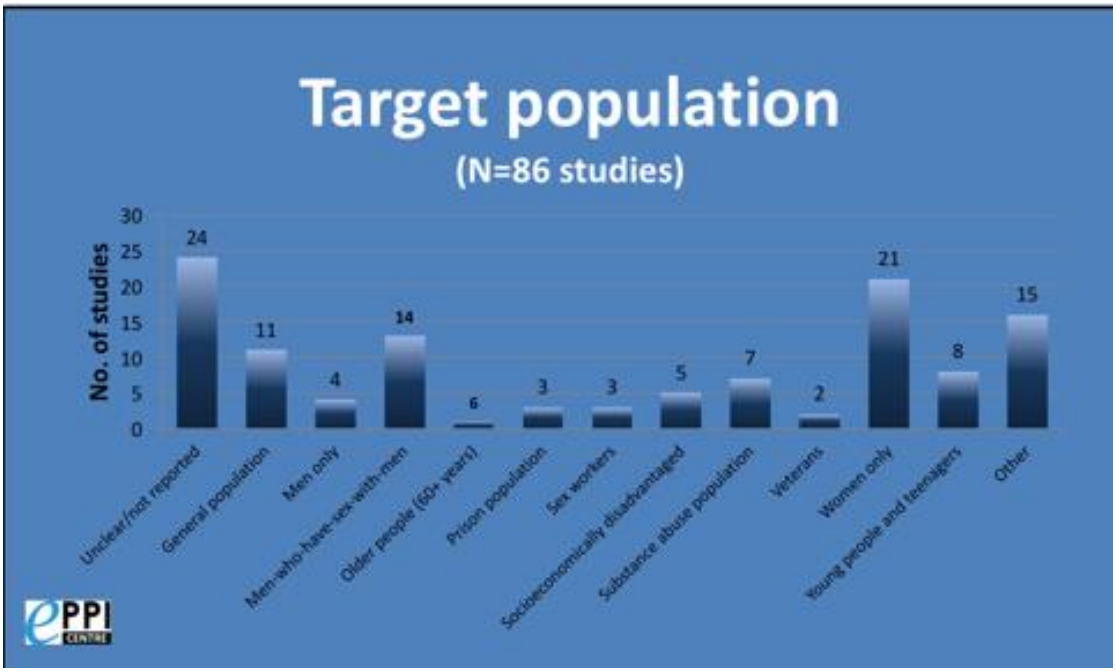
Characteristics of included economic evaluations



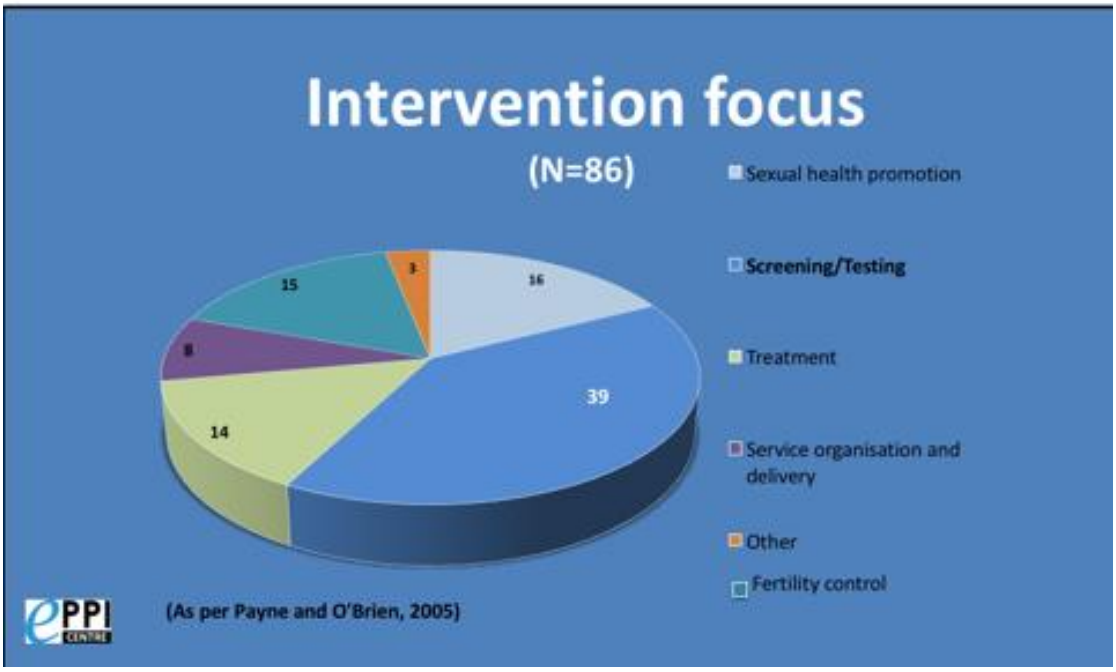
Characteristics of included economic evaluations



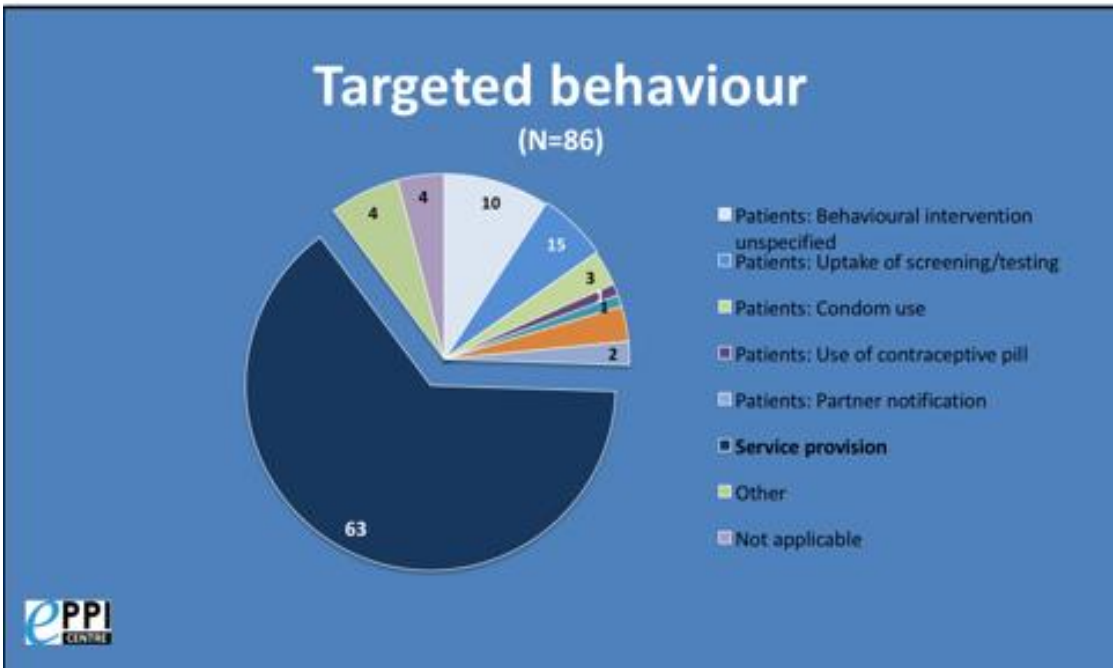
Characteristics of included economic evaluations



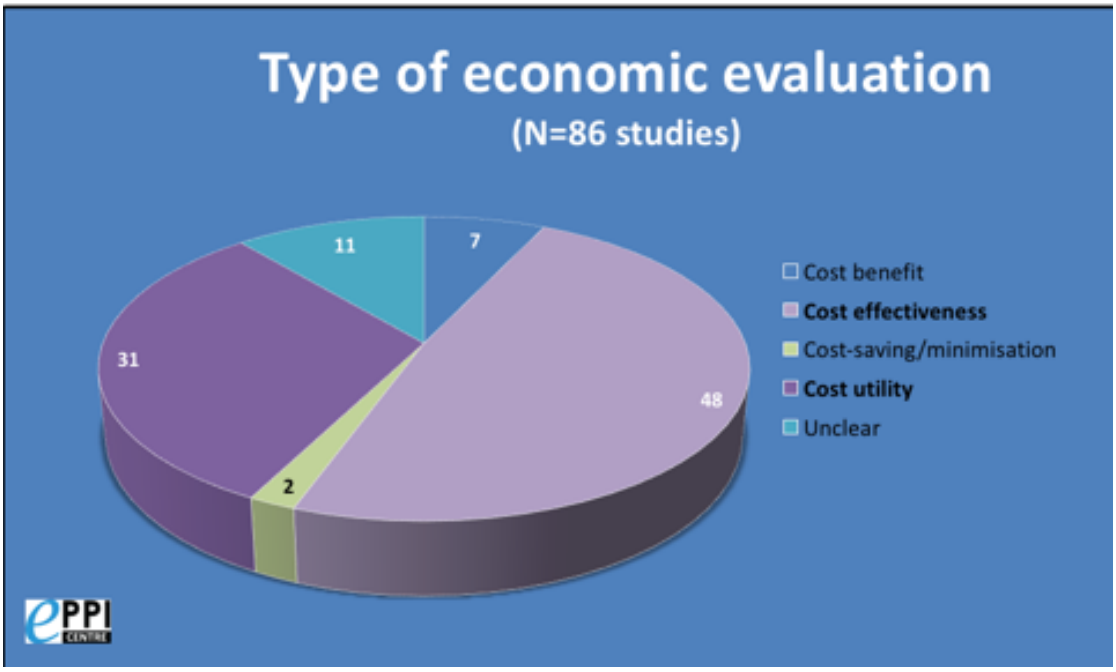
Characteristics of included economic evaluations



Characteristics of included economic evaluations



Characteristics of included economic evaluations



Appendix 5: Risk of bias/methodological quality assessment tools

NICE Intervention Study Checklist

1. Source population/source area well described?
Was the country (e.g. developed or non-developed, type of healthcare system), setting (primary schools, community centres etc.), location (urban, rural), population demographics etc. adequately described?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

2. Eligible population/area representative of source population/area?
Was the recruitment of individuals, clusters or areas well defined (e.g. advertisement, birth register)? Was the eligible population representative of the source? Were important groups under-represented?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

3. Do selected participants/areas represent the eligible population/ area?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

4. Allocation to exposure and comparison randomised?
Was allocation to exposure and comparison randomised? Was it truly random ++ or pseudo-randomised + (e.g. consecutive admissions)? If not randomised, was significant confounding likely (−) or not (+)? If a cross-over, was order of intervention randomised?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

5. Interventions (and comparisons) well described and appropriate?
Were interventions and comparisons described in sufficient detail (i.e. enough for study to be replicated)? Were comparisons appropriate (e.g. usual practice rather than no intervention)?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
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Not reported
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Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

6. Was allocation concealed?
Could the person(s) determining allocation of participants or clusters to intervention or comparison groups have influenced the allocation? Adequate allocation concealment (++) would include centralised allocation or computerised allocation systems.

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
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Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

7. Participants and/or investigators blind to exposure and comparison?
Were participants and investigators – those delivering or assessing the intervention – kept blind to intervention allocation? (Triple or double blinding score ++) If lack of blinding is likely to cause important bias, score −

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
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Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

8. Exposure to the intervention and comparison adequate?
Is reduced exposure to intervention or control related to the intervention (e.g. adverse effects leading to reduced compliance) or fidelity of implementation (e.g. reduced adherence to protocol)? Was lack of exposure sufficient to cause important bias?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
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Not reported
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Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

9. Contamination acceptably low?
Did any in the comparison group receive the intervention or vice versa? If so, was it sufficient to cause important bias? If a cross-over trial, was there a sufficient wash-out period between interventions?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

10. Other interventions similar in both groups?
Did either group receive additional interventions or have services provided in a different manner? Were the groups treated equally by researchers or other professionals? Was this sufficient to cause important bias?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

11. All participants accounted for at study conclusion?
Were those lost-to-follow-up (i.e. dropped or lost pre-, during or post-intervention) acceptably low (i.e. typically <20%)? Did the proportion dropped differ by group? For example, were drop-outs related to the adverse effects of the intervention?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
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Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

12. Does setting reflect usual UK practice?
Did the setting in which the intervention or comparison was delivered differ significantly from usual practice in the UK? For example, did participants receive intervention (or comparison) condition in a hospital rather than a community-based setting?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
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Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

13. Does intervention/comparison reflect usual UK practice?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

14. Outcome measures reliable?
Were outcome measures subjective or objective (e.g. biochemically validated nicotine levels ++ vs self-reported smoking −)? How reliable were outcome measures (e.g. inter- or intra-rater reliability scores)? Was there any indication that measures had been validated (e.g. validated against a gold standard measure or assessed for content validity)?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

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Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review

15. All outcome measurements complete?
Were all or most study participants who met the defined study outcome definitions likely to have been identified?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review

16. All important outcomes assessed?
Were all important benefits and harms assessed? Was it possible to determine the overall balance of benefits and harms of the intervention versus comparison?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
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Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

17. Outcomes relevant?
Where surrogate outcome measures were used, did they measure what they set out to measure? (e.g. a study to assess impact on physical activity assesses gym membership - a potentially objective outcome measure - but is it a reliable predictor of physical activity?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

18. Similar follow-up times in exposure and comparison groups?
If groups are followed for different lengths of time, then more events are likely to occur in the group followed-up for longer distorting the comparison. Analyses can be adjusted to allow for differences in length of follow-up (e.g. using person-years).

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

19. Follow-up time meaningful?
Was follow-up long enough to assess long-term benefits or harms? Was it too long, e.g. participants lost to follow-up?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

20. Exposure and comparison groups similar at baseline?
Were there any differences between groups in important confounders at baseline? If so, were these adjusted for in the analyses (e.g. multivariate analyses or stratification). Were there likely to be any residual differences of relevance?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

21. Intention to treat (ITT) analysis conducted?
Were all participants (including those that dropped out or did not fully complete the intervention course) analysed in the groups (i.e. intervention or comparison) to which they were originally allocated?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

22. Study sufficiently powered?
Was the study sufficiently powered to detect an intervention effect (if one exists)? A power of 0.8 (that is, it is likely to see an effect of a given size if one exists, 80% of the time) is the conventionally accepted standard. Is a power calculation presented? If not, what is the expected effect size? Is the sample size adequate?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

23. Effect size given or calculable?
Were effect estimates (e.g. relative risks, absolute risks) given or possible to calculate?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

24. Analytical methods appropriate?
Were important differences in follow-up time and likely confounders adjusted for? If a cluster design, were analyses of sample size (and power), and effect size performed on clusters (and not individuals)? Were subgroup analyses pre-specified?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

25. Precision of intervention effects given or calculable?
Was the precision of intervention effects given or calculable? Were they meaningful? Were confidence intervals or p values for effect estimates given or possible to calculate? Were CIs wide or were they sufficiently precise to aid decision-making? If precision is lacking, is this because the study is under-powered?

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

Not reported
Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

Not applicable
Should be reserved for those study design aspects that are not applicable given the study design under review.

26. Study results internally valid (i.e. unbiased)?
How well did the study minimise sources of bias (i.e. adjusting for potential confounders)? Were there significant flaws in the study design?

++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter.
+ Some of the checklist criteria have been fulfilled, where they have not been fulfilled, or not adequately described, the conclusions are unlikely to alter.
− Few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter.

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

27. Study results externally valid (i.e. generalisable to source population)?
Are the findings generalisable to the source population (i.e. externally valid)? Are there sufficient details given about the study to determine if the findings are generalisable to the source population? Consider: participants, interventions and comparisons, outcomes, resource and policy implications.

++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter.
+ Some of the checklist criteria have been fulfilled, where they have not been fulfilled, or not adequately described, the conclusions are unlikely to alter.
− Few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter.

++
Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.

+
Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

-
Should be reserved for those aspects of the study design in which significant sources of bias may persist.

AMSTAR Systematic Reviews Checklist

1 Was an 'a priori' design provided?
The research question and inclusion criteria should be established before the conduct of the review.
Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."

- Yes
- No
- Not reported
- Not applicable

2 Was there duplicate study selection and data extraction?
There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.

Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.

- Yes
- No
- Not reported
- Not applicable

3 Was a comprehensive literature search performed?
At least two electronic sources should be searched. The report must include years and databases used (e.g., Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. Note: If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary)

- Yes
- No
- Not reported
- Not applicable

4 Was the status of publication (i.e. grey literature) used as an inclusion criterion?
The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. Note: If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.

- Yes
- No
- Not reported
- Not applicable

5 Was a list of studies (included and excluded) provided?
A list of included and excluded studies should be provided. Note: Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no."

- Yes
- No

- Not reported
- Not applicable

6 Were the characteristics of the included studies provided?
In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. Note: Acceptable if not in table format as long as they are described as above.

- Yes
- No
- Not reported
- Not applicable

7 Was the scientific quality of the included studies assessed and documented?
'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant. Note: Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable)

- Yes
- No
- Not reported
- Not applicable

8 Was the scientific quality of the included studies used appropriately in formulating conclusions?
The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.

- Yes
- No
- Not reported
- Not applicable

9 Were the methods used to combine the findings of studies appropriate?
For the pooled results, a test should be done to ensure the studies were combinable, to

assess their homogeneity (i.e., Chi-squared test for homogeneity, I2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Note: Indicate "yes" if they mention or describe heterogeneity, i.e., if they explain that they cannot pool because of heterogeneity/variability between interventions.

- Yes
- No
- Not reported
- Not applicable

10 Was the likelihood of publication bias assessed?
An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.

- Yes
- No
- Not reported
- Not applicable

11 Was conflict of interest included?
Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.
Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies.

- Yes
- No
- Not reported
- Not applicable

Overall quality
Score 1 for not applicable. Score 0 for not reported.

- **Sound**
  Must score 'yes' for question 1, 3, 7 and 9 and 'yes' for more than 5 questions overall.
- **Unsound**
  Does NOT score 'yes' for questions 1, 3, 7 and 9, and/or scores 5 or less overall

Combined Health Economic Evaluation Checklist

Section 1. Applicability

For all questions:

-answer 'yes' if the study fully meets the criterion

-answer 'partly' if the study largely meets the criterion but differs in some important respect

-answer 'no' if the study deviates substantively from the criterion

-answer 'unclear' if the report provides insufficient information to judge whether the study complies with the criterion

-answer 'NA (not applicable)' if the criterion is not relevant in a particular instance.

For 'partly' or 'no' responses, use the comments column to explain how the study deviates from the criterion.

1.1 Is the study population appropriate?

The study population should be defined as precisely as possible and should be in line with that specified in the guideline scope and any related review protocols.

This includes consideration of appropriate subgroups that require special attention. For many interventions, the capacity to benefit will differ for participants with differing characteristics. This should be explored separately for each relevant subgroup as part of the base-case analysis by the provision of estimates of clinical and cost-effectiveness. The characteristics of participants in each subgroup should be clearly defined and, ideally, should be identified on the basis of an a priori expectation of differential clinical or cost-effectiveness as a result of biologically plausible known mechanisms, social characteristics or other clearly justified factors.

Answer 'yes' if the study population is fully in line with that in the guideline question(s) and if the study differentiates appropriately between important subgroups. Answer 'partly' if the study population is similar to that in the guideline question(s) but: (i) it differs in some important respects; or (ii) the study fails to differentiate between important subgroups. Answer 'no' if the study population is substantively different from that in the guideline question(s).

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

1.2 Are the interventions and services appropriate?

All relevant alternatives should be included, as specified in the guideline scope and any related review protocols. These should include routine and best practice in the NHS, existing NICE guidance and other feasible options.

Answer 'yes' if the analysis includes all options considered relevant for the guideline, even if it also includes other options that are not relevant. Answer 'partly' if the analysis omits one or more relevant options but still contains comparisons likely to be useful for the guideline. Answer 'no' if the analysis does not contain any relevant comparisons.

- Yes
- No/Unclear
- Partly
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

1.3 Is the healthcare system in which the study was conducted sufficiently similar to the current UK NHS context?

This relates to the overall structure of the healthcare system within which the interventions were delivered. For example, an intervention might be delivered on an inpatient basis in one country whereas in the UK it would be provided in the community. This might significantly influence the use of healthcare resources and costs, thus limiting the applicability of the results to a UK setting. In addition, old UK studies may be severely limited in terms of their relevance to current NHS practice.

Answer 'yes' if the study was conducted within the UK and is sufficiently recent to reflect current NHS practice. For non-UK or older UK studies, answer 'partly' if differences in the healthcare setting are unlikely to substantively change the cost-effectiveness estimates. Answer 'no' if the healthcare setting is so different that the results are unlikely to be applicable in the current NHS.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

1.4 Are costs measured from the societal, health care and personal social services (PSS) perspective?

The decision-making perspective of an economic evaluation determines the range of costs that should be included in the analysis. NICE works in a specific context; in particular, it does not set the budget for the NHS. The objective of NICE is to offer guidance that represents an efficient use of available NHS and PSS resources. For these reasons, the perspective on costs used in the NICE reference case is that of the NHS and PSS. Productivity costs and costs borne by patients and carers that are not reimbursed by the NHS or PSS are not included in the reference case. The reference case also excludes costs to other government bodies, although these may sometimes be presented in additional analyses alongside the reference case.

Answer 'yes' if the study only includes costs for resource items that would be paid for by the NHS and PSS. Also answer 'yes' if other costs have been included in the study, but the

results are presented in such a way that the cost-effectiveness can be calculated from an NHS and PSS perspective. Answer 'partly' if the study has taken a wider perspective but the other non-NHS/PSS costs are small in relation to the total expected costs and are unlikely to change the cost-effectiveness results. Answer 'no' if non-NHS/PSS costs are significant and are likely to change the cost-effectiveness results.

Some interventions may have a substantial impact on non-health outcomes or costs to other government bodies (for example, treatments to reduce illicit drug misuse may have the effect of reducing drug-related crime). In such situations, if the economic study includes non-health costs in such a way that they cannot be separated out from NHS/PSS costs, answer 'no' but consider retaining the study for critical appraisal. If studies containing non-reference-case costs are retained, use the comments column to note why.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

1.5 Are non-direct health effects on individuals excluded?

In the NICE reference case, the perspective on outcomes should be all direct health effects, whether for patients or, when relevant, other people (principally carers). This is consistent with an objective of maximising health gain from available healthcare resources. Some features of healthcare delivery that are often referred to as 'process characteristics' may ultimately have health consequences; for example, the mode of treatment delivery may have health consequences through its impact on concordance with treatment. Any significant characteristics of healthcare technologies that have a value to people that is independent of any direct effect on health should be noted. These characteristics include the convenience with which healthcare is provided and the level of information available for patients.

This question should be viewed in terms of what is excluded in relation to the NICE reference case; that is, non-health effects.

Answer 'yes' if the measure of health outcome used in the analysis excludes non-health effects (or if such effects can be excluded from the results). Answer 'partly' if the analysis includes some non-health effects but these are small and unlikely to change the cost-effectiveness results. Answer 'no' if the analysis includes significant non-health effects that are likely to change the cost-effectiveness results.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

1.6 Are both costs and health effects discounted at an annual rate of 3.5%?

NOTE: 3.0% is also considered an acceptable rate. The need to discount to a present value is widely accepted in economic evaluation, although the specific rate varies across jurisdictions and over time. NICE considers it appropriate to discount costs and health effects at the same rate. The annual rate of 3.5%, based on the recommendations of the UK Treasury for the discounting of costs, applies to both costs and health effects.

Answer 'yes' if both costs and health effects (for example, quality-adjusted life years [QALYs]) are discounted at 3.5% per year. Answer 'partly' if costs and health effects are discounted at a rate similar to 3.5% (for example, costs and effects are both discounted at 3% per year). Answer 'no' if costs and/or health effects are not discounted, or if they are discounted at a rate (or rates) different from 3.5% (for example, 5% for both costs and effects, or 6% for costs and 1.5% for effects). Note in the comments column what discount rates have been used. If all costs and health effects accrue within a short time (roughly a year), answer 'NA'.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

1.7 Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?

The QALY is a measure of a person's length of life weighted by a valuation of their health-related quality of life (HRQoL) over that period. Given its widespread use, the QALY is considered by NICE to be the most appropriate generic measure of health benefit that reflects both mortality and effects on HRQoL. It is recognised that alternative measures exist (such as the healthy-year equivalent), but few economic evaluations have used these methods and their strengths and weaknesses are not fully established.

NICE's position is that an additional QALY should be given the same weight regardless of the other characteristics of the patients receiving the health benefit.

Answer 'yes' if the effectiveness of the intervention is measured using QALYs; answer 'no' if not. There may be circumstances when a QALY cannot be obtained or where the assumptions underlying QALYs are considered inappropriate. In such situations answer 'no', but consider retaining the study for appraisal. Similarly, answer 'no' but retain the study for appraisal if it does not include QALYs but it is still thought to be useful for Guideline Development Group decision-making: for example, if the clinical evidence indicates that an intervention might be dominant, and estimates of the relative costs of the interventions from a cost-minimisation study are likely to be useful. When economic evaluations not using QALYs are retained for full critical appraisal, use the comments column to note why.

- Yes
- Partly
- No/Unclear

- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

1.8 Are changes in health-related quality of life (HRQoL) reported directly from patients and/or carers?

In the NICE reference case, information on changes in HRQoL as a result of treatment should be reported directly by patients (and directly by carers when the impact of treatment on the carer's health is also important). When it is not possible to obtain information on changes in patients' HRQoL directly from them, data should be obtained from carers (not from healthcare professionals).

For consistency, the EQ-5D is NICE's preferred measure of HRQoL in adults. However, when EQ-5D data are not available or are inappropriate for the condition or the effects of treatment, other multi-attribute utility questionnaires (for example, SF6D, QWB or HUI) or mapping methods from disease-specific questionnaires may be used to estimate QALYs. For studies not reporting QALYs, a variety of generic or disease-specific methods may be used to measure HRQoL.

Answer 'yes' if changes in patients' HRQoL are estimated by the patients themselves. Answer 'partly' if estimates of patients' HRQoL are provided by carers. Answer 'no' if estimates come from healthcare professionals or researchers. Note in the comments column how HRQoL was measured (EQ-5D, QWB, HUI and so on). Answer 'NA' if the cost-effectiveness study does not include estimates of HRQoL (for example, studies reporting 'cost per life year gained' or cost-minimisation studies).

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

1.9 Is the valuation of changes in HRQoL (utilities) obtained from a representative sample of the general public?

The NICE reference case specifies that the valuation of changes in HRQoL (utilities) reported by patients should be based on public preferences elicited using a choice-based method (such as the time trade-off or standard gamble) in a representative sample of the UK population.

Answer 'yes' if HRQoL valuations were obtained using the EQ-5D UK tariff. Answer 'partly' if the valuation methods were comparable to those used for the EQ-5D. Answer 'no' if other valuation methods were used. Answer 'NA' if the study does not apply valuations to HRQoL (for studies not reporting QALYs). In the comments column note the valuation method used (such as time trade-off or standard gamble) and the source of the preferences (such as patients or healthcare professionals).

- Yes
- Partly

- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

1.10 Section 1 judgement

Classify the applicability of the economic evaluation to the clinical guideline, the current NHS situation and the context for NICE guidance as one of the following:

Directly applicable – the study meets all applicability criteria, or fails to meet one or more applicability criteria but this is unlikely to change the conclusions about cost-effectiveness.

Partially applicable - the study fails to meet one or more applicability criteria, and this could change the conclusions about cost-effectiveness.

Not applicable – the study fails to meet one or more applicability criteria, and this is likely to change the conclusions about cost-effectiveness. Such studies would usually be excluded from further consideration and there is no need to continue with the rest of the checklist.

- Directly applicable=1
- Partially applicable=0.5
- No applicability=0

Section 2. Study limitations

For all questions:

-answer 'yes' if the study fully meets the criterion

-answer 'partly' if the study largely meets the criterion but differs in some important respect

-answer 'no' if the study deviates substantively from the criterion

-answer 'unclear' if the report provides insufficient information to judge whether the study complies with the criterion

-answer 'NA (not applicable)' if the criterion is not relevant in a particular instance. For 'partly' or 'no' responses, use the comments column to explain how the study deviates from the criterion.

2.1 Does the model structure adequately reflect the nature of the health condition under evaluation?

This relates to the choice of model and its structural elements (including cycle length in discrete time models, if appropriate). Model type and its structural aspects should be consistent with a coherent theory of the health condition under evaluation. The selection of treatment pathways, whether health states or branches in a decision tree, should be

based on the underlying biological processes of the health issue under study and the potential impact (benefits and adverse consequences) of the intervention(s) of interest.

Answer 'yes' if the model design and assumptions appropriately reflect the health condition and intervention(s) of interest. Answer 'partly' if there are aspects of the model design or assumptions that do not fully reflect the health condition or intervention(s) but these are unlikely to change the cost-effectiveness results. Answer 'no' if the model omits some important aspect of the health condition or intervention(s) and this is likely to change the cost-effectiveness results. Answer 'NA' for economic evaluations based on data from a clinical study which do not extrapolate treatment outcomes or costs beyond the study context or follow-up period.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?

The time horizon is the period of analysis of the study: the length of follow-up for participants in a trial-based evaluation, or the period of time over which the costs and outcomes for a cohort are tracked in a modelling study. This time horizon should always be the same for costs and outcomes, and should be long enough to include all relevant costs and outcomes relating to the intervention. A time horizon shorter than lifetime could be justified if there is no differential mortality effect between options, and the differences in costs and HRQoL relate to a relatively short period (for example, in the case of an acute infection).

Answer 'yes' if the time horizon is sufficient to include all relevant costs and outcomes. Answer 'partly' if the time horizon may omit some relevant costs and outcomes but these are unlikely to change the cost-effectiveness results. Answer 'no' if the time horizon omits important costs and outcomes and this is likely to change the cost-effectiveness results.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

2.3 Are all important and relevant health outcomes included?

All relevant health outcomes should include direct health effects relating to harms from the intervention (adverse effects) as well as any potential benefits.

Answer 'yes' if the analysis includes all relevant and important harms and benefits. Answer 'partly' if the analysis omits some harms or benefits but these would be unlikely to change the cost-effectiveness results. Answer 'no' if the analysis omits important harms and/or benefits that would be likely to change the cost-effectiveness results.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

2.4 Are the estimates of baseline health outcomes from the best available source?

The estimate of the overall net treatment effect of an intervention is determined by the baseline risk of a particular condition or event and/or the relative effects of the intervention compared with the relevant comparator treatment. The overall net treatment effect may also be determined by other features of the people comprising the population of interest.

The process of assembling evidence for economic evaluations should be systematic – evidence must be identified, quality assessed and, when appropriate, pooled, using explicit criteria and justifiable and reproducible methods. These principles apply to all categories of evidence that are used to estimate clinical and cost-effectiveness, evidence for which will typically be drawn from a number of different sources.

The sources and methods for eliciting baseline probabilities should be described clearly. These data can be based on 'natural history' (patient outcomes in the absence of treatment or with routine care), sourced from cohort studies. Baseline probabilities may also be derived from the control arms of experimental studies. Sometimes it may be necessary to rely on expert opinion for particular parameters.

Answer 'yes' if the estimates of baseline health outcomes reflect the best available evidence as identified from a recent well-conducted systematic review of the literature. Answer 'partly' if the estimates are not derived from a systematic review but are likely to reflect outcomes for the relevant group of patients in routine NHS practice (for example, if they are derived from a large UK-relevant cohort study). Answer 'no' if the estimates are unlikely to reflect outcomes for the relevant group in routine NHS practice.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

2.5 Are the estimates of relative treatment effects from the best available source?

The objective of the analysis of clinical effectiveness is to produce an unbiased estimate of the mean clinical effectiveness of the interventions being compared.

The NICE reference case indicates that evidence on outcomes should be obtained from a systematic review, defined as the systematic location, inclusion, appraisal and synthesis of evidence to obtain a reliable and valid overview of the data relating to a clearly formulated question.

Synthesis of outcome data through meta-analysis is appropriate provided that there are sufficient relevant and valid data obtained using comparable measures of outcome.

Head-to-head randomised controlled trials (RCTs) provide the most valid evidence of relative treatment effect. However, such evidence may not always be available. Therefore, data from non-randomised studies may be required to supplement RCT data. Any potential bias arising from the design of the studies used in the assessment should be explored and documented.

Data from head-to-head RCTs should be presented in the base-case analysis, if available. When head-to-head RCTs exist, evidence from indirect or mixed treatment comparison analyses may be presented if it is considered to add information that is not available from the head-to-head comparison. This indirect or mixed treatment comparison must be fully described and presented as additional to the base-case analysis. (A 'mixed treatment comparison' estimates effect sizes using both head-to-head and indirect comparisons.)

If data from head-to-head RCTs are not available, indirect treatment comparison methods should be used. (An 'indirect treatment comparison' is a synthesis of data from a network of trials that compare the interventions of interest with other comparators.)

When multiple interventions are being assessed that have not been compared within a single RCT, data from a series of pairwise head-to-head RCTs should be presented. Consideration should also be given to presenting a combined analysis using a mixed treatment comparison framework if it is considered to add information that is not available from the head-to-head comparison.

Only indirect or mixed treatment comparison methods that preserve randomisation should be used. The principles of good practice for standard meta-analyses should also be followed in mixed and indirect treatment comparisons.

The methods and assumptions that are used to extrapolate short-term results to final outcomes should be clearly presented and there should be documentation of the reasoning underpinning the choice of survival function.

Evidence for the evaluation of diagnostic technologies should normally incorporate evidence on diagnostic accuracy. It is also important to incorporate the predicted changes in health outcomes and costs resulting from treatment decisions based on the test result. The general principles guiding the assessment of the clinical and cost-effectiveness of diagnostic interventions should be the same as for other technologies. However, particular consideration of the methods of analysis may be required, particularly in relation to evidence synthesis. Evidence for the effectiveness of diagnostic technologies should include the costs and outcomes for people whose test results lead to an incorrect diagnosis, as well as for those who are diagnosed correctly.

As for other technologies, RCTs have the potential to capture the pathway of care involving diagnostic technologies, but their feasibility and availability may be limited. Other study designs should be assessed on the basis of their fitness for purpose, taking into consideration the aim of the study (for example, to evaluate outcomes, or to evaluate sensitivity and specificity) and the purpose of the diagnostic technology.

Answer 'yes' if the estimates of treatment effect appropriately reflect all relevant studies of the best available quality, as identified through a recent well-conducted systematic review of the literature. Answer 'partly' if the estimates of treatment effect are not derived from a systematic review but are similar in magnitude to the best available estimates (for example, if the economic evaluation is based on a single large study with treatment effects similar to pooled estimates from all relevant studies). Answer 'no' if the estimates of treatment effect are likely to differ substantively from the best available estimates.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

2.6 Are all important and relevant costs included?

Costs related to the condition of interest and incurred in additional years of life gained as a result of treatment should be included in the base-case analysis. This should include the costs of handling non-adherence to treatment and treating side effects. Costs that are considered to be unrelated to the condition or intervention of interest should be excluded. If introduction of the intervention requires additional infrastructure to be put in place, consideration should be given to including such costs in the analysis.

Answer 'yes' if all important and relevant resource use and costs are included given the perspective and the research question in the economic study under consideration. Answer 'partly' if some relevant resource items are omitted but these are unlikely to affect the cost-effectiveness results. Answer 'no' if important resource items are omitted and these are likely to affect the cost-effectiveness results.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

2.7 Are the estimates of resource use from the best available source?

It is important to quantify the effect of the interventions on resource use in terms of physical units (for example, days in hospital or visits to a GP) and valuing those effects in monetary terms using appropriate prices and unit costs. Evidence on resource use should

be identified systematically. When expert opinion is used as a source of information, any formal methods used to elicit these data should be clearly reported.

Answer 'yes' if the estimates of resource use appropriately reflect all relevant evidence sources of the best available quality, as identified through a recent well-conducted systematic review of the literature. Answer 'partly' if the estimates of resource use are not derived from a systematic review but are similar in magnitude to the best available estimates. Answer 'no' if the estimates of resource use are likely to differ substantively from the best available estimates.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

2.8 Are the unit costs of resources from the best available source?

Resources should be valued using the prices relevant to the NHS and PSS. Given the perspective of the NICE reference case, it is appropriate for the financial costs relevant to the NHS/PSS to be used as the basis of costing, although these may not always reflect the full social opportunity cost of a given resource. A first point of reference in identifying costs and prices should be any current official listing published by the Department of Health and/or the Welsh Government.

When the acquisition price paid for a resource differs from the public list price (for example, pharmaceuticals and medical devices sold at reduced prices to NHS institutions), the public list price should be used in the base-case analysis. Sensitivity analysis should assess the implications of variations from this price. Analyses based on price reductions for the NHS will only be considered when the reduced prices are transparent and can be consistently available across the NHS, and if the period for which the specified price is available is guaranteed.

National data based on healthcare resource groups (HRGs) such as the Payment by Results tariff can be used when they are appropriate and available. However, data based on HRGs may not be appropriate in all circumstances (for example, when the definition of the HRG is broad, or the mean cost probably does not reflect resource use in relation to the intervention(s) under consideration). In such cases, other sources of evidence, such as micro-costing studies, may be more appropriate. When cost data are taken from the literature, the methods used to identify the sources should be defined. When several alternative sources are available, a justification for the costs chosen should be provided and discrepancies between the sources explained. When appropriate, sensitivity analysis should have been undertaken to assess the implications for results of using alternative data sources.

Answer 'yes' if resources are valued using up-to-date prices relevant to the NHS and PSS. Answer 'partly' if the valuations of some resource items differ from current NHS/PSS unit costs but this is unlikely to change the cost-effectiveness results. Answer 'no' if the valuations of some resource items differ substantively from current NHS/PSS unit costs and this is likely to change the cost-effectiveness results.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?

An appropriate incremental analysis is one that compares the expected costs and health outcomes of one intervention with the expected costs and health outcomes of the next-best non-dominated alternative.

Standard decision rules should be followed when combining costs and effects, and should reflect any situation where there is dominance or extended dominance. When there is a trade-off between costs and effects, the results should be presented as an incremental cost-effectiveness ratio (ICER): the ratio of the difference in mean costs to the difference in mean outcomes of a technology compared with the next best alternative. In addition to ICERs, expected net monetary or health benefits can be presented using values placed on a QALY gained of £20,000 and £30,000.

For cost-consequence analyses, appropriate incremental analysis can only be done by selecting one of the consequences as the primary measure of effectiveness.

Answer 'yes' if appropriate incremental results are presented, or if data are presented that allow the reader to calculate the incremental results. Answer 'no' if: (i) simple ratios of costs to effects are presented for each alternative compared with a standard intervention; or (ii) if options subject to simple or extended dominance are not excluded from the incremental analyses.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?

There are a number of potential selection biases and uncertainties in any evaluation (trial- or model-based) and these should be identified and quantified where possible. There are three types of bias or uncertainty to consider:

Structural uncertainty – for example in relation to the categorisation of different states of health and the representation of different pathways of care. These structural assumptions should be clearly documented and the evidence and rationale to support them provided.

The impact of structural uncertainty on estimates of cost-effectiveness should be explored by separate analyses of a representative range of plausible scenarios.

Source of values to inform parameter estimates - the implications of different estimates of key parameters (such as estimates of relative effectiveness) must be reflected in sensitivity analyses (for example, through the inclusion of alternative scenarios). Inputs must be fully justified, and uncertainty explored by sensitivity analysis using alternative input values.

Parameter precision - uncertainty around the mean health and cost inputs in the model. Distributions should be assigned to characterise the uncertainty associated with the (precision of) mean parameter values. Probabilistic sensitivity analysis is preferred, as this enables the uncertainty associated with parameters to be simultaneously reflected in the results of the model. In non-linear decision models - when there is not a straight-line relationship between inputs and outputs of a model (such as Markov models) - probabilistic methods provide the best estimates of mean costs and outcomes. Simple decision trees are usually linear. The mean value, distribution around the mean, and the source and rationale for the supporting evidence should be clearly described for each parameter included in the model. Evidence about the extent of correlation between individual parameters should be considered carefully and reflected in the probabilistic analysis. Assumptions made about the correlations should be clearly presented.

Answer 'yes' if an extensive sensitivity analysis was undertaken that explored all key uncertainties in the economic evaluation. Answer 'partly' if the sensitivity analysis failed to explore some important uncertainties in the economic evaluation. Answer 'no' if the sensitivity analysis was very limited and omitted consideration of a number of important uncertainties, or if the range of values or distributions around parameters considered in the sensitivity analysis were not reported.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

2.11 Is there no potential conflict of interest?

The British Medical Journal (BMJ) defines competing interests for its authors as follows: "A competing interest exists when professional judgment concerning a primary interest (such as patients' welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or personal rivalry). It may arise for the authors of a BMJ article when they have a financial interest that may influence, probably without their knowing, their interpretation of their results or those of others."

Whenever a potential financial conflict of interest is possible, this should be declared.

Answer 'yes' if the authors declare that they have no financial conflicts of interest. Answer 'no' if clear financial conflicts of interest are declared or apparent (for example, from the stated affiliation of the authors). Answer 'unclear' if the article does not indicate whether or not there are financial conflicts of interest.

- Yes
- Partly
- No/Unclear
- Not applicable
  This should rate as 1 so as not to disadvantage a study which rightly does not assess this.

2.12 Section judgement

The overall methodological study quality of the economic evaluation should be classified as one of the following:

Minor limitations - the study meets all quality criteria, or fails to meet one or more quality criteria but this is unlikely to change the conclusions about cost-effectiveness.

Potentially serious limitations - the study fails to meet one or more quality criteria, and this could change the conclusions about cost-effectiveness.

Very serious limitations - the study fails to meet one or more quality criteria, and this is highly likely to change the conclusions about cost-effectiveness. Such studies should usually be excluded from further consideration.

- Minor limitations=1
- Potentially serious limitations=0.5
- Very serious limitations=0

Section 3. Modelling appraisal

3.1 Have methodological uncertainties been addressed?

Methodological uncertainty relates to whether particular analytical steps taken in the analysis are the most appropriate. Have methodological uncertainties been addressed by running alternative versions of the model with different methodological assumptions?

- Yes
- Partly
- No
- Not applicable

3.2 Have structural uncertainties been addressed?

Is there evidence that structural uncertainties have been addressed via sensitivity analysis?

- Yes
- Partly
- No

- Not applicable

3.3 Have heterogeneity uncertainties been addressed?

It is important to distinguish between uncertainty resulting from the process of sampling from a population and variability due to heterogeneity (i.e. systematic differences between patient subgroups). Has heterogeneity been dealt with by running the model separately for different subgroups?

- Yes
- Partly
- No
- Not applicable

3.4 Have internal and external consistency issues been considered?

There should be evidence that the internal consistency of the model has been evaluated in terms of its mathematical logic. In addition, the results of a model should be explicable. Either results should make intuitive sense or counterintuitive results should be fully explained.

All relevant available data should be incorporated into a model. Data should not be withheld for purposes of assessing external consistency.

The results of a model should be compared with those of previous models and any differences should be explained.

Consider:

-Is there evidence that the mathematical logic of the model has been tested thoroughly before use?

-Are any counterintuitive results from the model explained and justified?

-If the model has been calibrated against independent data, have any differences been explained and justified?

-Have the results of the model been compared with those of previous models and any differences in results explained?

- Yes
- Partly
- No
- Not applicable

3.5 Section judgement

The overall methodological study quality of the economic evaluation should be classified as one of the following:

Minor limitations – the study meets all quality criteria, or fails to meet one or more quality criteria but this is unlikely to change the conclusions about cost-effectiveness.

Potentially serious limitations – the study fails to meet one or more quality criteria, and this could change the conclusions about cost-effectiveness.

Very serious limitations – the study fails to meet one or more quality criteria, and this is highly likely to change the conclusions about cost-effectiveness. Such studies should usually be excluded from further consideration.

- Minor limitations=1
- Potentially serious limitations=0.5
- Very serious limitations=0

Section 4. Overall quality rating

FOR AN INTRINSIC OR EXTRINSIC TRIAL
Section 1 + Section 2

- High
  Rating Sections 1+2=2
- Medium
  Rating Sections 1+2=1 or 1.5
- Low
  Rating Sections 1+2=0 or 0.5

FOR MODELLING STUDIES

Section 1 + Section 2 + Section 3
HIGH=2.5-3 / MEDIUM=1.5-2 / LOW=0-0.5

Appendix 6: Risk of bias ratings: Trials and systematic reviews

Trials

Study (year)	Internal validity rating	External validity rating	Overall validity
Burgos (2010)	+	+	+
Crawford (2015)	++	+	++
Han (2014)	-	-	-
Holtgrave (2013)	-	-	-
Jackson (2015)	+	+	+
Marseille (2011)	-	-	-
Roberts (2012)	-	+	-
Rodriguez (2010b)	-	-	-
Ruger (2014)	-	-	-
Sanders (2010)	-	-	-
Schackman (2013)	+	+	+
Thomas & Cameron (2013)	++	++	++

++ All or most of the checklist criteria have been fulfilled; where they have not been fulfilled the conclusions are very unlikely to alter.

+ Some of the checklist criteria have been fulfilled; where they have not been fulfilled, or not adequately described, the conclusions are unlikely to alter.

− Few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter.

Systematic reviews

Study (year)	1. A priori question	3. Literature search	7. QA included studies	9. Appropriate synthesis	Two other criteria score 'yes'	Overall Validity
NCC (2013)	NR	Y	Y	Y	N	Unsound
Pilgrim (2010)	Y	Y	Y	Y	N	Unsound

Sound Review must score 'yes' for question 1, 3, 7 and 9 and 'yes' for more than 5 questions overall.

Unsound Review does NOT score 'yes' for questions 1, 3, 7 and 9, and/or scores 5 or less overall.

Appendix 7: Quality assessment ratings: Combined Health Economic Evaluation Checklist

Study (year)	Applicability	Study limitations	Modelling appraisal	Overall score	Rating
Bayer (2013)	0.5	0.5	0	1	Low
Burgos (2010)	0.5	0.5	1	2	Medium
Cooper (2012)	1	1	1	3	High
Crawford (2015)	1	1	1	3	High
Foster (2010)	0.5	0.5	0.5	1.5	Medium
Foster (2013)	0.5	0.5	0.5	1.5	Medium
Han (2014)	0.5	0	0	0.5	Low
Holtgrave (2012)	1	1	0.5	2.5	High
Holtgrave (2013)	0	0	0	0	Low
Jackson (2015)	0.5	0.5	0.5	1.5	Medium
Kessler (2013)	1	1	1	3	High
Lasry (2012)	0.5	0.5	0	1	Low
Long (2014)	1	1	0.5	2.5	High
Marseille (2011)	1	1	1	3	High
NCC (2013)	1	0.5	0.5	2	Medium
Pilgrim (2010)	0.5	0.5	0.5	1.5	Medium
Roberts (2012)	1	0.5	0	1.5	Medium
Rodriguez (2010a)	0.5	0	0	0.5	Low
Rodriguez (2010b)	0.5	0	0.5	1	Low
Ruger (2014)	1	1	1	3	High
Salcedo (2013)	0.5	0.5	0.5	1.5	Medium
Sanders (2010)	0.5	0.5	1	2	Medium
Schackman (2013)	1	1	1	3	High
Thomas (2012)	0.5	0.5	0.5	1.5	Medium

Study (year)	Applicability	Study limitations	Modelling appraisal	Overall score	Rating
Thomas and Cameron (2013)	0.5	0.5	0	1	Low
Trussell (2013)	0.5	0.5	0.5	1.5	Medium
Trussell (2014)	0.5	0	0.5	1	Low
Trussell (2015)	0.5	0.5	0.5	1.5	Medium
Turner (2014)	1	1	1	3	High

1: All or most of the checklist criteria have been fulfilled; where they have not been fulfilled the conclusions are very unlikely to alter.

0.5: Some of the checklist criteria have been fulfilled; where they have not been fulfilled, or not adequately described, the conclusions are unlikely to alter.

0: Few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter.

Appendix 8: Included studies: UK-based interventions

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Cooper et al. (2012) **Aim of study:** To assess the cost-effectiveness of school-based behavioural interventions for the prevention of STIs in young people through the development of an economic model **Type of economic analysis:** Cost-effectiveness **Economic perspective:** National Health Service (NHS) and Personal Social Services (PSS)	**Source populations:** Boys and girls aged 15 years old **Setting:** UK **Data sources:** *HRQoL*: Previous utility studies using validated tools for groups of patients who developed STI complications *Costs*: published studies *Prevalence and transmission probabilities of STIs:* National Chlamydia Screening programme and Health Protection Agency, case series study, literature	**Intervention description:** **Teacher-led:** Twenty sessions taking place over a 2-year period (10 sessions at age 13–14 years, and 10 sessions at age 14–15 years). It involved active learning (small group work and games), information leaflets on sexual health, and development of skills, primarily through the use of interactive video and role playing **Peer-led:** Three sessions led by peer educators lasting 1 hour each, over one school term. The sessions covered relationships, sexually transmitted infections, and use of condoms and contraception. They were	**Outcomes:** Total number of STI cases averted, QALY, savings in medical costs **Time horizon:** 1 year **Costing year(s) and currency:** 2011-2012 Euro **Discount rates:** Not applicable as the time horizon is for one year **Perspective:** National Health Service (NHS) and Personal Social Services (PSS) **Measures of uncertainty:** Deterministic and probabilistic sensitivity and scenario analysis **Modelling method:** Bernoulli statistical model	**Primary analysis:** *Teacher-led intervention:* - Total cost: £7,672 (€10,320) - Total medical costs averted: £1,297 (€1,745) - Net additional cost: £6,375 (€8,575) - Cost per case averted (all STIs): £3,017 (€4,058) - Incremental cost per QALY gained: £18,041 (€24,268) *the intervention averted an extra two STI cases with a corresponding quality of life gain of 0.35 QALY compared with standard sex education *Peer-led intervention:* - Total cost: £26,762 (€36,000)	**Limitations identified by author:** - Effectiveness data drawn from a meta-analysis did not show a statistically significant effect on behavioural outcomes - The model compares teacher-led to standard sexual health education and peer-led interventions to standard sexual health education, but no direct evidence is available directly comparing peer-led and teacher-led interventions - The intervention effect was assumed to be the same for both interventions so differences in outcomes are due primarily to

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Quality score: High **Applicability:** Directly applicable	review, assumptions *Effectiveness:* Systematic review and meta-analysis *Proportion of sexually active young people in England and their condom use at last intercourse*: Cross-national Health Behaviour in School-aged Children (HBSC) survey *Number of sexual partners that young people have has been:* Multi-purpose survey in Great Britain *Number of occasions of heterosexual sex in the past 4 weeks:*	designed to be informal using small group work, role plays, and condom use skills demonstrations **Comparator/control description:** Standard sexual health education, which is generally provided by teachers in British schools as part of the SRE curriculum. Standard sexual health education generally provides basic information on STIs and sexual health, but does not necessarily teach safer sex negotiation skills. It is, therefore, the teaching of safer sex skills and other broader activities that distinguishes the behavioural intervention from standard education		- Total medical costs averted: £1,297 (€1745) - Net additional cost: £25,465 (€34,255) - Cost per case averted (all STI): £12,050 (€16,210) - Incremental cost per QALY gained: £72,062 (€96,938) * the intervention had the same health gains, in terms of cases averted and QALYs gained when compared with the base case. In conclusion, the peer-led behavioural intervention is less cost-effective than the teacher-led intervention compared with standard sex education **Secondary analysis:** None **Sensitivity analysis:**	differences in costs. The differences costs were because there was less need for training in the teacher-led intervention - Due to a lack of data for the <16-year-old age group, the parameters for this age group are based on assumptions and extrapolations from other age groups **Limitations identified by review team:** Sensitivity analyses showing large uncertainty around the results **Evidence gaps and/or recommendations for future research:** Given the uncertainties surrounding the results, further studies are necessary to define

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
	The UK National Survey of Sexual Attitudes and Lifestyles (NATSAL) *Interventions:* Scottish study (the SHARE trial- teacher-led) and English trial (the RIPPLE trial- peer-led) *Others:* Systematic searches, administrative databases for the United Kingdom, and prospective studies, assumptions	**Sample sizes:** Simulated cohort of 1,000 boys and 1,000 girls		*Deterministic sensitivity analysis:* The results were most sensitive to the intervention effect, the transmission probability, and the number of sexual partners *Scenario analysis for older teenagers*: In this age group, there are more STI cases averted, QALYs gained, and medical costs averted that in the younger age group *Probabilistic sensitive analysis:* - The teacher-led intervention had an ICER between £0 and £26,762 (€36,000) per QALY for 48% of iterations, more than £26,762 (€36,000) per QALY for 28% of iterations and was	cost-effective interventions **Source of funding:** KC, JS, JP, JJ, AH, EB-P, AC, DH and AP received an NIHR Health Technology Assessment Programme grant

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				associated with a QALY loss for 24% of iterations - The peer-led intervention had an ICER between £0 and £26,762 (€36,000) per QALY for 16 percent of iterations	
Crawford et al. (2015) **Aim of study:** To examine the clinical and cost-effectiveness of brief advice for excessive alcohol consumption among people who attend sexual health clinics **Type of economic analysis:** Cost-utility analysis **Economic perspective:**	**Source populations:** 802 people aged 19 years or over attending one of three sexual health clinics and drinking excessively **Setting:** Sexual health clinics in London, UK **Data sources:** Computer-assisted self-completion questionnaire; EuroQol-5D scale; Adult Service Use Schedule; national UK unit costs	**Intervention description:** Brief advice: feedback on alcohol and health, written information, offer of an appointment with an alcohol health worker **Comparator/control description:** Leaflet on health and lifestyle **Sample sizes:** Total N = 802 Intervention N = 402 Control N = 400	**Outcomes:** Outcomes measured 6 months after randomisation and assessed behaviour in the 3 months prior to the date of the assessment (objective measures) **Primary**: Mean weekly alcohol consumption **Secondary**: Proportion of participants who reported any unprotected sex; mean units of alcohol consumed per drinking day; percentage days abstinent; whether the participant was drinking excessively	**Primary outcomes:** *benefits:* -QALY for control = 0.475 -QALY for intervention = 0.450 -Incremental QALY (QALY intervention *minus* QALY control = -0.007) *Costs:* -Average costs for control group: £310.87; average cost for intervention group: £319.28 -Incremental cost (cost intervention minus cost control = £8.41)	**Limitations identified by author:** - Participants were recruited at sexual health clinics. In order to limit exposure of control participants to questions about alcohol consumption, very little baseline data on alcohol-related behaviour was collected. Analysis of available data suggests groups were comparable. - No follow-up was collected for approximately 25% of

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
NHS/Personal Social Service perspective **Quality score:** High **Applicability:** Directly applicable			**Sexual behaviour outcomes**: Number of sexual partners; number of unprotected sexual partners; any incidence of regretted sex; any incidence of unprotected sex after drinking alcohol or while drunk; how long they knew their last sexual partner before they had sex with them; unplanned pregnancy; any new diagnosis of a sexually transmitted infection **Cost and cost-effectiveness outcomes:** Cost of the brief advice; QALY **Time horizon:** 6 months **Costing year(s) and currency:** 2010-2011 GBP **Discount rates:** Not applicable as time horizon was less than one year	-No significant difference in costs or QALY **Secondary analysis:** Not presented as cost/QALY Because the difference in costs and QALY were not significant, acceptability curves were used to estimate the probability that the intervention would be cost-effective for given thresholds of willingness to pay (WTP) per QALY gained; the results showed no evidence of this at any WTP values **Sensitivity analysis:** Statistical model used and inclusion of missing data gave similar findings of a small difference around statistical significance for the primary outcome	intervention participants. These participants were excluded from the final analysis, which may have biased estimates of intervention effectiveness **Limitations identified by review team:** Short time horizon to capture behaviour change **Evidence gaps and/or recommendations for future research:** Authors could have modelled potential scenarios for behaviour change based on available data in the literature **Source of funding:** NIHR Health Technology Assessment programme and the Department of Health, Chelsea and

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
			Perspective: NHS/Personal Social Service **Measures of uncertainty:** Sensitivity analysis: non-parametric bootstrapping and non-hierarchical linear models **Modelling method:** Random-effects linear regression, ordinary parametric models		Westminster NHS Foundation Trust, Central and North West London NHS Foundation Trust, Turning Point, and Imperial College Academic Health Sciences Centre
Jackson et al. (2015) **Aim of study:** To compare the costs and outcomes of two sexually transmitted infection screening interventions targeted at men in football club settings in	**Source populations:** Men ≥18 years in six London amateur football clubs **Setting:** UK **Data sources:** *Costs:* Unit Costs of Health and Social Care 2013; other primary costing data collection *Consequences*:	**Intervention description:** 1. Captain-led and poster STI screening promotion. 2. Sexual health adviser-led and poster STI screening promotion **Comparator/control description:** Poster-only STI screening promotion. **Sample sizes:** Total N = 153 Intervention N = 56+46	**Primary outcome (objective):** proportion of eligible men accepting screening **Time horizon:** Not clearly stated, but probably equal to the intervention (one year) **Costing year(s) and currency:** 2012-2013 GBP **Discount rates:** Discount rates were not applied. Only start-up costs (costs	**Primary analysis:** *benefits*: Number and proportion of men accepting screening: - Captain-led and poster STI screening promotion: 28 (50%) - Sexual health adviser-led and poster STI screening promotion: 31 (67%)	**Limitations identified by author:** - Uptake of screening could not be accurately estimated for intervention arms - Variability in the acceptability of screening intervention between clubs limited ability to estimate acceptability

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
England, including screening promoted by team captains **Type of economic analysis:** Cost-consequence analysis **Economic perspective:** Health service perspective **Quality score:** Medium **Applicability:** Partially applicable	Three-arm trial and results from blood sample	Control N = 51	with the posters) were annuitised at 3% (for 3 years) **Perspective:** NHS **Measures of uncertainty:** One-way deterministic sensitivity analysis for costs and outcomes **Modelling method:** Not applicable	- Poster-only STI screening promotion: 31 (61%) *Costs:* (average cost per player tested): -Captain-led and poster STI screening promotion: £88.99 -Sexual health adviser-led and poster STI screening promotion: £88.33 -Poster-only STI screening promotion: £81.87 **Secondary analysis:** None **Sensitivity analyses:** Variables affecting the overall cost: Time needed for club recruitment; incentive of £1,000 for each club to help maximise participation; costs for team captains to deliver	- Difficulty in recruitment meant that target sample size was not reached - Subsequent testing that may have occurred outside of the intervention but been motivated by intervention materials was not captured, meaning that the uptake of STI testing linked to the intervention may be an underestimate - No cases of chlamydia or gonorrhoea were identified as part of the intervention making it impossible to estimate a cost per case diagnosed - The influence of captains on uptake of testing was not

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				the promotion; intervention costs; cost of the test kit boxes; sample processing costs	anticipated. However, this appears to have played a substantial role with some captains encouraging players to participate in screening in team-wide communications **Limitations identified by review team:** None **Evidence gaps and/or recommendations for future research:** Authors clearly stated this analysis was conducted for the pilot phase, and that was the reason for a cost-consequence analysis. A full cost-effectiveness analysis with a probabilistic analysis might help with uncertainties around the costs and consequences,

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
					especially between the captain-led and the health adviser–led interventions **Source of funding:** SPORTSMART study, part of NIHR-funded BALLSEYE Programme 'Targeting Men for Better Sexual Health'; no competing interests declared
Long et al. (2014) **Aim of study:** To estimate the effectiveness and cost-effectiveness of HIV testing in the UK **Type of economic analysis:** Cost-utility analysis	**Source populations:** UK adult population 15 to 64 years Categorised by risk behaviours or country of origin: MSM; PWID; men from HIV-endemic countries with high HIV prevalence; women from HIV-endemic countries;	**Intervention description:** -Universal testing every 3 years -Universal testing every 2 years -Universal testing every year -Universal testing every year + ART -High-risk testing every year, low-risk testing every 2 years	**Outcomes:** HIV prevalence and incidence; QALYs gained; lifetime healthcare costs; costs of voluntary counselling and testing (VCT) and antiretroviral therapy (ART)/person; HIV infections averted and incremental cost-effectiveness ratios (cost per QALY gained for various scenarios)	**Primary analysis:** *benefits (incremental QALY):* -Universal testing every 3 years: £13,000 -Universal testing every 2 years: £32,900 -Universal testing every year: £57,400 -Universal testing every year + ART: £161,700	**Limitations identified by author:** -Simplification of complex dynamics of HIV disease progression, development of resistance, and changes in viral suppression -Assumption of a standard proportional mixing model of partnership selection does not include preferential mixing by

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Economic perspective: Societal, healthcare and personal social services perspective **Quality score:** High **Applicability:** Directly applicable	other men; and other women Population groups subdivided by HIV infection status: uninfected, acute HIV infection, asymptomatic HIV with CD4 count 350 cells/mm3, symptomatic HIV with CD4 count 200–350 cells/mm3, or AIDS with CD4 count 200 cells/mm3; HIV diagnosis status; ART status if infected; and male circumcision status **Setting:** UK **Data sources:** Previously published studies, assumptions and calculations	-High-risk testing every year, low-risk testing once -High-risk testing every year, low-risk testing once + ART **Comparator/control description:** *Current scenario (assumption):* 25% of MSM, 25% of people from HIV-endemic countries, 77% of PWID and 10% of other adults in the population receiving an HIV test in the last 12 months. Simulated various scaling-up scenarios under different HIV testing and treatment and accounted for various risk behaviour **Sample sizes:** Simulated cohort of individuals of unknown size	**Time horizon:** Projected HIV prevalence and incidence over a 10-year time horizon, and lifetime QALYs gained in the population **Costing year(s) and currency:** 2012 GBP **Discount rates:** Costs and benefits discounted at 3% **Perspective:** Societal **Measures of uncertainty:** Model calibration through comparison of the model projected outcomes with available data on prevalence, incidence, and diagnosis trends. All model parameters were varied in a sensitivity analysis **Modelling method:** Dynamic compartmental model based on a previously published	-High-risk testing every year, low-risk testing every 2 years: £53,100 -High-risk testing every year, low-risk testing once: £42,900 -High-risk testing every year, low-risk testing once + ART: £145,300 *Costs (incremental costs in billions):* -Universal testing every 3 years: £1.25 -Universal testing every 2 years: £2.18 -Universal testing every year: £4.61 -Universal testing every year + ART: £7.41 -High-risk testing every year, low-risk testing every 2 years: £2.37 -High-risk testing every year, low-risk testing once: £0.75	HIV status, race or immigration status -Differential condom use by HIV status not considered -Due to a lack of data on HIV prevalence among newly arrived immigrants, similar HIV prevalence levels for newly arriving immigrants and those already living in the UK were assumed -Cost of HIV testing, counselling and treatment inputs based on current estimates which are linked to the current model and volume of delivery. Changes in service delivery patterns may have an impact on costs and this has not been accounted for.

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
	(particularly a measure for initial distribution for acute HIV stage; calculation based on assumptions and published studies)		dynamic HIV epidemic model	-High-risk testing every year, low-risk testing once + ART: £3.49 ICERS (for CEA, CUA) (cost/QALY gained) -Universal testing every 3 years: £96,200 -Universal testing every 2 years: £66,300 -Universal testing every year: £80,300 -Universal testing every year + ART: £240,000 -High-risk testing every year, low-risk testing every 2 years: £44,700 -High-risk testing every year, low-risk testing once: £17,500 -High-risk testing every year, low-risk testing once + ART: £26,800 **Secondary analysis:** None	**Limitations identified by review team:** Limitations were comprehensively discussed, especially for the model simplification for HIV transmission rates, development of resistance and changes in viral suppression **Evidence gaps and/or recommendations for future research:** Additional attempts can be made to better explore implications of early HIV screening and treatment to better understand the impact of costs of ART in the long term for the control of HIV transmission **Source of funding:** EL, SA, and MB obtained grant funding from the

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Sensitivity analyses: All parameters were varied in a one-way sensitivity analysis and in a probabilistic analysis. The extent to which VCT reduces risky sexual partnerships among newly diagnosed people living with HIV was the primary driver of health outcomes and cost-effectiveness. Cost-effectiveness estimates were affected by reduction in sexual partnership across all risk-groups; epidemic's baseline trajectory; testing, counselling and ART costs; adherence level and ART effectiveness	US National Institute on Drug Abuse. The authors declare that the funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript
National Collaborating Centre (NCC) for	**Source populations:** Male	**Intervention description:** LARC methods: IDU, IUS: LNG-	**Outcomes:** Number of pregnancies averted by the use of one contraceptive	**Primary analysis:** (Comparison across reversible contraceptive	**Limitations identified by author:**

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Women's and Children's Health (2013) **Aim of study:** Overall aim was to provide (clinical and educational) guidance on LARC. The cost-effectiveness analysis aimed at assessing LARC methods compared to combined oral contraceptive pill (COC) **Type of economic analysis:** Cost-effectiveness **Economic perspective:** Public health (NHS)	and females in reproductive ages **Setting:** UK **Data sources:** *Costs:* COC use in England in 2002, 2004 NHS reference costs, British National Formulary (49, March 2005), GP fee schedule, opinion of the Guideline Development Group (GDG), published literature *Effectiveness:* systematic literature review, agreements between GDG members, national statistics, published literature	IUS (Mirena), injectable hormones, implant **Comparator/control description:** Combined oral contraceptive pill (COC), male condom and non-reversible contraceptive methods (female and male sterilisation) **Sample sizes:** Simulated cohort of 1,000 sexually active women choosing one method of contraception	method in comparison with another **Time horizon:** 1 to 15 years **Costing year(s) and currency:** 2004-2005 GBP **Discount rates:** 3.5% **Perspective:** NHS **Measures of uncertainty:** Sensitivity analysis, scenario analysis **Modelling method:** Decision-analytic model – Markov model	methods: LARC methods, COC, male condom) ***1 year of use:*** *Total pregnancy:* Implant: 14 IUS: 17 IUD: 18 Injectable: 33 COC: 91 Condom: 150 *Total costs:* Implant: £262,117 IUS: £270,749 IUD: £195,442 Injectable: £190,534 COC: £232,932 Condom: £212,658 *Incremental cost-effectiveness ratio:* - Implant vs IUD: £17,367/pregnancy averted	- The relative cost-effectiveness of LARC methods highly sensitive to changes in discontinuation rates in several cases - Adverse events, side effects associated with contraceptive use and non-contraceptive benefits are not considered in the model **Limitations identified by review team:** - Key parameters were not assessed individually in the sensitivity analysis, making it difficult to identify which parameter contributes more uncertainty in the model - Authors noted that LARC and COC or non-reversible methods may

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Quality score: Medium **Applicability:** **High**ly applicable				- IUS: dominated by implant - IUD vs injectable: £339/pregnancy averted - COC: dominated by IUD and injectable - Condom: dominated by IUD and injectable ***2 years of use:*** *Total pregnancy:* Implant: 51 IUD: 55 IUS: 57 Injectable: 99 COC: 190 Condom: 295 *Total costs:* Implant: £ 322,939 IUD: £256,572 IUS: £337,093 Injectable: £338,376 COC: £406,366 Condom: £418,125	not always be substitutes since not every woman will be eligible for all methods. This was acknowledged in discussion model structure and limitations, but this scenario was not incorporated in the sensitivity analysis - The model was adapted from a previous model but no discussion was carried out about validity and calibration **Evidence gaps and/or recommendations for future research:** Model can be validated and calibrated and variables should be assessed individually to check for uncertainty among parameters

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Incremental cost-effectiveness ratio: - Implant vs IDU: £17,866/pregnancy averted - IUS: Dominated by implant, IUD - Injectable: Dominated by implant, IUD, IUS - COC: Dominated by all LARC methods Condom: Dominated by all LARC methods ***3 years of use:*** *Total pregnancy:* Implant: 101 IUD:105 IUS: 109 Injectable: 167 COC: 289 Condom: 435 *Total costs:* Implant: £400,947	**Source of funding:** Not declared

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				IUD: £337,207 IUS: £418,616 Injectable: £482,178 COC: £575,320 Condom: £616,644 *Incremental cost-effectiveness ratio:* - Implant vs IUD: £14,730/pregnancy averted - IUS: Dominated by implant, IUD - Injectable: Dominated by implant, IUD, IUS - COC: Dominated by all LARC methods - Condom: Dominated by all LARC methods ***5 years of use:*** *Total pregnancy:* Implant: 215 IUS: 228 IUD: 232	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Injectable: 302 COC: 482 Condom: 707 *Total costs:* Implant: £667,275 IUS: £603,534 IUD: £534,555 Injectable: £760,600 COC: £899,697 Condom: £993,769 *Incremental cost-effectiveness ratio:* - Implant vs IUD: £7,574/pregnancy averted, extended dominance - Implants vs IUS: £4,598/pregnancy averted - IUS vs IUD: £18,845/pregnancy averted	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- Injectable: Dominated by implant, IUD, IUS - COC: Dominated by all LARC methods - Condom: Dominated by all LARC methods ***10 years of use:*** *Total pregnancy:* Implant: 483 IUS:522 IUD: 551 Injectable: 635 COC: 932 Condom: 1291 *Total costs:* Implant: £1,210,419 IUS: £1,119,079 IUD: £1,050,425 Injectable: £1,401,818 COC: £1,632,762 Condom: 1,830,496 *Incremental cost-effectiveness ratio:*	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- Implant vs IUD: £2,342/pregnancy averted/ extended dominance - Implant vs IUS: £2,339/pregnancy averted - IUS vs IUD: £2,346/pregnancy averted - Injectable: Dominated by implant, IUD, IUS - COC: Dominated by all LARC methods - Condom: Dominated by all LARC methods ***15 years of use:*** *Total pregnancy:* Implant: 719 IUS: 778 IUD: 828 Injectable: 948 COC: 1330 Condom: 1788	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Total costs: Implant: £1,622,769 IUS: £1,563,548 IUD: £1,469,754 Injectable: £1,965,220 COC: £2,260,880 Condom: £2,534,998 *Incremental cost-effectiveness ratio:* - Implant vs IUD: £1,403/pregnancy averted/ extended dominance - Implant vs IUS: £999/pregnancy averted - IUS vs IUD: £1,884/pregnancy averted - Injectable: Dominated by implant, IUD, IUS - COC: Dominated by all LARC methods - Condom: Dominated by all LARC methods	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Secondary analysis: (Comparison of LARC methods with non-reversible contraceptive methods) ***1 year of use:*** *Total pregnancies:* Male sterilisation: 7 Female sterilisation: 19 Implant: 719 IUS: 778 IUD: 828 Injectable: 948 *Total costs:* Male sterilisation: £466,776 Female sterilisation: £750,191 Implant: £1,622,769 IUS: £1,563,548 IUD: £1,469,754 Injectable: £1,965,220	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Incremental cost-effectiveness ratio: Implant: Dominated by male and female sterilisation IUS: Dominated by male and female sterilisation IUD: Dominated by male and female sterilisation Injectable: Dominated by male and female sterilisation **Sensitivity analysis:** *Comparison across reversible contraceptive methods: LARC methods, COC, male condom:* - Varying the failure rates of COC and male condom by ±10%: no impact in the base-case results - Varying the failure rates of LARC methods by ±10%: no impact in the cost-effectiveness of the	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				base-case results relative to the COC and male condom. No impact in the ranking of LARC methods in terms of effectiveness or the case dominance across LARC methods - Varying the failure rate of IUD: moderate impact on the ICERs of the implant versus IUD only for short periods of contraceptive use (3-4 years) *Comparison of LARC methods with non-reversible contraceptive methods:* - Varying the failure rates of female and male sterilisation by ±10%: no impact in the base-case results - Varying the failure rates of LARC methods by	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				±10%: no impact in the cost-effectiveness results	
Pilgrim et al. (2010) **Aim of study:** To assess the cost-effectiveness of a range of interventions to encourage young people, especially socially disadvantaged young people, to use contraceptives or contraceptive services **Type of economic analysis:** Cost-effectiveness **Economic perspective:** Public sector	**Source populations:** 1. Young people aged 14-16 who have not previously been a parent (but who may or may not have been pregnant without carrying to term) within secondary school 2. Young mothers within a secondary school 3. Young people aged 15–19 who are sexually active **Setting:** UK **Data sources:** *Probability of abortion and birth:* national	**Intervention description:** 1. School-based dispensing of hormonal contraceptives within the school (DH); school-based dispensing of condoms (**DC**) 2. Intensive case management to prevent repeat pregnancy (includes a culturally matched school-based social worker [including home visits], weekly school-based peer education support and comprehensive medical care including contraception) (ICM) 3. Advance provision of emergency hormonal contraception (AP)	**Primary outcomes:** Cost per pregnancy averted, cost per abortion averted **Secondary outcomes:** Cost of the intervention and additional contraception required as a result of the intervention; cost of maternity care; cost of abortion; cost of miscarriage/ ectopic pregnancy/ stillbirth; cost of treatment for low birth weight babies; cost of treatment of STIs; cost of government-funded benefits **Time horizon:** Lifetime **Costing year(s) and currency:** 2007-2008 GBP **Discount rates:** 3.5% **Perspective:** Public sector	**Primary analysis:** ***Model 1: Deterministic results (discounted)*** *Total cost (billions):* - ND: £1,527 - DC: £1,519 - DH: £1,417 *Cost per abortion averted:* - DC: £815 - DH: £1,514 (compared with DC) *Cost per pregnancy averted (excluding benefits):* - DC: £32 - DH: £441 (compared with DC) *Cost per pregnancy averted (including benefits):*	**Limitations identified by author:** - A lack of data on the long-term employment and education impacts of teenage pregnancy meant that this could not be included in the analysis. If negative impacts on future productivity were included, the intervention may appear more cost-effective. - Only primary transmission of STIs is considered in the model. Consideration of additional infections averted could improve the cost-effectiveness ratio.

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Quality score: Medium **Applicability:** Partly applicable	government statistics for England and Wales *Probability of miscarriage and ectopic pregnancy:* Hospital Episode Statistics (HES); a Denmark study was used to parameterise the miscarriage rates *Long term outcomes of a teenage birth:* Literature review including only UK papers, and elicitation technique with programme development group (PDG) at NICE *Sexually transmitted infection (STI)*	**Comparator/control description:** 1. School nurse only (ND) 2. No follow-up following first pregnancy 3. No advance provision of EHC (No AP) **Sample sizes:** Simulated cohort of 100,000 young individuals	**Measures of uncertainty:** One-way and probabilistic sensitivity analysis **Modelling method:** Cost-effectiveness modelling study with a hypothetical cohort over a lifetime from the age at which the intervention is provided; the following scenarios were modelled: 1. School-based interventions for nulliparous young people 2. School-based interventions to prevent repeat pregnancy 3. Interventions to encourage the use of emergency hormonal contraception following unprotected sex	- DN: dominated by DC - DC: dominated by DH - DH: dominates DC and ND ***Model 2: Deterministic results (discounted)*** *Total costs (millions):* - no follow-up: £655,572 - ICM: £705,730 *Cost per repeat teenage pregnancy averted (excluding benefits):* ICM: £15,155 *Cost per repeat teenage pregnancy averted (including benefits):* ICM: £4,031 ***Model 3: Deterministic results (discounted)*** *Total cost (billions):* - No AP: £1,524 - AP: £1,447 *Cost per abortion averted:* AP: £2,795	- The long term implications of the interventions are not well known. For example, it is not clear if teenage pregnancies are averted or delayed. - Available evidence on contraceptive effectiveness in teenagers has been generated based on 6-12 months of follow-up - Outcomes are not reported in terms of QALYs gained, limiting the extent to which they can be compared with other interventions using this outcome - Variability in baseline health and risk factors is not captured in the model - The comparison within Model 1 is highly

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
	outcomes: NICE Sex and Relationship Education (SRE) public health guidance *Effectiveness:* National statistics assumptions *Benefits:* Office for National Statistics (ONS, 2009), previous published studies, assumptions *Costs:* British National Formulary (BNF 58, 2009), NICE assessment of LARCs, health economic model developed for the NICE SRE public health guidance, NHS reference costs			*Cost per age pregnancy averted:* AP (excluding benefits): £310 *Cost per age pregnancy averted:* AP (including benefits) dominates **Secondary analysis:** ***Model 1: Expected results (discounted)*** *Total cost (billions):* - DN: £1,524 - DC: £1,517 - DH: £1,515 *Cost per abortion averted:* - DC: £822 - DH: £1,495 (compared with DC) *Cost per pregnancy averted (excluding benefits):* - DC: £38	dependent upon the true effectiveness of each of the methods of contraception - Research comparing the cost-effectiveness of different methods of contraception in terms of both STIs and contraception is sparse due to the limitations around which outcome measure can reasonably capture both effects - the cost of maternity services may differ for teenage mothers compared with older mothers **Limitations identified by review team:** Authors stated that no preterm births were assessed which may be more common amongst young people; however,

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- DH: £443 (compared with DC) *Cost per pregnancy averted (including benefits):* - DN: dominated by DC - DC: dominated by DH - DH: dominates DC and ND ***Model 1: Expected results (undiscounted):*** *Total cost (billions):* - DN: £2,307 - DC: £2,297 - DH: £2,295 *Cost per abortion averted:* - DC: £848 - DH: £1,535 (compared with DC) *Cost per pregnancy averted (excluding benefits):*	this statement seems odd since multiples and low birth weight are included - unless low-birth weight is the same as preterm. Other adverse events associated with teen pregnancy such as fistula were not mentioned. **Evidence gaps and/or recommendations for future research:** Modelling was based on previous model (NICE), but no discussion of model calibration has been provided **Source of funding:** Not declared

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- DC: £92 - DH: £488 (compared with DC) *Cost per pregnancy averted (including benefits):* - DN: dominated by DC - DC: dominated by DH - DH: dominates DC and ND ***Model 2: Expected results (discounted)*** *Total cost (millions):* - no follow-up: £654,756 - ICM: £705,164 *Cost per repeat teenage pregnancy averted (excluding benefits):* ICM: £15,175 *Cost per repeat teenage pregnancy averted (including benefits):* ICM: £4,052	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Model 2: Expected results (undiscounted) *Total cost (millions):* - no follow-up: £825,978 - ICM: £866,883 *Cost per repeat teenage pregnancy averted (excluding benefits):* ICM: £15,186 *Cost per repeat teenage pregnancy averted (including benefits):* ICM: £2,935 ***Model 3: Expected results (discounted)*** *Total cost (billions):* - no AP: £1,522 - AP: £1,445 *Cost per abortion averted:* AP: £2,803 *Cost per age pregnancy averted:* AP (excluding benefits): £314	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Cost per age pregnancy averted: AP (including benefits) dominates ***Model 3: Expected results (undiscounted)*** *Total cost (billions):* - no AP: £2,303 - AP: £2,198 *Cost per abortion averted:* AP: £2,948 *Cost per age pregnancy averted:* AP (excluding benefits): £395 *Cost per age pregnancy averted:* AP (including benefits) dominates **Sensitivity analysis:** ***Model 1:*** *PSA:* The analysis shows very little difference in both costs and effectiveness between dispensing condoms within schools and dispensing hormonal	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				contraceptives within schools. There is the possibility that either one could be more effective and/or more costly than the other *One-way:* -Delay in births averted (14-16 years to 17-19 years): (1) DC would remain cost saving compared with ND for the cost per age 14–16 pregnancy averted including government-funded benefits; (2) DH would remain cost saving compared with DC within schools for this outcome - Pregnancies averted at ages 14–16 years would have been additional: cost-effectiveness ratio for the cost per abortion averted decreases	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- Probability of condom failure is doubled: DC results in greater net costs than DH - Doubled risk of miscarriage: DC is estimated to result in net cost savings compared with ND - Increase in medical abortions: net cost savings of DC compared with ND - Increase in relative risk of both interventions: higher cost-effectiveness ratios than the base case analysis ***Model 2*** *PSA:* - ICM is unlikely to result in net cost savings when excluding benefit payments	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- 20% probability that ICM will result in net cost savings (with government-funded benefits) compared with no follow-up after first teenage pregnancy *One way:* - Reducing cost of intervention: cost per repeat teenage pregnancy averted (excluding benefits) of £6,844 - Including benefits: ICM will dominate no follow-up after a teenage birth - Other variations do not have substantial impact upon the model results ***Model 3*** *PSA:* - AP is unlikely to result in net cost savings using	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				the cost per abortion averted outcome - 24% probability AP will result in net cost savings when using the cost per age 15–19 pregnancy averted outcome (excluding benefit payments) - AP is likely to be cost saving using a cost per age 15–19 pregnancy averted outcome (including benefit payments) *One way:* - Increasing the baseline usage of EHC following unprotected sex: AP dominates including and excluding government-funded benefit payments; estimated cost per abortion averted associated with AP decreases to £688	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- Other variations do not have substantial impact upon the model results	
Roberts et al. (2012) **Aim of study:** To assess two new models of partner notification (PN), known as Accelerated Partner Therapy (APT Hotline and APT Pharmacy), as compared with routine patient referral PN, for sex partners of people with chlamydia, gonorrhoea and non-gonococcal urethritis **Type of economic analysis:** Cost-	**Source populations:** Clients in 2 GUM clinics and 6 community pharmacies participating in a clinical trial in the UK **Setting:** UK **Data sources:** -Effectiveness measures data come from a trial -Data on resources use comes from Chlamydia Screening Studies (ClaSS) project and Unit Costs of Health and Social Care 2008	**Intervention description:** -APT Hotline: Telephone assessment of sex partner by a clinic-based nurse-qualified health adviser. In Clinic B, majority of advisers were not nurse-qualified and a clinic doctor needed to conduct a short additional telephone consultation with the patient to ensure safe prescribing -APT Pharmacy assessment of sex partner by a trained community pharmacist **Comparator/control description:** Routine PN (patient referral, which included infection-specific information,	**Primary outcome:** Average cost/partner treated **Secondary outcomes:** Number of partners treated by allocated method; median time from diagnosis to treatment **Time horizon:** Unclear, but it seems to be one year **Costing year(s) and currency:** 2008 GBP **Discount rates:** No discount rate applied to costs and outcomes as the analysis seems to be for one year; cost of telephone device was annuitised for 3 years at 3% interest rate **Perspective:** NHS	**Primary analysis:** ***Benefits:*** *Number partners treated by allocated method:* APT hotline: 47 APT pharmacy: 15 Routine PN: 13 *Median time from diagnosis to treatment (days):* APT hotline: 1 APT pharmacy: 1 Routine PN: 4 ***Average costs:*** APT Hotline: £2558 APT pharmacy: £799 Routine PN: £597 ***ICERS (for CEA, CUA):*** *Cost-consequence analysis:* APT strategies	**Limitations identified by author:** -Analysis is carried out on data collected in an exploratory trial where there was no randomisation of index cases or partners to the alternative strategies, which provides considerable potential for bias in the results -In some cases the outcome data relied on reported results from the index patient **Limitations identified by review team:** The authors stated that, because it was an exploratory analysis, a sensitivity analysis was not carried out. The

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
consequence analysis **Economic perspective:** NHS perspective **Quality score:** Medium **Applicability:** Directly applicable		advice that sex partner should attend clinic for testing and treatment and, in one clinic, a standard letter detailing antibiotic treatment options for the sex partner to give to his/her general practitioner if appropriate) **Sample sizes:** *Total N (APT+PN):* 296 *Intervention N:* APT hotline: 135 APT pharmacy: 44 Total: 179 *Control N:* Routine PN: 117	**Measures of uncertainty:** No sensitivity analysis was carried out **Modelling method:** Not applicable; cost-consequence analysis	were more costly and more effective in terms of treating partners compared to routine PN; PN was the least cost strategy, but had the fewest partners treated; there was no strategy that was either clearly dominant or dominated: APT Hotline: £54.42 per partner treated APT pharmacy: £53.29 per partner treated Routine PN: £45.89 per partner treated **Secondary analysis:** None **Sensitivity analysis:** No sensitivity analysis was carried out	review team disagrees and see a sensitivity analysis as a way to better identify parameters that generate more uncertainty for further exploration in a future economic evaluation for these strategies **Evidence gaps and/or recommendations for future research:** We would suggest that effectiveness and costs parameters are further explored in a sensitivity analysis **Source of funding:** Department of Health, through the Sexual Health and HIV Research Strategy Committee of the Medical Research

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
					Council; no competing interests declared
Thomas and Cameron (2013) **Aim of study:** To calculate the cost of an unintended pregnancy in 2011 and use this cost in a cost-effectiveness model comparing ulipristal acetate (UPA) with levonorgestrel (LNG) for emergency hormonal contraception (EHC) **Type of economic analysis:** Cost-effectiveness analysis	**Source populations:** Women in England presenting in primary care for EHC within 24 to 72 hours of unprotected sexual intercourse **Setting:** English primary care **Data sources:** *Health outcome:* Probabilities of unintended pregnancies from clinical trials of EHC and published data sources and studies conducted on pregnancy intention in women in UK.	**Intervention description:** Ulipristal acetate (UPA) 30 mg indicated for EC within 120 hrs of unprotected sexual intercourse (UPSI) **Comparator/control description:** Levonorgestrel (LNG) 1.5 mg, which is indicated for EC if taken within 72 hrs of UPSI **Sample sizes:** Not described clearly	**Primary outcome:** Number of unintended pregnancies and direct and indirect costs of unintended pregnancy **Secondary outcome:** Consequence of unintended pregnancy (miscarriage, abortion, ectopic pregnancy, stillbirth or live birth) **Time horizon:** One year **Costing year(s) and currency:** 2011 GBP **Discount rates:** Not applicable as time horizon was one year **Perspective:** Healthcare and societal **Measures of uncertainty:** Sensitivity analysis: failure rates of EHC and costs of unintended pregnancies	**Primary analysis:** *Direct health costs of a pregnancy:* £3.9 billion (average cost: £3,903) -Cost per event: Miscarriage: £554; abortion: £714; ectopic pregnancy: £1,228; stillbirth: £3,765; live birth: £5,337 *Indirect health costs:* Government expenditure on maternal health benefits: £2.3 billion plus £34 billion in tax credits and child benefits *Overall analysis:* -Cost of treating woman with UPA instead of LGN: Healthcare cost: £1,469; health and societal costs: £1,469 (same)	**Limitations identified by author:** -Post-natal care costs for the mother were not included in the analysis -Cost estimates are based on average pregnancy costs, which may be different from the costs associated with an unintended pregnancy **Limitations identified by review team:** No additional limitations identified for this type of analysis **Evidence gaps and/or recommendations for future research:** Long-term implications for the interventions could

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Economic perspective: Healthcare only or health plus social care **Quality score:** Low **Applicability:** Partially applicable	Measure of effectiveness was number needed to treat *Costs:* Records from the NHS hospitals; NHS national Schedule of Reference Costs		**Modelling method:** N/A - not a modelling study	-Avoided costs (pregnancy averted): Healthcare costs: £1,663, health and societal costs: £2,992 -ICER (net benefit) costs of treating minus avoided costs: Healthcare costs: −£194; Health and societal costs: −£1,453 **Secondary analysis:** None **Sensitivity analysis:** All main parameters were varied. The sensitivity analysis did not change the results and has produced negative ICERs for the main outcomes of analysis, indicating robustness of the cost-saving analysis	be explored in a modelling study **Source of funding:** Funded by HRA Pharma UK & Ireland Ltd, manufacturers of ellaOne (UPA) CT has worked as a consultant for HRA Pharma Ltd, the manufacturer of UPA. SC has received lecture fees from HRA Pharma Ltd and was the principal investigator for the clinical studies of UPA, which were also sponsored by HRA Pharma Ltd
Turner et al. (2014)	**Source populations:** Simulated cohort	**Intervention description:** POC NAAT for chlamydia	**Primary outcome:** Total cost per QALY gained	**Primary analysis:** *QALY:*	**Limitations identified by author:** -Difficulty in obtaining

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Aim of study: To estimate the costs and benefits of clinical pathways incorporating a point of care (POC) nucleic acid amplification test (NAAT) for chlamydia and gonorrhoea in genitourinary medicine (GUM) clinics compared with standard off-site laboratory testing **Type of economic analysis:** Cost-utility analysis and cost-effectiveness analysis	of 1.2 million index patients at GUM clinics **Setting:** England national health service GUM clinic **Data sources:** *Epidemiological data:* based on the Genitourinary Medicine Clinic Activity Dataset 2011 *Utilities:* Assumptions and published data *Costing data:* Published data	and gonorrhoea in GUM clinics **Comparator/control description:** Standard off-site laboratory testing **Sample sizes:** Simulated cohort of 1.2 million hypothetical index patients	(incremental cost-effectiveness ratio) **Secondary outcome:** Number of inappropriate treatments, complications and transmissions averted **Time horizon:** The model cycle length was 1 day with an overall length of 28 days **Costing year(s) and currency:** 2013 GBP **Discount rates:** Not applicable as time horizon was less than one year **Perspective:** NHS GUM clinic **Measures of uncertainty:** -Scenario analysis -Univariate sensitivity analysis (disease progression and transmission) **Modelling method:** Decision analytic model	-POC NAAT: 184.059 -Standard care: 184,012 *Costs:* -POC NAAT: £103.9 million -Standard care: £115.6 million *ICERS (for CEA, CUA):* POC NAAT dominates (negative ICER, which means the intervention is cost saving) *Inappropriate treatments avoided:* POC NAAT: 95,382 *Complications averted (Cases of pelvic inflammatory disease prevented):* POC NAAT: 189 *Transmission averted (onward transmissions averted annually):* POC NAAT: 17 561	accurate patient management parameter estimates from the literature due to reliance on presumptive treatment data - The only complication considered was pelvic inflammatory disease in women -Both tests were assumed to have equivalent sensitivity and specificity -Changes in uptake of testing due to POC testing were not considered -Patient costs associated with repeat visits or returning to collect treatment were not considered -The cost of changing testing protocol was not considered

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Economic perspective: National Health Service **Quality score:** High **Applicability:** Directly applicable				**Secondary analysis:** None **Sensitivity analysis:** Depending on the assumptions on prevalence rates and level of infectivity, the ICERs vary, but POC NAAT is still cost-effective	**Limitations identified by review team:** None **Evidence gaps and/or recommendations for future research:** -Combination of qualitative and quantitative research to better capture changes in uptake over time - Impact of POC NAAT tests on patient experience - New generation POC NAAT tests need to be evaluated independently -Impact of POC NAAT on prevalence of complications by type of complication **Source of funding:** Cepheid, the manufacturer of the POC NAAT testing equipment

Appendix 9: Included studies table: Health promotion interventions

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Burgos et al. (2010) **Aim of study:** To investigate the cost-effectiveness of Mujer Segura (Healthy Woman) intervention to reduce incidence of HIV and STIs in the border region of northern Mexico **Type of economic analysis:** Cost-effectiveness **Economic perspective:** Government healthcare payer **Quality score:** Medium **Applicability:** Partly applicable	**Source populations:** Female sex workers (FSWs) **Setting:** Tijuana and Cuidad Juarez, Mexico **Data sources:** *Individual characteristics:* Randomly assigned using distributions derived from the Mujer Segura cohort and other studies *Costs:* Observed costs per screening during the Mujer Segura study, National Center for AIDS Prevention in Mexico (CENSIDA) and published	**Intervention description:** Mujer Segura (Healthy Woman) intervention (once only or annually): brief (35-minute) behavioural intervention focused on increasing condom negotiation skills and reducing incidence of HIV and STIs among FSWs **Comparator/control description:** No intervention **Sample sizes:** Intervention: 409 Control: 460 Total: 869	**Outcomes:** Incidence HIV infection and QALY; HIV cases prevented, changes in quality-adjusted life expectancy (QALE), and costs per additional QALY gained **Time horizon:** Lifetime **Costing year(s) and currency:** 2009 USD **Discount rates:** 3% **Perspective:** Government healthcare payer **Measures of uncertainty:** One-, two- and multi-way sensitivity analyses; second-order Monte Carlo simulation for a multivariate probabilistic sensitivity analysis; probabilistic sensitivity analysis using Monte Carlo simulation methods and	**Primary analysis:** *No intervention* - Cost: £12,730 ($19,200) - QALYs gained: 21,863 *Mujer Segura intervention offered once only* - Cost: £64,576 ($97,400) - Incremental cost: £51,847 ($78,200) - HIV infections prevented: 33 - Increase in the QALE per FSW: 151 days - Incremental cost per HIV case prevented: £1,571 ($2,370) - QALY: 22,290 - incremental QALY: 427 - incremental cost per QALY: £121 ($183) *Mujer Segura intervention offered annually* - Cost: £322,483 ($486,400)	**Limitations identified by author:** - The assessment of intervention effectiveness relies on only 6 months of follow-up and modelling assumes sustained effect, which may not be realistic - Mujer Segura participants are at high risk for HIV and STI infection meaning that the results may not be generalisable to other lower risk populations or to other settings - Multivariate sensitivity analyses generate present confidence intervals; however, published data from the US and Africa were used to parameterise HIV

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
	reports from Mexico *Other parameters:* Published literature		multi-way sensitivity analyses **Modelling method:** Markov Model and Monte Carlo simulation	- Incremental cost: £257,907 ($389,000) - HIV infections prevented: 62 - Increase in the QALE per FSW: 283 days - Incremental cost per HIV case prevented: £8,893 ($13,413) - QALY: 22,652 - Incremental QALY: 362 - Incremental cost per QALY: £713 ($1,075) **Secondary analysis:** Base-case results considering universal access to HAART *Incremental cost per HIV case averted:* - Mujer Segura annual: cost-saving - Mujer Segura once: dominated - no-intervention: dominated *Incremental cost per QALY:*	progression in the model **Limitations identified by review team:** Authors have covered major issues; model was calibrated, as it was adapted from previous model **Evidence gaps and/or recommendations for future research:** To better capture complications of HIV, analysis could also consider assessments by CD4 levels **Source of funding:** Funding for the Mujer Segura study provided by the National Institute of Mental Health. JB funded by the National Institute of Drug Abuse

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				- Mujer Segura annual: net-saving - Mujer Segura once: dominated - No intervention: dominated **Sensitivity analysis:** *1. Two-way sensitivity analysis - base case results considering universal access to HAART, ignoring added costs for antiretroviral medications:* Incremental cost per HIV case averted: - Mujer Segura once: $2,370 - No intervention: $13,258 Incremental cost per QALY: - Mujer Segura once: $2,435 - No-intervention: $14,136 *2. One-way sensitivity analyses:* Results were sensitive to changes in HIV incidence	

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				3. *Probabilistic sensitivity analysis:* The cost-effectiveness acceptability curve indicated that there was a greater than 95% probability of a cost per QALY gained less than £16,906 ($25,499) for the intervention offered once and £10,078 ($15,200) for the intervention offered annually 4. Mujer Segura intervention is no longer cost-effective with changes in incidence of HIV, STI, syphilis, gonorrhoea and chlamydia	
Cooper et al. (2012) **Aim of study:** To assess the cost-effectiveness of school-based behavioural interventions for the prevention of STIs in young	**Source populations:** Boys and girls aged 13 to 15 years old **Setting:** UK **Data sources:** *HRQoL:* Previous utility studies using validated tools for	**Intervention description:** *Teacher-led:* Twenty sessions delivered over two years: 10 sessions at age 13–14 years, and 10 sessions at age 14–15 years. Active learning (small group work and games), information leaflets on sexual health, and development of skills, using	**Outcomes:** Total number of STI cases averted, QALY, savings in medical costs **Time horizon:** 1-year **Costing year(s) and currency:** 2011-2012 Euro	**Primary analysis:** *Teacher-led intervention:* - Total cost: £7,672 (€10,320) - Total medical costs averted: £1,297 (€1,745) - Net additional cost: £6,375 (€8,575) - Cost per case averted (all STIs): £3,017 (€4,058)	**Limitations identified by author:** -Effectiveness data drawn from a meta-analysis did not show a statistically significant effect on behavioural outcomes -The model compares teacher-led to standard

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
people through the development of an economic model **Type of economic analysis:** Cost-effectiveness **Economic perspective:** National Health Service (NHS) and Personal Social Services (PSS) **Quality score:** High **Applicability:** Directly applicable	groups of patients who developed STI complications *Costs:* Published studies *Prevalence and transmission probabilities of STIs:* National Chlamydia Screening programme and Health Protection Agency, case series study, literature review, assumptions *Effectiveness:* Systematic review and meta-analysis *Proportion of sexually active young people in England and their condom use at last intercourse:* Cross-	interactive video and role playing *Peer-led:* Three one-hour peer-educator-led sessions delivered over one school term. Topics: relationships, sexually transmitted infections and use of condoms and contraception. Informal format using small group work, role plays and condom use skills demonstrations **Comparator/control description:** Standard sexual health education provided by teachers in British schools as part of the SRE curriculum. Topics: basic information on STIs and sexual health, which may or may not teach safer sex negotiation skills. **Sample sizes:** Simulated cohort of individuals of unclear size	**Discount rates:** Not applicable as the time horizon is for one year **Perspective:** National Health Service (NHS) and Personal Social Services (PSS) **Measures of uncertainty:** Deterministic and probabilistic sensitivity and scenario analysis **Modelling method:** Bernoulli statistical model	- Incremental cost per QALY gained: £18,041 (€24,268) *the intervention averted an extra two STI cases with a corresponding gain of 0.35 QALY compared with standard sex education *Peer-led intervention:* - Total cost: £26,762 (€36,000) - Total medical costs averted: £1,297 (€1,745) - Net additional cost: £25,465 (€34,255) - Cost per case averted (all STIs): £12,050 (€16,210) - Incremental cost per QALY gained: £72,062 (€96,938) * the intervention had the same health gains, in terms of cases averted and QALYs gained when compared with the base case **Secondary analysis:** None	sexual health education and peer-led interventions to standard sexual health education, but no direct evidence is available directly comparing peer-led and teacher-led interventions - The intervention effect was assumed to be the same for both interventions so differences in outcomes are due primarily to differences in costs. The differences in costs were primarily because a lower frequency of training was needed in the teacher-led intervention - Due to a lack of data for the <16-year-old age group, the parameters for this age group are

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
	national Health Behaviour in School-aged Children (HBSC) survey *Number of sexual partners that young people have had:* Multi-purpose survey in Great Britain *Number of occasions of heterosexual sex in the past 4 weeks:* The UK National Survey of Sexual Attitudes and Lifestyles (NATSAL) *Interventions:* Scottish study (the SHARE trial- teacher-led) and English trial (the RIPPLE trial- peer-led)			**Sensitivity analysis:** *Deterministic sensitivity analysis:* Results most sensitive to intervention effect, transmission probability, and number of sexual partners *Scenario analysis for older teenagers:* In this age group, there are more STI cases averted, QALYs gained and medical costs averted than in the younger age group *Probabilistic sensitive analysis:* - The teacher-led intervention ICER was between £0 and £26,762 (€36,000) per QALY for 48% of iterations, more than £26,762 (€36,000) per QALY for 28% of iterations and was associated with a QALY loss for 24% of iterations	based on assumptions and extrapolations from other age groups **Limitations identified by review team:** Sensitivity analyses showing large uncertainty around the results **Evidence gaps and/or recommendations for future research:** Given the uncertainties surrounding the results, further studies are necessary to define cost-effective interventions **Source of funding:** KC, JS, JP, JJ, AH, EB-P, AC, DH and AP received an NIHR Health Technology Assessment Programme grant

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
	Others: Systematic searches, administrative databases for the United Kingdom and prospective studies, assumptions			- The peer-led intervention ICER between £0 and £26,762 (€36,000) per QALY for 16% of iterations	
Crawford et al. (2015) **Aim of study:** To examine the clinical and cost-effectiveness of brief advice for excessive alcohol consumption among people who attend sexual health clinics **Type of economic analysis:** Cost-utility analysis **Economic perspective:** NHS/Personal	**Source populations:** 802 people aged 19+ years attending one of three sexual health clinics and drinking excessively **Setting:** Sexual health clinics in London, UK **Data sources:** Computer-assisted self-completion questionnaire; EuroQol-5D scale; Adult Service Use	**Intervention description:** Brief advice: feedback on alcohol and health, written information, offer of an appointment with an alcohol health worker **Comparator/control description:** Leaflet on health and lifestyle **Sample sizes:** Total N = 802 Intervention N = 402 Control N = 400	**Outcomes:** Outcomes measured 6 months after randomisation and assessed behaviour in the 3 months prior to the date of the assessment (objective measures) **Primary outcome**: Mean weekly alcohol consumption **Secondary outcomes**: Proportion of participants who reported any unprotected sex; mean units of alcohol consumed per drinking day; percentage days abstinent; whether the	**Primary outcomes:** *Benefits:* -QALY for control = 0.475 -QALY for intervention = 0.450 -Incremental QALY (QALY intervention *minus* QALY control): −0.007 *Costs:* -Average costs for control group: £310.87 -Average cost for intervention group: £319.28 -Incremental cost (cost of intervention minus cost of control): £8.41	**Limitations identified by author:** -Participants were recruited at sexual health clinics. In order to limit exposure of control participants to questions about alcohol consumption, very little baseline data on alcohol-related behaviour was collected. Analysis of available data suggests groups were comparable. -No follow-up was collected for

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Social Service perspective **Quality score:** High **Applicability:** Directly applicable	Schedule; national UK unit costs		participant was drinking excessively **Sexual behaviour outcomes:** Number of sexual partners; number of unprotected sexual partners; any incidence of regretted sex; any incidence of unprotected sex after drinking alcohol or while drunk; how long they knew their last sexual partner before they had sex with them; unplanned pregnancy; any new diagnosis of a sexually transmitted infection **Cost and cost-effectiveness outcomes:** Cost of the brief advice; QALY **Time horizon:** 6 months **Costing year(s) and currency:** 2010-2011 GBP	-No significant difference in costs or QALY **Secondary analysis:** Not presented as cost/QALY. Because the difference in costs and QALY were not significant, acceptability curves were used to estimate the probability that the intervention would be cost-effective for given thresholds of willingness to pay (WTP) per QALY gained; the results showed no evidence of this at any WTP values **Sensitivity analysis:** Statistical model used and inclusion of missing data gave similar findings of a small difference around statistical significance for the primary outcome	approximately 25% of intervention participants. These participants were excluded from the final analysis, which may have biased estimates of intervention effectiveness **Limitations identified by review team:** Short time horizon to capture behaviour change **Evidence gaps and/or recommendations for future research:** Authors could have modelled potential scenarios for behaviour change based on available data in the literature **Source of funding:** NIHR Health Technology Assessment programme and the Department of

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
			Discount rates: Not applicable as time horizon was less than one year **Perspective:** NHS/Personal Social Service **Measures of uncertainty:** Sensitivity analysis: non-parametric bootstrapping and non-hierarchical linear models **Modelling method:** Random-effects linear regression, ordinary parametric models		Health, Chelsea and Westminster NHS Foundation Trust, Central and North West London NHS Foundation Trust, Turning Point, and Imperial College Academic Health Sciences Centre
Holtgrave et al. (2012) **Aim of study:** To examine the affordability, performance standards and cost-effectiveness of female condom	**Source population:** Women **Setting:** Washington, DC, USA **Data sources:** Female Health Company and MAC	**Intervention description:** Female condom distribution and education programme **Comparator/control description:** No intervention **Sample sizes:** Not clearly stated but understood as a simulation using eligible	**Primary outcome:** Costs saved **Secondary outcomes:** Total costs, HIV infections averted, net cost-savings per QALY averted **Time horizon:** 1 year and lifetime **Costing year(s) and currency:** 2012 USD	**Primary analysis:** *Benefits (HIV infections averted):* -Female to female transmission: 5.08 -No STI, male to male: 6.61 -Non ulcerative STI, male to female: 6.54	**Limitations identified by author:** -Retrospective analysis meant that uncertainty was explored using mathematical modelling techniques -Simplified assumption of random distribution of sexual acts

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
(FC2) provision and education **Type of economic analysis:** Cost analysis, cost-effectiveness and cost-utility analysis **Economic perspective:** Societal and public sector payer perspectives, USA **Quality score:** High **Applicability:** Directly applicable	AIDS Fund for all cost elements	population (men and women of reproductive age)	**Discount rates:** 3% **Perspective:** Societal and public sector payer perspectives, USA **Measures of uncertainty:** Sensitivity analysis (type not mentioned, but understood as one-way sensitivity analysis) **Modelling method:** Cost analysis; threshold analysis	-Ulcerative STI, male to female: 5.13 -Total HIV infections averted: 23.35 *Total cost:* -Total overall programme cost: £279,575 ($414,186) -Cost per female condom using during sex: £2.15 ($3.19) *Threshold analysis (cost saving per HIV infection averted) - cost-utility:* -Societal perspective: net savings of £5.51 million ($8.16 million) -Payer perspective: net savings of £4.06 million ($6.017 million) *Allowance for male condom crowd-out:* -Total HIV infection averted: 20.32	-Prevention of secondary transmission of HIV not considered. This is likely to lead to conservative estimates of effectiveness **Limitations identified by review team:** - Authors have only stated that the results were robust in terms of benefits gained and costs averted -We suggest that the sensitivity analysis be more detailed and informative in terms of showing which parameter(s) bring more uncertainty to the model/estimates **Evidence gaps and/or recommendations for future research:** When alternatives are dominant, present this

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				-Societal perspective (cost-utility analysis): net savings of £4.76 million ($7.046 million) -Payer perspective: net savings of £3.5 million ($5.181 million) **Sensitivity analysis:** *Threshold analysis:* From the societal perspective, 1.13 infections would need to be averted for the intervention to be cost saving and 0.46 infections averted for the intervention to fall below a threshold of £67,500 ($100,000) per QALY gained. From the payer perspective, 1.5 infections would need to be averted for the intervention to be cost saving *Crowding out:* If increased uptake of FC2 leads to a 13% decrease in male condom use (known as crowding out), the intervention would still be	and subsequent alternatives that were not dominant **Source of funding:** Female Health Company, the producer of the female condom product, FC2, provided support for the economic evaluation, education and dissemination. The MAC AIDS fund provided funding for the educational project

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				associated with 20.32 infections averted which means it would still be cost saving *Reduced FC2 effectiveness:* If the effectiveness of FC2 dropped as low as 7.04%, the intervention would still be cost-effective.	
Holtgrave et al. (2013) **Aim of study:** To present a cost-utility analysis of supportive housing for homeless and unstably housed persons living with HIV, through the combination of three favourable outcomes (undetectable HIV viral load, less use of emergency rooms as a source	**Source populations:** Homeless and unstably housed persons living with HIV in Baltimore, Chicago and Los Angeles **Setting:** Baltimore, Chicago and Los Angeles/ USA **Data sources:** Previously published cost and effectiveness data	**Intervention description:** Supportive housing for homeless and unstably housed persons living with HIV: people who did not spend any night homeless during the past 6 months **Comparator/control description:** Persons living with HIV who spent at least one night homeless during the past 6 months **Sample sizes:** Simulated cohort of individuals of unspecified size	**Primary outcome:** Cost per QALY saved by the Housing and Health intervention **Secondary outcomes:** - Average cost per client per year to receive the Housing and Health services (C) - Average medical cost savings per client accrued because of lowered emergency department use (E) - Number of HIV transmissions averted to	**Primary analysis:** -Average per-client cost across Baltimore, Chicago and Los Angeles: C = £7,975 ($12,288) E = £63 ($97) A = 0.01567 T = £205,022 ($315,904) Q_{PSS} = 0.0324 Q_{TA} = 5.33 (discounted) - Cost per QALY saved by the HIV-related housing services: £40,558 ($62,493) **Secondary analysis:** None	**Limitations identified by author:** - Estimates of the number of infections averted is based on estimates obtained from the literature as this could not be observed directly - The study used results from the as-treated analysis, rather than the intent-to-treat analysis, so is not possible to establish a causal relationship between housing status

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
of medical care, and lower perceived stress) with information on the costs of service delivery and mathematical model estimates of the cost per QALY saved by the intervention **Type of economic analysis:** Cost-utility **Economic perspective:** Not clear **Quality score:** Low **Applicability:** Partly applicable	from the Housing and Health Study		HIV seronegative partners of HIV seropositive clients (A) - Net present value of downstream medical care costs saved when an HIV infection is averted (T) - Average number of QALYs saved for each client living with HIV due to improvements in perceived stress (Q_{PSS}) - Net present value of the downstream QALYs saved each time an HIV transmission is averted from one HIV seropositive client in the study to an HIV seronegative partner (Q_{TA}) **Time horizon:** Not clear **Costing year(s) and currency:** 2005 USD **Discount rates:** 3% **Perspective:** Not clear	**Sensitivity analysis:** The threshold analysis for the parameter A indicated that even if A sank as low as 0.01054, the cost-utility ratio would be £64,900 ($100,000) or less. This is also true if the value for Q_{TA} decreased to as low as 2.56.	and the outcomes of interest - Estimates of the net present value of QALYs saved due to averted transmissions (Q_{TA}) were based on available literature at the time of analysis; however, more recent CDC estimates suggest that a higher value could be used, meaning that the estimates in the present study are conservative -Secondary HIV transmissions averted are not included in the model, meaning that estimates of the number of transmissions averted are conservative -It is assumed that no HIV transmissions occur from a seropositive

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
			Measures of uncertainty: Sensitivity analysis: threshold analysis **Modelling method:** Mathematical modelling		individual with an undetectable viral load to a seronegative partner, though it is theoretically possible that this could occur, but the risk of transmission per sex act is expected to be very low. The threshold analysis for number of HIV transmissions averted to HIV seronegative partners of HIV seropositive clients (A) suggests that the results are robust to this assumption - Study participants were recruited through HIV service organisations which may have resulted in a sample that is more able to negotiate access to services compared to

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
					the general population of homeless and unstably housed individuals **Limitations identified by review team:** Main limitations already identified by authors **Evidence gaps and/or recommendations for future research:** To assess complications of HIV and long-terms costs and benefits of interventions, we suggest adding an analysis by CD4 levels **Source of funding:** Funding received from the US Centers for Disease Control and Prevention and the Department of Housing and Urban Development

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Jackson et al. (2015) **Aim of study:** To compare the costs and outcomes of two sexually transmitted infection screening interventions targeted at men in football club settings in England, including screening promoted by team captains **Type of economic analysis:** Cost-consequence analysis **Economic perspective:** Health service perspective	**Source populations:** Men ≥18 years in six London amateur football clubs **Setting:** UK **Data sources:** *Costs:* Unit Costs of Health and Social Care 2013; other primary costing data collection *Consequences:* Three-arm trial and results from blood sample	**Intervention description:** 1. Captain-led and poster STI screening promotion 2. Sexual health adviser-led and poster STI screening promotion **Comparator/control description:** Poster-only STI screening promotion **Sample sizes:** Total N = 153 Intervention N = 56+46 Control N = 51	**Primary outcome (objective):** Proportion of eligible men accepting screening **Time horizon:** Not clearly stated, but probably equal to the intervention (one year) **Costing year(s) and currency:** 2012-2013 GBP **Discount rates:** Only start-up costs (costs with the posters) were discounted at 3% (for 3 years) **Perspective:** NHS **Measures of uncertainty:** One-way deterministic sensitivity analysis for costs and outcomes **Modelling method:** Not applicable	**Primary analysis:** *Benefits: Number and proportion of men accepting screening:* -Captain-led and poster STI screening promotion: 28 (50%) -Sexual health adviser-led and poster STI screening promotion: 31 (67%) -Poster-only STI screening promotion: 31 (61%) *Costs (average cost per player tested):* -Captain-led and poster STI screening promotion: £88.99 -Sexual health adviser-led and poster STI screening promotion: £88.33 -Poster-only STI screening promotion: £81.87 **Secondary analysis:** None **Sensitivity analyses:** Variables affecting the overall cost: Time needed for club	**Limitations identified by author:** -Uptake of screening could not be accurately estimated for intervention arms -Variability in the acceptability of screening intervention between clubs limited ability to estimate acceptability -Difficulty in recruitment meant that target sample size was not reached -Subsequent testing that may have occurred outside of the intervention but been motivated by intervention materials was not captured, meaning that the uptake of STI testing linked to the

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Quality score: Medium **Applicability:** Partially applicable				recruitment; incentive of £1000 for each club to help maximise participation; costs for team captains to deliver the promotion; intervention costs; cost of the test kit boxes; sample processing costs	intervention may be an underestimate -No cases of chlamydia or gonorrhoea were identified as part of the intervention, making it impossible to estimate a cost per case diagnosed -The influence of captains on uptake of testing was not anticipated. However, this appears to have played a substantial role, with some captains encouraging players to participate in screening in team-wide communications **Limitations identified by review team:** - Only one outcome was explored: the proportion of eligible

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
					men accepting screening - Time horizon was unclear, although the analysis seems to be for one year. If analysis was conducted for one year, costs might be overestimated, as costs for posters were discounted for three years; authors had not stated if only a proportion or the full costs were allocated into the analysis **Evidence gaps and/or recommendations for future research:** Authors clearly stated that this analysis was conducted for the pilot phase, and that was the reason for a cost-consequence analysis. A full cost-effectiveness

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
					analysis with a probabilistic analysis might help with uncertainties around the costs and consequences, especially between the captain-led and the health adviser-led interventions **Source of funding:** SPORTSMART study, part of NIHR-funded BALLSEYE Programme 'Targeting Men for Better Sexual Health'; no competing interests declared
Kessler et al. (2013) **Aim of study:** To inform HIV prevention planning in the jurisdiction by comparing cost-per	**Source populations:** HIV infected; HIV infected, high risk; HIV infected, hazardous alcohol users; HIV infected and partners; HIV	**Intervention description:** Increases in investment in HIV prevention programmes - CD - Condom distribution - SM - Social marketing - CI - community intervention	**Outcomes:** -Number and percentage of infections averted -Cost per infection averted * threshold of £243,000 ($360,000) per infection	**Primary analysis:** *Base case:* - 58,632 new cases of HIV infection over a 20-year time period - Average incidence of 2,932 new infections per year	**Limitations identified by author:** - Not all inputs are known with certainty, and results are partially dependent on the assumptions embedded in the model

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
infection averted between the various Enhanced Comprehensive HIV Prevention Planning (ECHPP) strategies and by identifying the optimal package of prevention services in NYC **Type of economic analysis:** Cost-effectiveness analysis **Economic perspective:** NYC Department of Health and Mental Hygiene (NYC DOHMH) **Quality score:** High	infected on ART; HIV uninfected; HIV uninfected, high risk; providers; all population **Setting:** New York City, USA **Data sources:** *Population of NYC in 2009:* NYC HIV surveillance data *Costs:* Estimates of programmatic expenditures within the DOHMH *Other inputs:* Literature; discussion and consensus amongst the study team	- SD - Prioritised use of surveillance data - CF - Cofactors (brief screening and treatment for co-morbid STDs) - SBIRT - Screening, brief intervention and referral for treatment for unhealthy alcohol use - LC - Linkage to care - LS - Linkage to support - PS - Partner services - RR - risk reduction - STD screening - TC - Testing – clinical - TNC - Testing – non-clinical - CC - Care coordination - SS - Social services - PEP - Post-exposure prophylaxis (provision of post-exposure prophylaxis to populations) **Comparator/control description:** Current scenario:	averted was selected as cost-saving **Time horizon:** 20 years **Costing year(s) and currency:** 2010 USD **Discount rates:** Apparently no discount rate was applied **Perspective:** NYC Department of Health and Mental Hygiene (NYC DOHMH) **Measures of uncertainty:** Sensitivity analyses with alternative time horizons of potential interest for policy decisions (5 years and 10 years); costs (±50%) **Modelling method:** Deterministic compartmental model of HIV transmission/micro-simulation HIV disease progression model	- 16,159 persons were predicted to have died of AIDS-related conditions over 20-year simulation - Average 808 deaths per year *Increases in investment in HIV prevention programmes:* Cost per infection averted/cost-saving? CD1: £2,004 ($2,969) / YES CD2: £2,345 ($3,474) / YES CD3: £86,883 ($128,715) / YES CD4: £126,368 ($187,212) / YES SM1: £2,345 ($3,474) / YES SM2: £54,888 ($81,315) / YES SM3: £55,709 ($82,532) / YES SM4: £228,843 ($339,026) / YES CI1: £4,482 ($7,173) / YES SD1: £18,673 ($27,663) / YES CF1: £21,130 ($31,304) / YES	- Costs were not addressed from the comprehensive societal perspective and therefore may not be inclusive or reflective of all costs incurred by society or payers outside the NYC DOHMH - Recently approved biomedical interventions and modalities still under investigation were not considered in the model (for example, rapid HIV self-testing and pre-exposure prophylaxis, microbicides and HIV vaccine) - Modelled interventions are not mutually exclusive as the implementation of one intervention may

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Applicability: Directly applicable.		without incremental investment in HIV prevention programmes or strategies **Sample sizes:** Simulated cohort of individuals. Number of individuals in cohort not reported.		CF2: £2,451,098 ($3,631,257) / NO SBIRT1: £24,821 ($36,772) / YES SBIRT2: £2,629,434 ($3,895,458) / NO LC1: £257,112 ($380,906) / YES LS1: £83,896 ($124,291) / YES PS1: £133,821 ($198,253) / YES RR1: £518,016 ($767,431) / NO STD1: £228,843 ($339,026) / YES STD2: £322,639 ($477,984) / NO STD3: £7,698,044 ($11,404,509) / NO STD4: £11,907,321 ($17,640,475) / NO TC1: £1,190,066 ($1,763,061) / NO	impact on pathways or outcomes of another - Per-person costs in the model were derived from programmatic estimates from the DOHMH and were applied in a 'pre purchased' approach. This neither accounts for the potential economies of scale that may be operational nor the actual utilisation of an intervention. Therefore, potential bias towards overestimation of costs of interventions may occur, leading to a more conservative estimate of portfolios of interventions that may be 'cost-saving' - The model does not explicitly consider costs

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				TNC1: £2,099,507 ($3,110,381) / NO CC1: £781,784 ($1,158,199) / NO SS1: £706,311 ($1,046,387) / NO PEP1: £7,698,044 ($11,404,509) / NO PEP2: £9,812,825 ($14,537,519) / NO **Secondary analysis:** *Analysis with cost-saving intervention:* - CD (high-risk HIV infected persons), SM (HIV-infected persons), CI, CF (HIV-infected persons), and LS (HIV-infected persons, partner) are interventions included in different packages located on the efficiency frontier - CI+LS (HIV+)+STD (HIV infected, high risk)+PS is the package to prevent the most infections (20,211 and cost	of the antiretroviral medications or the routine care needed by a person living with HIV/AIDS, although these costs informed the estimation of the £243,000 ($360,000) threshold - Assumptions that the authors have made may have also contributed to the model's limitations - There are little to no reliable data to inform how different interventions would impact on each other if implemented in tandem. - A conservative approach was chosen by research team **Limitations identified by review team:** Main

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				per infection averted £71,805 ($106,378) Analysis including all interventions PEP (HIV-), LS, SM (HIV+), CI and TC is the package to prevent the greatest number of infections (33,004 infections averted) and cost per infection averted £6.075 million ($9 million) **Sensitivity analysis:** - Several of the interventions had >10% absolute change in their projected effectiveness in one-way sensitivity analysis - Varying all parameters and evaluating the effects of all interventions under these conditions demonstrated that the prevention interventions considered to be of favourable value were robust - No intervention with a cost per infection averted greater	limitations covered by authors **Evidence gaps and/or recommendations for future research:** Future research could include an assessment of reduction in number of complications of HIV taking into account levels of CD4 and effects on lifetime costs and health outcomes **Source of funding:** The study was sub-contracted by the Department of Health and Mental Hygiene, Bureau of HIV/AIDS Prevention and Control

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				than the £243,000 ($360,000) threshold under base case assumptions crossed this threshold under any other conditions. - Several of the interventions (CD, LS, PS and STD) that were considered cost-saving under base case assumptions had cost-per-infection ratios which increased above the threshold considered as cost-saving under other, specific conditions - Under conditions where ART initiation was not restricted by CD4 count there were no differences in the list of interventions that were considered to be cost-saving or in the relative rankings of interventions by cost per infections averted - Variation in the time horizon did not change the	

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				group of interventions considered cost-saving	
Lasry et al. (2012) **Aim of study:** To support the planning efforts of the Division of HIV/AIDS Prevention (DHAP) and inform the decision-making process for HIV resource allocation **Type of economic analysis:** Cost-saving **Economic perspective:** Government **Quality score:** Low **Applicability:** Partly applicable	**Source populations:** HIV transmission risk group and gender: male high risk heterosexuals (HRH), female HRH, men who have sex with men (MSM), male injection drug users (IDUs) and female IDUs (black, Hispanic and all others – whites, Asians, Pacific Islanders, Alaska natives and American Indians) and general U.S. population **Setting:** USA-wide **Data sources:**	**Intervention description:** Allocation for: - HIV testing - Individual and group-level counselling and education **Comparator/control description:** No allocation **Sample sizes:** Simulated cohort of individuals of unspecified size	**Outcomes:** - Projection of HIV infections over time given a specific funding allocation scenario - Amounts to allocate each year toward interventions and population subgroups to minimise new infections - General population: Per-person cost of testing based on the cost of opt-out testing in emergency department settings and the cost of a CDC-led expanded testing programme targeted to high risk populations -Cost of testing in STD clinic settings and the	**Primary analysis:** New infections averted, £216.8 ($327 million) budget - Baseline allocation: 13% - Optimised allocation: 31% ***HIV resource allocation model:*** Allocated proportion of budget ($327 million) *Allocation by intervention (counselling+testing) and risk group* - Baseline: 29% to the general US adult population; 23% to MSM; 11% to IDUs and 36% to HRH - Optimised: entire budget allocated to the MSM, IDU and HHR (51%, 11% and 38% respectively) *Allocation by intervention (counselling+testing) and race ethnicity:*	**Limitations identified by author:** -An underlying assumption of the model is that interventions can be scaled up to effectively reach 100% of the target population. However, some individuals in high-risk populations may be more difficult and therefore more costly to reach - The cost of antiretroviral treatment and variation in the risk of transmission per sex act according to viral load are not considered in the model. Since early diagnosis and treatment reduces HIV

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
	-Cycle 6 (2002) of the National Survey of Family Growth (NSFG), Division of HIV/AIDS -Prevention (DHAP) data, other previously published studies and assumptions		cost of testing in outreach settings **Time horizon:** Five years **Costing year(s) and currency:** 2009 USD **Discount rates:** Apparently not used; results were presented as undiscounted values **Perspective:** CDC **Measures of uncertainty:** Univariate sensitivity analysis function **Modelling method:** - HIV resource allocation model - Dynamic compartmental model: epidemic model - Optimisation model	- Baseline: 32% for blacks, 17% Hispanics and 22% others - Optimised: 36% for blacks; 29% for Hispanics and 35% others *Allocation to counselling and education by serostatus:* - Baseline: 11% of the budget targeted for diagnosed positives and 89% for those susceptible - Optimised: 100% of the budget targeted for diagnosed positives * current baseline and the optimal allocation of funds can be considered cost-saving when compared to the HIV lifetime treatment costs **Secondary analysis:** Incremental Budget Constraint Scenario (from £66.3 million ($100 million) to £331.5 million ($500 million) *By intervention:*	transmission, the benefits of HIV diagnoses may be underestimated. This may mean that a greater focus on testing may be warranted - For most interventions considered, the cost per person was derived using a microcosting approach which does not take into account the higher level management and administrative costs associated with allocating and channelling funds **Limitations identified by review team:** Time horizon too short to account for all benefits generated by reduction in infection

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				- At £66.3 million ($100 million), the budget is allocated to testing only but as the budget increases, more funds are allocated to counselling and education interventions - At a budget of £331.5 million ($500 million) more funds are allocated to counselling and education interventions than to testing *By risk group:* - At £66.3 million ($100 million), 84% of the budget is allocated to MSM and the remainder to IDUs; as the budget increases, more funds are allocated to all three risk groups - At a budget of £331.5 million ($500 million) the proportion of funds allocated to MSM, IDUs and HRH is 55%, 16% and 29% respectively	**Evidence gaps and/or recommendations for future research:** Future research could include an assessment of reduction in number of complications of HIV, taking into account levels of CD4 and effects on lifetime costs and health outcomes **Source of funding:** No support or funding reported

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				New infections: The marginal infections averted decrease from 38,506 to 5,906 and represent the reduction in HIV incidence for each additional £66.3 million ($100 million) made available in the annual budget **Sensitivity analysis:** Of over 100 sensitivity analysis scenarios conducted, only 9 scenarios altered the key results	
Marseille et al. (2011) **Aim of study:** To reports the cost-effectiveness of the demonstration sites. It addresses the following questions: 1. What were the total and unit costs over the 3 years of the	**Source populations:** HIV-infected patients seen in clinical settings: All patients (including new and returning patients); Male patients reporting sexual activity with other males in the last 6 months; All returning patients;	**Intervention description:** Counselling based interventions: - Primary care provider-based (clinical provider): brief risk assessments administered by computer to patients in private while they waited for their medical appointments. It was based on proven effective health behaviour change theories that helped clinicians to identify the best points of	**Outcomes:** Unit costs for each of the intervention types; average cost per dose-minute of service; HIV infections averted **Time horizon:** 3 years **Costing year(s) and currency:** 2010 USD **Discount rates:** not clear **Perspective:** Healthcare system	**Primary analysis:** *Total average costs:* - Clinical provider: £98,601 ($146,075) - Specialist: £228,070 ($337,881) - Mixed: £181,515 ($268,911) - Total costs for all 13 sites: £2,473,197 ($3,663,995) *Average cost/dose-minute of service:*	**Limitations identified by author:** - Because the site was the unit of analysis, our sample was too small to yield definitive results - assessing the cost of prevention with positive (PWP) activities required the allocation of expenditures across the categories, direct services, training,

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
demonstration project and how did costs vary across the three intervention types? 2. What was the cost-effectiveness of the Services Administration's Special Projects of National Significance (SPNS) demonstration project considered as a whole? 3. What was the incremental cost-effectiveness among the three intervention types? Secondarily, to understand the specific cost elements that accounted for variations in unit	All men who have sex with men (MSM) patients; Patients diagnosed with HIV for at least 3 months; Patients older than age 45 years reporting unprotected sex in the last 12 months; Patients reporting sexual activity or drug use in the last 3 months; Female patients; Patients reporting risk in the last 6 months; Patients with sex or drug risk in the last 6 months; Patients reporting sexual activity or IDU in last 6 months **Setting:** USA:	intervention with brief counselling sessions for a particular patient - social worker or peer educator-based (specialist): one-on-one client-oriented sessions, group session or a combination. Individual sessions were led by either social workers or trained HIV-infected peer interventionists. Group sessions were usually co-led by a social worker and peers - mix of primary care and specialist-based (mixed): Interventions using both strategies, provider-delivered and specialist-delivered interventions **Comparator/control description:** Standard care **Sample sizes:** Clinical provider: 768 Specialist: 975	**Measures of uncertainty:** Multivariate sensitivity analyses, Monte Carlo simulation, threshold analysis, scenario analysis **Modelling method:** Computer-based epidemic model of HIV transmission	- Clinical provider: £11.79 ($17.46) - Specialist: £4.97 ($7.37) - Mixed: £9.30 ($13.78) *HIV cases averted:* - Clinical provider: 2.71 - Specialist: 1.11 - Mixed: 3.02 *Cost-effectiveness ($ per HIV case averted):* - Clinical provider x standard of care: £72,668 ($107,656) - Clinical provider x mixed: Clinical provider sites dominate - Clinical provider x specialist: Clinical provider sites dominate - All sites combined x standard of care: 361,653 ($535,782) **Secondary analysis:** None **Sensitivity analysis:**	research and administration/ overhead. These allocations were not based on standard or pre-existing accounting templates and therefore required personal judgement by staff members. Although we reviewed and discussed the allocations and their rationales carefully, this method is imperfect. However, most of the potential misallocations do not affect our primary results - Misallocations between PWP and non-PWP activities at the same sites would affect the accuracy of our results, but these are

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
cost and the relationship between programme scale and unit costs **Type of economic analysis:** Cost-effectiveness **Economic perspective:** Healthcare system **Quality score:** High **Applicability:** Directly applicable	-Medical care provider only: Johns Hopkins University, Baltimore, University of Alabama Birmingham -HIV specialist only: El Rio/Special Immunology Health Center, Tucson; St. Luke's Roosevelt Hospital, New York; University of Washington, Seattle; Fenway Community Health Center, Boston; Mt. Sinai Hospital, Chicago, University of Miami -Medical care provider and HIV specialist: DeKalb County Board of	Mixed: 758 Standard care: 1,055		*Monte Carlo simulation:* - With 50,000 trials, the cost-effectiveness of the clinical provider sites at the 80% confidence level varied from £53,900 ($79,852) to £99,500 ($147,482) using beta distributions for the three variables and from £39,492 ($58,507) to £139,596 ($206,809) using uniform distributions (both under the threshold of £204,593 ($303,100)) - Considering the average cost-effectiveness of all sites, cost-effectiveness ranges from £268,890 ($398,355) to £503,675 ($746,185) (beta) and from £197,049 ($291,925) to £710,947 ($1,053,255) (uniform). The low end of the range using uniform distributions is thus just on the favourable side of the threshold	unlikely to have occurred to a significant degree because accounting reports were required by Health Resources and Services Administration to track PWP expenditures and because intervention staff can readily distinguish between these two types of activities - Estimates of intervention effect are based on self-reported changes in behaviour. Although these methods are standard in low-prevalence settings, they contain potential for social desirability bias, which may inflate the estimates of intervention benefit

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	Health, Decatur; Drexel University, Philadelphia; University of California San Diego, Owen Clinic; University of California, Davis; University of North Carolina, Chapel Hill **Data sources:** *Annual costs:* Intervention expenditure records *Number of clients served in each programme year:* Standardised reporting documents required by the Health Resources and Services Administration			*Multivariable threshold analysis:* - even if programme effectiveness was only 50% of that found, costs could also rise by almost 50% before the clinical provider interventions stopped being cost-effective compared with no intervention *Scenario analysis using only sites showing benefit:* - Four sites exhibited increased risky behaviour and thus had 'negative benefits'. Two of these were specialist and two were mixed sites. If these sites are disregarded, the incremental cost-effectiveness ratio of mixed versus provider is £661,457 $979,936 per case averted. In this scenario, both provider and mixed dominate specialist	- It was assumed that all averted infections are truly averted, not merely postponed. Estimating the portion of cases that are postponed is rarely done in the assessment of HIV interventions. Obtaining a precise estimate requires a number of assumptions about the evolution of partners' risk profiles - Estimates of risk reduction are limited to patients who participated in the interventions and do not estimate the effects on the community **Limitations identified by review team:** Time horizon too short to account for all benefits associated with the

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
	Costs: Standard cost data collection protocol and accompanying manual				reduction in risk transmission **Evidence gaps and/or recommendations for future research:** Future research could include an assessment of reduction in number of complications of HIV taking into account levels of CD4 and effects on lifetime costs and health outcomes **Source of funding:** This publication is supported by grant number 5 H97 HA00261 from the Health Resources and Services Administration (HRSA) Special Projects of National Significance (SPNS) Program
Pilgrim et al. (2010) **Aim of study:** To assess the cost-	**Source populations:** 1. Young people aged 14-16 years	**Intervention description:** 1. School-based dispensing of hormonal contraceptives within the school (DH); school-	**Primary outcome:** Cost per age pregnancies averted, cost per abortions averted	**Primary analysis:** ***Model 1: Deterministic results (discounted):***	**Limitations identified by author:** - There are several key structural uncertainties

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
effectiveness of a range of interventions to encourage young people, especially socially disadvantaged young people, to use contraceptives or contraceptive services **Type of economic analysis:** Cost-effectiveness **Economic perspective:** Public sector **Quality score:** Medium **Applicability:** Partly applicable	who have not previously been a parent (but who may or may not have been pregnant without carrying to term) within secondary school 2. Young mothers within a secondary school 3. Young people aged 15–19 years who are sexually active **Setting:** UK **Data sources:** *Probability of abortion and birth:* National government statistics for England and Wales	based dispensing of condoms (DC) 2. Intensive case management to prevent repeat pregnancy (this involves a culturally matched school-based social worker, including home visits, weekly school-based peer education support and comprehensive medical care including contraception) (ICM) 3. Advance provision of emergency hormonal contraception (AP) **Comparator/control description:** 1. School nurse only (ND) 2. No follow-up following first pregnancy 3. No advance provision of EHC (No AP) **Sample sizes:** Simulated cohort of 100,000 young individuals	*Secondary outcomes:* Cost of the intervention and additional contraception required as a result of the intervention; cost of maternity care; cost of abortion; cost of miscarriage/ ectopic pregnancy/ stillbirth; cost of treatment for low birth weight babies; cost of treatment of STIs; cost of government-funded benefits **Time horizon:** Lifetime **Costing year(s) and currency:** 2007-2008 GBP **Discount rates:** 3.5% **Perspective:** Public sector **Measures of uncertainty:** One-way and probabilistic sensitivity analysis **Modelling method:** Cost-effectiveness modelling	*Total cost (billions):* - ND: £1,527 - DC: £1,519 - DH: £1,417 *Cost per abortion averted:* - DC: £815 - DH: £1,514 (compared with DC) *Cost per pregnancy averted (excluding benefits):* - DC: £32 - DH: £441 (compared with DC) *Cost per pregnancy averted (including benefits):* - DN: dominated by DC - DC: dominated by DH - DH: dominates DC and ND ***Model 2: Deterministic results (discounted)*** *Total costs (millions):* - no follow-up: £655,572 - ICM: £705,730	within the model which it was not feasible to assess within the PSA and these key uncertainties are likely to underestimate rather than overestimate the effectiveness of the interventions; this suggests that cost-effectiveness ratios are more likely to be overestimated than underestimated - There are a large number of uncertainties within the model due to a paucity of evidence - The effectiveness evidence generally reports the percentage of young people either using contraceptives or becoming pregnant over a relatively short period

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
	Probability of miscarriage and ectopic pregnancy: Hospital Episode Statistics (HES); a Denmark study was used to parameterise the miscarriage rates *Long term outcomes of a teenage birth:* Literature review including only UK papers and elicitation technique with programme development group (PDG) at NICE *Sexually transmitted infection (STI) outcomes:* NICE Sex and Relationship Education (SRE)		study with a hypothetical cohort of 100,000 young people over a lifetime from the age at which the intervention is provided; the following scenarios were modelled: 1. School-based interventions for nulliparous young people 2. School-based interventions to prevent repeat pregnancy 3. Interventions to encourage the use of emergency hormonal contraception following unprotected sex	*Cost per repeat teenage pregnancy averted (excluding benefits):* ICM: £15,155 *Cost per repeat teenage pregnancy averted (including benefits):* ICM: £4.031 ***Model 3: Deterministic results (Discounted)*** *Total cost (billions):* - no AP: £1,524 - AP: £1,447 *Cost per abortion averted:* AP: £2,795 *Cost per age pregnancy averted:* AP (excluding benefits): £310 *Cost per age pregnancy averted:* AP (including benefits) dominates **Secondary analysis:** ***Model 1: Expected results (discounted)*** *Total cost (billions):* - DN: £1,524	- The evidence around the long-term outcomes of a teenage birth is varied in terms of quality and results, leading to considerable uncertainty around the negative consequences of teenage births - Limited evidence exists around the outcomes of the child of a teenage birth, adjusting for the characteristics which might predispose a woman to teenage birth - It was not feasible to express model outcomes in terms of a measure which would enable comparisons of the cost-effectiveness of interventions across different health topics/

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
	public health guidance *Effectiveness:* National statistics and assumptions *Benefits:* Office for National Statistics (ONS, 2009), previous published studies, assumptions *Costs:* British National Formulary (BNF 58, 2009), NICE assessment of LARCs, health economic model developed for the NICE Sex and Relationship Education (SRE) public health guidance, NHS reference costs			- DC: £1,517 - DH: £1,515 *Cost per abortion averted:* - DC: £822 - DH: £1,495 (compared with DC) *Cost per pregnancy averted (excluding benefits):* - DC: £38 - DH: £443 (compared with DC) *Cost per pregnancy averted (including benefits):* - DN: dominated by DC - DC: dominated by DH - DH: dominates DC and ND ***Model 1: Expected results (undiscounted):*** *Total cost (billions):* - DN: £2,307 - DC: £2,297 - DH: £2,295 *Cost per abortion averted:*	diseases such as the QALY - the health economic model does not capture the variability between young people - The comparison within Model 1 is highly dependent upon the true effectiveness of each method of contraception - Research comparing the cost-effectiveness of different methods of contraception in terms of both STIs and contraception is sparse due to the limitations around which outcome measure can reasonably capture both effects. - the cost of maternity services may differ for teenage mothers

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				- DC: £848 - DH: £1,535 (compared with DC) *Cost per pregnancy averted (excluding benefits):* - DC: £92 - DH: £488 (compared with DC) *Cost per pregnancy averted (including benefits):* - DN: dominated by DC - DC: dominated by DH - DH: dominates DC and ND ***Model 2: Expected results (discounted)*** *Total cost (millions):* - No follow-up: £654,756 - ICM: £705,164 *Cost per repeat teenage pregnancy averted (excluding benefits):* ICM: £15,175	compared with older mothers **Limitations identified by review team:** - Authors stated that no preterm births were assessed, which may be more common amongst young people - Other adverse events associated with teen pregnancy, such as fistula, were not mentioned **Evidence gaps and/or recommendations for future research:** Modelling was based on previous model (NICE), but no mention about calibration of the model, e.g., tuning of probabilities or parameters that have

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				Cost per repeat teenage pregnancy averted (including benefits): ICM: £4,052 ***Model 2: Expected results (undiscounted):*** *Total cost (millions):* - No follow-up: £825,978 - ICM: £866,883 *Cost per repeat teenage pregnancy averted (excluding benefits):* ICM: £15,186 *Cost per repeat teenage pregnancy averted (including benefits):* ICM: £2,935 ***Model 3: Expected results (discounted)***: *Total cost (billions):* - No AP: £1,522 - AP: £1,445 *Cost per abortion averted:* AP: £2,803 *Cost per age pregnancy averted:* AP (excluding benefits): £314	caused uncertainties in previous models **Source of funding:** Not declared

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				Cost per age pregnancy averted: AP (including benefits) dominates ***Model 3: Expected results (undiscounted)*** *Total cost (billions):* - No AP: £2,303 - AP: £2,198 *Cost per abortion averted: AP:* £2,948 *Cost per age pregnancy averted: AP (excluding benefits):* £395 *Cost per age pregnancy averted:* AP (including benefits) dominates **Sensitivity analysis:** ***Model 1*** *PSA:* The analysis shows very little difference in both costs and effectiveness between dispensing condoms within schools and dispensing	

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				hormonal contraceptives within schools. There is the possibility that either one could be more effective and/or more costly than the other *One-way:* -Delay in births averted (14-16 years to 17-19 years): (1) DC would remain cost saving compared with ND for the cost per age 14–16 pregnancy averted including government-funded benefits; (2) DH would remain cost saving compared with DC within schools for this outcome - Pregnancies averted at ages 14 – 16 years would have been additional: cost-effectiveness ratio for the cost per abortion averted decreases	

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				- Probability of condom failure is doubled: DC results in greater net costs than DH - Doubled risk of miscarriage: DC is estimated to result in net cost savings compared with ND - Increase in medical abortions: net cost savings of DC compared with ND - Increase in relative risk of both interventions: higher cost-effectiveness ratios than predicted within the base case analysis ***Model 2*** *PSA:* - ICM is unlikely to result in net cost savings when excluding benefit payments - There is around a 20% probability that ICM will result in net cost savings when including government-funded benefits compared	

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				with no follow-up after first teenage pregnancy *One way:* - Reducing cost of intervention: results in a cost per repeat teenage pregnancy averted excluding benefits of £6,844 - Including benefits: ICM will dominate no follow-up after a teenage birth - Other variations do not have substantial impact upon the model results ***Model 3*** *PSA:* - AP is unlikely to result in net cost savings using the cost per abortion averted outcome - There is around a 24% probability AP will result in net cost savings when using the cost per age 15–19 pregnancy averted outcome	

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				and benefit payments are excluded from the analysis - AP is likely to be cost saving using a cost per age 15–19 pregnancy averted outcome when benefit payments are included *One way:* - Increasing the baseline usage of EHC following unprotected sex: AP dominates including and excluding government-funded benefit payments; estimated cost per abortion averted associated with AP decreases to £688 - Other variations do not have substantial impact upon the model results	
Ruger et al. (2014) **Aim of study:** To assesses cost-effectiveness of	**Source populations:** Drug-using women (cocaine, heroin, amphetamines or	**Intervention description:** - WWE – standard intervention (SI) and a field-based well woman examination (WWE): SI + breast and routine pelvic	**Outcomes:** Total number of primary and secondary infections prevented by the intervention; cost of achieving an additional	**Primary analysis:** ***Randomised controlled trial results:*** *Baseline for HIV:* -SI ***x*** WWE: WWE dominated	**Limitations identified by author:** *Statistical analysis:* - Bernoullian model predicting infection

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
behavioural interventions for reducing HIV and STDs infections among injection drug-using women **Type of economic analysis:** Cost-effectiveness and cost-utility **Economic perspective:** Societal and provider **Quality score:** High **Applicability:** Directly applicable	other injection drug use), age 18 or older and sexual activity in the prior 4 months **Setting:** St. Louis area residency, USA **Data sources:** *Cost:* Previous study developing a microcosting methodology and conducting cost analyses *Effectiveness:* randomised trial and literature	examination with cervical cytological testing (Pap smear) provided by a nurse practitioner, who also obtained a short medical history - 4ES - SI, WWE, plus four educational sessions (4ES): SI + WWE + 4ES delivered by a peer facilitator paired with a health professional, based on the Health Belief Model. The facilitator used a holistic approach emphasising substance abuse, HIV/AIDS, health and nutrition, and stress and coping **Comparator/control description:** SI - modified National Institute on Drug Abuse (NIDA) cooperative agreement standard intervention: 20 minutes of HIV pre-test counselling, blood collection and the NIDA SI; and	unit of outcome compared to the next least costly intervention; the cost per additional QALY saved **Time horizon:** Trial - 12 months; model – lifetime **Costing year(s) and currency:** 2003 USD **Discount rates:** Only QALYs were discounted at 3% **Perspective:** Societal and provider **Measures of uncertainty:** One-way, bivariate and multivariate sensitivity analyses, acceptability curves **Modelling method:** Bernoullian mathematical model estimates of infections averted	-WWE *x* 4ES: 4ES cost-effective and cost-saving: £62,098 ($94,230) per additional infection averted *STDs total:* -SI *x* WWE: WWE dominated -WWE *x* 4ES: 4ES cost-effective: £5,509 ($8,359) per additional infection averted *Hepatitis C:* -SI *x* WWE: WWE cost-effective and cost-saving: £72,034 ($109,308) per additional infection averted and £27,996 ($42,482) per additional QALY saved -WWE *x* 4ES: 4ES dominated *Syphilis:* -SI *x* WWE: WWE dominated -WWE *x* 4ES: 4ES cost-effective: £28,838 ($43,760) per additional infected averted *Chlamydia:*	rates based on sexual conduct assumes independence - Nesting of overlapping partners was not considered - The number of partners used in predicting secondary infections is based on participants' number of partners *Study:* - Its location in a single urban centre limits its generalisability - data constraints prevented incorporating future costs, except for those from the literature included in the Bernoullian model (e.g. lifetime HIV and STD treatment costs), suggesting an

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
		2 weeks later, test results and HIV post-test counselling **Sample sizes:** SI = 144 WWE = 153 4ES = 157 Total = 454		-SI *x* WWE: WWE dominated -WWE *x* 4ES: 4ES cost-effective and cost saving: £19,530 ($29,636) per additional infection averted and £ 2,273,217 ($3,449,495) per additional QALY saved *Gonorrhoea:* -SI *x* WWE: WWE cost-effective and cost saving: £6,235 ($9,461) per additional infection averted and £706,949 ($1,072,760) per additional QALY -WWE *x* 4ES: 4ES dominated **Secondary analysis:** ***Bernoullian model results*** *HIV primary:* -SI *x* WWE: WWE cost-effective and cost-saving: £137,280 ($208,316) per additional infection averted -WWE *x* 4ES: 4ES dominated *HIV total:*	underestimation of the intervention's results - by focusing on HIV and STD prevention and substance abuse, the intervention incorporated significant interactions, but might have sacrificed the clarity possible in studying HIV and/or STDs exclusively - the model results were highly sensitive to input parameters, especially prevalence and transmission probability - baseline assessment determined STD prevalence, which may underestimate the prevalence among partners because the participants were all HIV-negative,

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				-SI *x* WWE: WWE cost-effective and cost-saving: £33,460 ($50,774) per additional infection averted -WWE *x* 4ES: 4ES dominated *Hepatitis C:* -SI *x* WWE: WWE cost-effective and cost-saving: £3,965 ($6,016) per additional infection averted -WWE *x* 4ES: 4ES dominated *Syphilis:* -SI *x* WWE: WWE cost-effective: £11,257 ($17,082) per additional infection averted -WWE *x* 4ES: 4ES dominated *Chlamydia:* -SI *x* WWE: WWE cost-effective and cost-saving: £113,548 ($172,303) per additional infection averted and £13,334,149	suggesting they have fewer STDs than their peers - QALY measures and their estimation have many disadvantages when used for health policy evaluation **Limitations identified by review team:** Main limitations identified by the authors **Evidence gaps and/or recommendations for future research:** Complications of STIs could be explored in to the model **Source of funding:** - National Institutes of Health (NIH) (National Institute on Drug Abuse (NIDA) Grant R01DA11622, and

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				($20,233,913) per additional QALY saved -WWE *x* 4ES: 4ES dominated *Gonorrhoea:* -SI *x* WWE: WWE cost-effective and cost-saving: £9,255 ($14,044) per additional infection averted and £1,062,241 ($1,611,898) per additional QALY saved -WWE *x* 4ES: 4ES dominated **Sensitivity analysis:** ***One-way*** *Trial results*: - WWE and 4ES sensitive to small effectiveness changes in preventing hepatitis C - WWE is sensitive for HIV and syphilis and very robust for chlamydia and gonorrhoea - 4ES is robust for other diseases (except hepatitis C) ***Bernoullian model:***	K01DA01635810 to J.P.R.) - the Patrick and Catherine Weldon Donaghue Medical Research Foundation (Grant DF06-112 to J.P.R.)

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				- Model HIV results require large changes in effectiveness to show domination for WWE and to relieve domination for 4ES Bi- and multivariate: WWE is cost-effective or cost-saving relative to SI in all model scenarios ***Acceptability curves:*** *-Preventing total STD:* -WWE x 4ES: WWE has a 0.80 probability at £19,770 ($30,000) -WWE x SI: WWE less than 0.20 probability *Preventing hepatitis C*: The probabilities of being cost-effective are considerably higher for WWE than 4ES, but at £13,180 ($20,000), the two curves begin to report increasingly similar probabilities	

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Sanders et al. (2010) **Aim of study:** To examine the costs and benefits of strategies to improve HIV testing and receipt of results **Type of economic analysis:** Cost-effectiveness **Economic perspective:** Insurer and patient **Quality score:** Medium **Applicability:** Partly applicable	**Source populations:** Patients from two Departments of Veterans Affairs in California, aged 18–65 years, with unknown HIV status **Setting:** USA/ Southern California **Data sources:** *Costs:* Centres for Medicare and Medicaid (CMS) reimbursement rates for the VA, Abbott Laboratories, earlier analysis, Bureau of Labour Statistics *Others:* Randomised clinical trial, 'high-quality published literature' (quality	**Intervention description:** -Model B = nurse-initiated routine screening with traditional HIV testing and counselling -Model C = nurse-initiated routine screening with rapid HIV testing and streamlined counselling **Comparator/control description:** Model A = traditional HIV counselling and testing **Sample sizes:** Total: 251	**Outcomes:** Life-years, QALYs, costs and incremental cost-effectiveness (cost/QALY) **Time horizon:** Lifetime **Costing year(s) and currency:** 2007 USD **Discount rates:** 3% **Perspective:** Insurer and patient (although authors assumed the perspective as societal) **Measures of uncertainty:** One-way, multi-way and probabilistic sensitivity analyses **Modelling method:** Adapted Markov model	**Primary analysis:** ***Benefits to partners excluded:*** *Model B (compared to Model A):* Incremental cost-effectiveness (cost/QALY): extended dominance *Model C (compared to Model A):* Incremental cost-effectiveness (cost/QALY): £23,472 ($36,390) ***Benefits to partners included:*** *Model B (compared to Model A):* - Incremental cost-effectiveness (cost/QALY): extended dominance *Model C (compared to Model A):* - Incremental cost-effectiveness (cost/QALY): £6,876 ($10,660) **Secondary analysis:**	**Limitations identified by author:** - The trial was performed in Veterans Affairs (VA) primary and urgent care settings, which have different patient populations than many primary or urgent care practices - The requirements for follow-up may have discouraged some patients from participating. Thus, the implications for implementation of screening outside a trial are not known - The VA populations studied do not reflect the distributions or the risk groups in some other populations or settings

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
	criteria not reported) and expert clinical judgement			***Benefits to partners excluded:*** *Model A:* - Lifetime costs: £31,379 ($48,650) - Life years (LY): 18.8330 - QALY: 16.2714 *Model B:* - Lifetime costs: £31,418 ($48,710) - Incremental costs: £34 ($53) - Life years (LY): 18.8348 - Incremental life years: 0.0018 - Incremental cost-effectiveness (LY): Extended dominance - QALY: 16.2727 - Incremental QALY: 0.0013 - Increase in life expectancy: 0.64 years - Quality-adjusted life expectancy (QALE): 0.47	**Limitations identified by review team:** - Complications associated with HIV were not included - Costs were modelled based on reimbursement costs not real costs, which may have an influence on the final results (costs maybe either under- or over-estimated) **Evidence gaps and/or recommendations for future research:** It was not clear if interventions would have lifetime effects on complications depending on levels of CD4 **Source of funding:** Department of Veterans Affairs Health Services

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				Model C: - Lifetime costs: £31,424 ($48,720) - Incremental costs: £8 ($13) - Life years (LY): 18.8355 - Incremental life years: 0.0007 - Incremental cost-effectiveness (LY): £17,228 ($26,710) - QALY: 16.2732 - Incremental QALY: 0.0005 - Increase in life expectancy: 0.87 years - QALE: 0.63 ***Benefits to partners included:*** *Model A:* - Lifetime costs: £31,631 ($49,040) - Life years (LY): 18.8153 - QALY: 16.2530 *Model B:*	Research and Development Service and the National Institute on Drug Abuse (R01 DA15612-01). Dr Bayoumi was supported by a career scientist award from the Ontario HIV Treatment Network

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				- Lifetime costs: £31,644 ($49,060) - Incremental costs: £27 $27 - Life years (LY): 18.8178 - Incremental life years: 0.0025 - Incremental cost-effectiveness (LY): Extended dominance - QALY: 16.2551 - Incremental QALY: 0.0021 *Model C:* - Lifetime costs: £31,650 ($49,070) - Incremental costs: £3 ($4) - Life years (LY): 18.8187 - Incremental life years: 0.0009 - Incremental cost-effectiveness (LY): £5,960 ($9,240) - QALY: 16.2559 - Incremental QALY: 0.0008	

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				Sensitivity analysis: - Varying prevalence of unidentified HIV: cost-effectiveness of Model C less favourable - Varying probability of a patient receiving an HIV test and HIV test acceptance rate: cost-effectiveness ratio of Model C increases from £6,876 ($10,660)/QALY to £8,540 ($13,240)/QALY - Varying other variables: no substantial change in the model results	
Schackman et al. (2013) **Aim of study:** To project the life expectancy gains, costs, and cost-effectiveness of HIV testing strategies (evaluated in a	**Source populations:** Substance abuse treatment programme users (12 community-based substance abuse treatment programmes) **Setting:** USA	**Intervention description:** 1. Referral for off-site HIV testing 2. Offer of an on-site rapid HIV test with information that describes the testing procedure but no counselling about risk behaviours 3. Brief participant-tailored risk-reduction counselling that	**Outcomes:** Life expectancy, lifetime costs and QALYs **Time horizon:** Lifetime **Costing year(s) and currency:** 2009 USD **Discount rates:** 3% **Perspective:** Societal **Measures of uncertainty:** One-way sensitivity	**Primary analysis:** (reference: no intervention) *Offer of off-site test:* - Cost-effectiveness ratio (cost/QALY): dominated *On-site test + information:* - Cost-effectiveness ratio (cost/QALY): £39,979 ($60,300)	**Limitations identified by author:** - Data were collected in a clinical trial conducted in community-based substance abuse treatment programmes that were diverse, but were not representative

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
trial) to provide guidance to policy makers and substance abuse treatment programmes **Type of economic analysis:** Cost-effectiveness modelling **Economic perspective:** Societal **Quality score:** High **Applicability:** Directly applicable	**Data sources:** *QALY:* SF-6D data derived from a national survey of HIV infected individuals *Costs:* medical service utilisation data from a national cohort and national costs *Population in substance abuse treatment being tested and other inputs:* The National Drug Abuse Treatment Clinical Trials Network (CTN) HIV Rapid Testing and Counselling Study (CTN 0032), Multicenter AIDS Cohort Study (MACS) and	includes a personalised examination of risk focused on whatever is salient to the risk behaviour of the participant and creation of an individualised risk-reduction plan followed by the offer of an on-site rapid HIV test **Comparator/control description:** No intervention **Sample sizes:** Total: trial population of 1,281 individuals	analysis (prevalence of undiagnosed HIV, CD4 counts, probability of acceptance, costs, HIV test frequency, test sensitivity and specificity, HIV RNA diagnosis for HIV-infected individuals, ART efficacy and costs); scenarios analysis **Modelling method:** First-order state-transition Monte Carlo simulation: cost-effectiveness of Preventing AIDS Complications (CEPAC) computer simulation model	*On-site test + counsel:* - Cost-effectiveness ratio (cost/QALY): dominated **Secondary analysis:** *Background screen:* - Undiscounted life expectancy per HIV-infected person (years): 17.05 - Cost per HIV infected person: £181,671 ($274,013) *Offer of off-site test:* - Undiscounted life expectancy per HIV-infected person (years): 17.85 - Cost per HIV infected person: £196,664 ($296,627) - Cost per HIV uninfected person: £7 ($11) - Incremental cost per person: £68 ($102) - Incremental QALY per person: 0.0016 *On-site test + information:*	of all programmes in the US - The trial was not powered to detect prevalence of undiagnosed HIV - Prevalence of undiagnosed HIV may be higher in settings where there is higher overall HIV prevalence and fewer substance users have been tested previously - Both the CD4 count at diagnosis and the frequency of testing elsewhere were unobserved - The model did not incorporate future HIV transmission behaviour - The authors did not project future advances in HIV care that

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
	published literature			- Undiscounted life expectancy per HIV-infected person (years): 20.75 - Cost per HIV infected person: £251,361 ($379,126) - Cost per HIV uninfected person: £27 ($41) - Incremental cost per person: £239 ($360) - Incremental QALY per person: 0.0060 *On-site test + counsel:* - Undiscounted life expectancy per HIV-infected person (years): 20.52 - Cost per HIV infected person: £247,168 ($372,802) - Cost per HIV uninfected person: £51 ($77) - Incremental cost per person: £7 ($11) - Incremental QALY per person: -0.0005	improve life expectancy nor future gaps in treatment that reduce life expectancy **Limitations identified by review team:** No additional comments. Authors clearly acknowledge main limitations **Evidence gaps and/or recommendations for future research:** Authors could explore some of their limitations in future research **Source of funding:** This research was supported by the National Institute on Drug Abuse (R01 DA027379, K23DA019809); the National Drug Abuse Treatment Clinical Trials Network (CTN)

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				Sensitivity analysis: One-way sensitivity analysis - Varying prevalence of undiagnosed HIV: on-site testing + information vs no intervention: cost-effectiveness ratios are higher - Varying probability of testing: cost-effectiveness ratio for on-site testing + information= £54,896/QALY ($82,800/QALY) - Other variations have little impact on cost-effectiveness ratios	(U10 DA013720, U10DA13720-09S, U10 DA020036, U10DA15815, U10DA13034, U10DA013038, U10 DA013732, U10 DA13036, U10 DA13727, U10DA015833, HHSN271200522081C, HHSN271200522071C); the National Institute of Mental Health (R01 MH063869); and the National Institute of Allergy and Infectious Diseases (R37 A1042006).
Thomas (2012) **Aim of study:** Stated as 'to assess the fiscal impact of three national-level policies designed to prevent unintended	**Source populations:** 10,000 individuals aged 15-44 whose demographic characteristics were nationally representative (of USA)	**Intervention description:** 1. Mass media campaign 2. Evidence-based teen pregnancy prevention programme 3/ Expanded access to Medicaid Family Planning	**Outcomes (linked to unattained pregnancies):** *Main:* benefit-cost ratio *Others:* % reduction in abortion; % reduction in births; % reduction in number of children born into poverty; programme	**Primary analysis:** *Benefits:* -% reduction in abortion: Mass media (3.9%); evidence-based teen pregnancy prevention programme (1.4%); expanded access to Medicaid Family Planning (3.5%)	**Limitations identified by author:** *Does not account for:* - Spending on children over the age of 5 - Private costs of unintended pregnancy

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
pregnancy'. In practice, the author assessed the financial benefit of implementing interventions to prevent unintended pregnancies **Type of economic analysis:** Cost-benefit analysis **Economic perspective:** Government and social **Quality score:** Medium **Applicability:** Partially applicable	**Setting:** United States **Data sources:** The General Social Survey and the National Survey of Family Growth; the Guttmacher Institute; the National Vital Statistics System; data from the Current Population Survey were used to parameterise the model that assigns a poverty status to each newborn child; meta-analysis for behaviour effects; Truth, VERB, and National Youth Anti-Drug Media (NYADMC)	**Comparator/control description:** N/A **Sample sizes:** Total N = 10,000 simulation cohort	costs, public savings, fiscal savings **Time horizon:** 5 years **Costing year(s) and currency:** 2008 USD **Discount rates:** 3% **Perspective:** Social and public sector government) **Measures of uncertainty:** One-way sensitivity analysis **Modelling method:** Cost-benefit analysis	**-** % reduction in births: Mass media (1.0%); evidence-based teen pregnancy prevention programme (0.6%); expanded access to Medicaid Family Planning (1.4%) - % reduction in number children born into poverty: Mass media (2.2%); evidence-based teen pregnancy prevention programme (1.4%); expanded access to Medicaid Family Planning (1.8%) *Costs:* **-**Programme costs: mass media**:** £65.3 million ($100 million); evidence-based teen pregnancy prevention programme: £94,685 million ($145 million); expanded access to Medicaid Family Planning: £153,455 million ($235 million) *Public savings:*	(e.g. lower earnings of mother) *Other potentially important societal costs:* - Does not consider likely effect on spread of STIs - Scale-up of small interventions may be less effective than assumed - Assumption of effectiveness of national media campaign may be incorrect - Programme costs and baseline parameters were uncertain. **Limitations identified by review team:** Author has identified main limitations

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
	campaigns (costs); literature for both benefits and costs			For pregnancy care alone: -Mass media: £24,164,437 ($37,005,263); benefit-cost ratio: £0.24 ($0.37) -Evidence-based teen pregnancy prevention programme: £241,597,209 ($369,980,412); benefit-cost ratio; £0.17 ($0.26) -Expanded access to Medicaid Family Planning: £79,455,150 ($121,677,106); benefit-cost ratio: £0.59 ($0.62) *Pregnancy care plus infant medical:* -Mass media: £58,929,344 ($90,244,018); benefit-cost ratio: £0.59 ($0.90) -Evidence-based teen pregnancy prevention programme: £51,856,523 ($79,412,746); benefit-cost ratio: £0.36 ($0.55) -Expanded access to Medicaid Family Planning:	**Source of funding:** The William and Flora Hewlett Foundation

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				£186,002,878 ($284,843,611); benefit-cost ratio: £0.79 ($1.21) *Pregnancy care plus children benefits:* -Mass media: £281,383,852 ($430,909,421); benefit-cost ratio: £2.81 ($4.31) -Evidence-based teen pregnancy prevention programme: £232,562,922 ($356,145,363); benefit-cost ratio: £1.61 ($2.46) -Expanded access to Medicaid family planning: £862,217,932 ($1,320,394,996); benefit-cost ratio: £3.67 ($5.62) **Secondary analysis:** Findings were relatively insensitive to large changes in the assumptions underlying the analysis. For example, the results of the preferred specifications suggest that, even if the cost of the	

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				Medicaid expansion was twice as high as it was assumed to be — or if the benefits of the teen pregnancy prevention programme were twice what they were estimated to be — the benefit-cost ratios for the former would still be at least as large as for the latter. On the other hand, the results from the preferred specifications that account for spending on children through age 5 suggest that, even if these programmes were half as effective (or twice as expensive) as they were assumed to be, all of them would have benefit-cost ratios of greater than 1.	

Appendix 10: Included studies table: Contraception interventions

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Bayer et al. (2013) **Aim of study:** To examine the cost-efficacy of ulipristal acetate (UPA) compared with levonorgestrel (LNG) **Type of economic analysis:** Cost-effectiveness analysis **Economic perspective:** All pregnancy costs were obtained from state Medicaid payments. It is unclear if costs are measured from the	**Source populations:** Women of reproductive age taking EC within 120 hours of unprotected intercourse **Setting:** US **Data sources:** *Probabilities inputs:* - Emergency contraception (EC) and pregnancy following the use of UPA or LNG: from a 2010 meta-analysis - Distribution of unintended pregnancy outcomes (vaginal vs caesarean delivery, spontaneous abortion, induced abortion, ectopic	**Intervention description:** Ulipristal acetate (UPA) **Comparator/control description:** Levonorgestrel (LNG) **Sample sizes:** Simulated cohort of 10,000 women	**Main outcome:** Number of unattained pregnancy averted **Secondary outcomes:** Pregnancy complications (vaginal vs caesarean delivery, spontaneous abortion, induced abortion, ectopic pregnancy) **Time horizon:** Unclear, but analysis included a single menstrual cycle for single episode of EC use and expands to the assessment of pregnancy outcomes (so at least 10 months, on average) **Costing year(s) and currency:** 2011 USD **Discount rates:** Both costs and benefits	**Primary analysis:** *UPA:* -Pregnancy rate: 54,295 -Costs: £270,251,630 ($399.19 million) -QALY: 111,813,707 *LNG:* -Pregnancy rate: 91,884 -Costs: £348,959,650 ($515.45 million) -QALY: 111,805,654 *Overall analysis (comparing EC and LNG):* -Unintended pregnancies averted (UPA over LNG): 37,589 -Costs saved: £78,735,100 ($116.3 million) -QALYs gained: 8,053 *-Incremental cost-effectiveness analysis:* UPA was a dominant intervention	**Limitations identified by author:** -For the probability of EC failure input there is no distinction between different time frames of taking EC after unprotected intercourse - The costs of LNG and UPA used in the decision model reflect the lower end of published drug prices -The decision model did not include the copper-releasing intrauterine device (IUD) **Limitations identified by review team:** -Measure of benefit (utilities and QALYs) were used without any disaggregation (by type of complication or contraceptive method) so benefits could not be fully assessed

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
societal, healthcare or personal social services perspective **Quality score:** Low **Applicability:** Partly applicable	pregnancy): literature *Costs inputs:* - All pregnancy costs were obtained from Medicaid payments and costs - Costs of EC and LNG: from the market (price women pay over the counter (also online, but only for EC) *Utilities and QALYs:* Assumed an overall 0.992 utility for unattained pregnancies from literature; not disaggregated by outcomes; authors said they used an average life expectancy of 55 additional years after taking EC		were discounted at 3% annually **Perspective:** Unclear (although assumed that it is societal) **Measures of uncertainty:** Univariate, multivariate and probabilistic sensitivity analyses **Modelling method:** Monte Carlo simulation for a cost-effectiveness analysis	**Secondary analysis:** -UPA dominates all scenarios -UPA is still a cost-effective intervention when the failure rate is 1.3%. There is a linear decrease of cost-effectiveness when UPA failure increases -Applying a threshold of £67,700 ($100,000) per QALY gained, UPA was more cost-effective when the UPA failure rate was less than 2.17% and the price of the medication was less than £179 ($265) -At a willingness-to-pay (WTP) threshold of £67,700 ($100,000) per QALY, UPA was the preferred EC 96% of the time	-Complications such as STIs were not included, so full benefits were not assessed -Perspective of analysis was unclear, so we could not assess if results could be extrapolated to the society or to Medicaid users only -Discount rate is not applicable in studies with a time horizon less than 1 year **Evidence gaps and/or recommendations for future research:** -To disaggregate benefits to better understand dominance of UPA over LNG -As discussed in the limitation, further analysis including other effective contraception methods should be undertaken **Source of funding:** None stated

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Foster et al. (2010) **Aim of study:** To determine the potential effect and cost-effectiveness of different means of accessing emergency contraceptive pills (ECP) on unintended pregnancy rates in sexually active women **Type of economic analysis:** Cost-benefit **Economic perspective:** Public payer of medical care **Quality score:** Medium	**Source populations:** Sexually active women who are at risk of having unprotected intercourse **Setting:** USA **Data sources:** *Probability of taking ECP:* Assumptions *Probability of conception:* Available data on conception rates, mean time to use of ECP, and ECP effectiveness after an episode of unprotected intercourse *Effectiveness data:* Single-use clinical trials of ECP *Costs:* Medi-Cal, California's Medicaid programme, and	**Intervention description:** - Advance provision: women who have ECP on hand to use if needed after an episode of unprotected intercourse - On-demand provision: women who must seek ECP from a clinic or pharmacy after an episode of unprotected intercourse * These categories are evaluated as high and low use of emergency contraception: *High use:* Women with advance provision take ECP after all episodes of unprotected intercourse, women with on-demand access take ECP after half of episodes	**Outcomes:** - Unintended pregnancy according to high and low use of ECP - Cost-saving ratio according to pharmacy dispensed and clinic dispensed - Sample size to test difference in pregnancies (advanced vs no ECP and advanced vs on-demand) **Time horizon:** 1 year **Costing year(s) and currency:** 2005 USD **Discount rates:** Not applicable **Perspective:** Public payer of medical care **Measures of uncertainty:** No measurement of	**Primary analysis:** ***Reduction in pregnancy rate comparing with No ECP:*** *High use of emergency contraception:* -Once per year Advance: −66 On demand: −38 -Once per month Advance: −39 On demand: −36 -Once per week Advance: −30 On demand: −30 *Low use of emergency contraception:* -Once per year Advance: −38 On demand: −20 -Once per month Advance: −21 On demand: −17 -Once per week	**Limitations identified by author:** - Recent trials have shown failure of ECP to reduce pregnancy rates. However, the current model suggests that these trials have not had sufficient power to detect differences in these rates - The discrepancy between the single-use trials and the advance provision trial can be due to the overestimation of ECP effectiveness - The inflated expected pregnancy rate would lead to an overestimate of the effectiveness of ECP - The cost savings of advance provision will be underestimated to the extent that women keep their ECP supplies for longer than a year - the cost savings associated with ECP use for advance provision and on demand

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Applicability: Partly applicable	Family PACT, California's Medicaid 1115 Waiver Program	*Low use:* Women with advance provision take ECP after half of episodes of unprotected intercourse, women with on-demand access take ECP after one quarter of episodes **Comparator/control description:** No use of ECP: women who do not have access to ECP and do not use ECP **Sample sizes:** Simulated cohort of individuals derived from multiple estimates	uncertainty was carried out **Modelling method:** Computer simulation model of pregnancies among sexually active women, Markov process	Advance: −15 On demand: −14 ***Costs-savings ratio: pharmacy-dispensed:*** *High use of emergency contraception:* -Once per year Advance: £1.25 ($1.92) On demand: £1.55 ($2.39) -Once per month Advance: £1.38 ($2.12) On demand: £1.35 ($2.08) -Once per week Advance: £1.04 ($1.60) On demand: £1.04 ($1.61) *Low use of emergency contraception:* -Once per year Advance: £0.83 ($1.28) On demand: £1.62 ($2.49) -Once per month Advance: £1.41 ($2.17) On demand: £1.32 ($2.04)	would be higher than projected because women are more likely to use ECP for acts that occur in the week before ovulation - Medical cost data may be lower than private health plan costs. Social, welfare, and private costs can be much higher - The study considered medical costs of an unintended pregnancy for up to 2 years after a birth - Changing behaviour was not considered in to the analysis **Limitations identified by review team:** - Only modelled intercourse where no contraception was used; cost effectiveness would be lower if emergency contraception used in situations where likelihood of conception is lower than with

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				-Once/week Advance: £1.07 ($1.65) On demand: £1.06 ($1.64) ***Costs-savings ratio: Clinic-dispensed:*** *High use of emergency contraception:* -Once per year Advance: £1.14 ($1.75) On demand: £0.979 ($1.50) -Once per month Advance: £0.90 ($1.39) On demand: £0.84 ($1.30) -Once per week Advance: £0.66 ($1.01) On demand: £0.65 ($1.00) *Low use of emergency contraception:* -Once per year Advance: £0.80 ($1.24) On demand: £1.01 ($1.56) -Once per month Advance: £0.97 ($1.50)	no contraception (e.g. missed pill) - Medicaid costs may be lower than private health plan costs - Only considered medical costs of unintended pregnancy for up to 2 years after a birth - Social, welfare and private costs likely to be much higher - Generic emergency contraception may reduce costs and increase cost saving **Evidence gaps and/or recommendations for future research:** To model scenarios assessing the limitations discussed above for a longer period and include complications of pregnancies and STI risks **Source of funding:** The California State Department of Public Health, Maternal, Child and Adolescent Health Branch (MCAH), Office of Family Planning.

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				On demand: £0.83 ($1.28) -Once per week Advance: £0.69 ($1.07) On demand: £0.67 ($1.03) **Secondary analysis:** The required size of a study designed to test differences in pregnancy rates between advance provision and no ECP access ranged from 133 to 4,370 in each arm and to test differences in pregnancy rates between advance provision and on-demand provision ranged from 4,556 to 320,926 in each arm **Sensitivity analysis:** Not reported	Funder did not participate in the design of the study or the collection, management, analysis, and interpretation of the data. The funder reviewed and approved the final manuscript
Foster et al. (2013) **Aim of study:** To examine the relative cost-benefit of specific methods and evaluate the	**Source populations:** Women aged 15 to 44, PACT clients **Setting:** USA, California **Data sources:** Paid claims data, Family	**Intervention description:** Contraceptive methods: Interval tubal ligation Tubal occlusion Copper intrauterine contraception (IUC)	**Outcomes:** Costs of providing contraceptive services for each method; pregnancies averted; cost-savings per dollar expenditure	**Primary analysis:** *Pregnancies averted:* Interval tubal ligation: 1,766 Tubal occlusion: 355 Copper intrauterine contraception (IUC): 10,264	**Limitations identified by author:** - The cost savings of long-acting methods were underestimated because women may use them for

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
relative contribution of each method to the number of unintended pregnancies averted within the Family PACT population **Type of economic analysis:** Cost-benefit **Economic perspective:** Public sector **Quality score:** Medium **Applicability:** Partly applicable	PACT Medical Record Review, published estimates for unintended pregnancies in California, medical records, assumptions	Hormonal IUC Implant Injectable Ring Patch Oral contraceptives Barriers (including on-site dispensing of male and female condoms, diaphragms, and spermicides) Emergency contraceptives **Comparator/control description:** *Comparator:* Doing-nothing scenario The intervention assumes a scenario where different contraceptive methods are provided to the simulated population through Family PACT (a reproductive health	**Time horizon:** 2 years **Costing year(s) and currency:** 2009 USD **Discount rates:** Not provided **Perspective:** Public sector **Measures of uncertainty:** Sensitivity analyses of method-specific savings from preventing unintended pregnancies **Modelling method:** Model to estimate the number of pregnancies expected among Family PACT clients	Hormonal IUC: 13,396 Implant: 2,808 Injectable: 26,053 Ring: 12,931 Patch: 9,005 Oral contraceptives: 102,573 Barriers: 17,564 Emergency contraceptives: 3,325 *Costs (thousands):* Interval tubal ligation: £1,785 ($2,692) Tubal occlusion: £813 ($1,226) Copper intrauterine contraception (IUC): (£7,893) $11,905 Hormonal IUC: £11,205 ($16,900) Implant: £2,532 ($3,819) Injectable: £29,085 ($43,869) Ring: £25,772 ($38,872) Patch: £17,976 ($27,113)	more than two years as assumed in the current study - The duration of contraceptive coverage was underestimated for barrier methods - It is not possible to state whether contraceptive supplies that were dispensed were actually used - The study did not include rebates from pharmaceutical companies on contraceptives dispensed at pharmacies. As a consequence, the cost of providing some contraceptives was not accurately captured **Limitations identified by review team:** Main limitations already identified by authors **Evidence gaps and/or recommendations for future research:** For a public health perspective, implications regarding complications

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
		programme in USA) and assess the potential costs savings from pregnancies averted, and public sector expenditures on unintended pregnancies borne by federal, state and local governments **Sample sizes:** Simulated cohort of women aged 15 to 44; no size given		Oral contraceptives: £138,352 ($208,676) Barrier methods: £51,412 ($77,545) Emergency contraceptives: £6,516 ($9,828) *Cost-savings per dollar expenditure:* Interval tubal ligation: £2.38 ($3.59) Tubal occlusion: £1.05 ($1.59) Copper intrauterine contraception (IUC): £3.36 ($5.07) Hormonal IUC: £3.24 ($4.89) Implant: £3.24 ($4.89) Injectable: £2.65 ($4.00) Ring: £1.46 ($2.20) Patch: £1.41 ($2.12) Oral contraceptives: £2.23 ($3.37) Barrier methods: £1.05 ($1.58)	(including STIs) should be included **Source of funding:** None

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Emergency contraceptives: £1.70 ($2.56) **Secondary analysis:** None **Sensitivity analysis:** *Scenario 1: Women use all methods dispensed:* Cost-benefit of the whole programme: £2.33 ($3.51) (16% higher) *Scenario 2: Medical costs through end of pregnancy only:* Cost-saving/dollar expenditure of the whole programme: £0.40 ($0.61)	
Han et al. (2014) **Aim of study:** To determine the cost-effectiveness of a hypothetical state-funded programme offering immediate	**Source populations:** Adolescents aged 13-22 years enrolled in a pre-natal-post-natal programme – CAMP, Colorado Adolescent Maternity Program	**Intervention description:** IPI insertion: subdermal contraception (etnogestrel) prior to hospital discharge or within 4 weeks after delivery **Comparator/control description:** Other	**Outcomes:** Total cost per 1,000 women, cost of repeated pregnancy, implant continuation rate at 6, 12, 24 and 36 months and pregnancy rates at 6, 12, 24 and 36 months	**Primary analysis:** *Total cost per 1,000 women (6, 12, 24, 36 months):* IPI group: £475,083 ($699,680); £672,006 ($989,700); £100,492,000 ($1.48 million) and £157,528,000 ($2.32 million) Control group: £425,783 ($627,073); £10,456,600	**Limitations identified by author:** - The results may be less generalisable because the analysis is based on actual outcomes rather than using hypothetical outcomes from the literature - Patients may have over- or under-reported both

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
postpartum implant (IPI) insertion for adolescent mothers at 6, 12, 24, and 36 months postpartum **Type of economic analysis:** Cost-effectiveness (cost-saving) **Economic perspective:** Colorado Medicaid **Quality score:** Low **Applicability:** Partly applicable	**Setting:** USA, University of Colorado Hospital **Data sources:** Electronic Report on Adolescent Pregnancy, participants' electronic medical records, questionnaires, Medicaid payment and reimbursement	contraceptive method according to standard clinical protocols: no contraception, condoms, depot medroxyprogesterone acetate, and progestin-only pills initiated at any time after delivery, combined hormonal contraception (pills, patch, ring) started at any time 4 or more weeks after delivery, implant insertion at 4 or more weeks after delivery, and levonorgestrel-intrauterine system or copper-T 380A (IUD) insertion any time 6 or more weeks after delivery **Sample sizes:** Total: 396 Intervention: 171	**Time horizon:** 36 months **Costing year(s) and currency:** 2013 USD **Discount rates:** Not reported **Perspective:** Colorado Medicaid **Measures of uncertainty:** Sensitivity analysis: Variation of repeat pregnancy rates **Modelling method:** N/A - not a modelling study	($1.54 million); £267,526,000 ($3.94 million); and £465,115,000 ($6.85 million) *Net cost per 1,000 women (6, 12, 24, 36 months):* -£49,299 ($72,606); £371,379 ($546,950); £167,034,000 ($2.46 million); and £307,587,000 ($4.53 million) * At 12, 24, and 36 months, £0.53 ($0.78), £2.40 ($3.54), and £4.41 ($6.50) were saved for every dollar spent on IPI insertion **Secondary analysis:** *Implant continuation rate at 6, 12, 24 and 36 months:* IPI group: 97%, 86%, 65% and 48% respectively Control group - by 6 months 43.7% (implants or IDU), 34% (short-acting method) and 16% (discontinued or elected not to use birth control)	spontaneous miscarriages and induced abortions incidence. Thus, pregnancy data can introduce potential source of bias -Loss to follow-up was lower in the comparison group at 3 years than the implant group - Pregnancy outcomes were cumulatively added over time and may result in bias from losing women who did not get pregnant, inflating overall pregnancy rates - The cost-effectiveness of IPI programmes may be less in the adult population because rates of unplanned repeat pregnancy are higher in adolescents than adults -Analysis used the Colorado Medicaid outpatient reimbursement rates for implant insertion and removal. Different inputs from

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
		Comparator: 225		*Pregnancy rates at 6, 12, 24 and 36 months:* IPI group: 0%, 2.6%, 8.1% and 17.7% respectively Control group: 9.9%, 20.1%, 46.5, and 83.7% respectively **Sensitivity analysis:** Cost savings were robust enough that only very large deviations in pregnancy rates would affect the overall result of a net savings to Medicaid	different payers may change the results **Limitations identified by review team:** -Benefits in terms of repeat pregnancy rates by type of complications were not reported, thus we could not assess the benefits generated by each outcome -Measures of uncertainties were only reported to one parameter, repeated pregnancy rates for the comparison group; we were therefore unable to assess robustness of the model and to assess which parameters brought more uncertainty to the results -Discount rate for a 3-year analysis was not reported and we were unsure if any was used

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
					Evidence gaps and/or recommendations for future research: -Benefits should be disaggregated and presented, as well as all their probabilities -Parameters tested in the sensitivity analysis should be presented and we suggested that one-way sensitivity analysis be conducted and results presented first before a multivariate or probabilistic sensitivity analysis. Thus, we would have the chance to better understand which parameters contribute the most to explaining the estimates **Source of funding:** Authors report no conflict of interest
National Collaborating Centre (NCC) for Women's and	**Source populations:** Male and females of reproductive age **Setting:** UK	**Intervention description:** LARC methods: IDU, IUS: LNG-	**Outcomes:** Number of pregnancies averted by the use of one contraceptive method	**Primary analysis: Comparison across reversible contraceptive**	**Limitations identified by author:** - The relative cost-effectiveness of LARC

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Children's Health (2013) **Aim of study:** Overall aim was to provide (clinical and educational) guidance on LARC. The cost-effectiveness analysis aimed at assessing LARC methods compared to combined oral contraceptive pill (COC) **Type of economic analysis:** Cost-effectiveness **Economic perspective:** Public health (NHS)	**Data sources:** *Costs:* COC use in England in 2002, 2004 NHS reference costs, British National Formulary (49, March 2005), GP fee schedule, opinion of the Guideline Development Group (GDG), published literature *Effectiveness:* systematic literature review, agreements between GDG members, national statistics, published literature	IUS (Mirena), injectable hormones, implant **Comparator/control description:** Combined oral contraceptive pill (COC), male condom, and non-reversible contraceptive methods (female and male sterilisation) **Sample sizes:** Simulated cohort of 1,000 sexually active women choosing one method of contraception	in comparison with another **Time horizon:** 1 to 15 years **Costing year(s) and currency:** 2004-2005 GBP **Discount rates:** 3.5% **Perspective:** NHS **Measures of uncertainty:** Sensitivity analysis, scenario analysis **Modelling method:** Decision-analytic model – Markov model	**methods: LARC methods, COC, male condom:** ***1 year of use:*** *Total pregnancy:* Implant: 14 IUS: 17 IUD: 18 Injectable: 33 COC: 91 Condom:150 *Total costs:* Implant: £262,117 IUS: £270,749 IUD: £195,442 Injectable: £190,534 COC: £232,932 Condom: £212,658 *Incremental cost-effectiveness ratio:* Implant vs IUD: £17,367/pregnancy averted IUS: dominated by implant	methods highly sensitive to changes in discontinuation rates in several cases - Adverse events, side effects associated with contraceptive use and non-contraceptive benefits are not considered in the model **Limitations identified by review team:** - Key parameters were not assessed individually in the sensitivity analysis, making it difficult to identify which parameter contributes more uncertainty in the model - Authors noted that LARC and COC or non-reversible methods may not always be substitutes since not every woman will be eligible for all methods. This was acknowledged in discussion of model structure and limitations, but this scenario

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Quality score: Medium **Applicability:** Partly applicable				IUD vs injectable: £339/pregnancy averted COC: dominated by IUD and injectable Condom: dominated by IUD and injectable ***2 years of use:*** *Total pregnancy:* Implant: 51 IUD: 55 IUS: 57 Injectable: 99 COC: 190 Condom: 295 *Total costs:* Implant: £ 322,939 IUD: £256,572 IUS: £337,093 Injectable: £338,376 COC: £406,366 Condom: £418,125 *Incremental cost-effectiveness ratio:*	was not incorporated in the sensitivity analysis - The model was adapted from a previous model but there was no discussion about validity and calibration **Evidence gaps and/or recommendations for future research:** Model can be validated and calibrated and variables should be assessed individually to check for uncertainty among parameters **Source of funding:** Not declared

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Implant vs IDU: £17,866/pregnancy averted IUS: Dominated by implant, IUD Injectable: Dominated by implant, IUD, IUS COC: Dominated by all LARC methods Condom: Dominated by all LARC methods ***3 years of use:*** *Total pregnancy:* Implant: 101 IUD:105 IUS: 109 Injectable: 167 COC: 289 Condom: 435 *Total costs:* Implant: £400,947 IUD: £337,207 IUS: £418,616 Injectable: £482,178	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				COC: £575,320 Condom: £616,644 *Incremental cost-effectiveness ratio:* Implant vs IUD: £14,730/pregnancy averted IUS: Dominated by implant, IUD Injectable: Dominated by implant, IUD, IUS COC: Dominated by all LARC methods Condom: Dominated by all LARC methods ***5 years of use:*** *Total pregnancy:* Implant: 215 IUS: 228 IUD: 232 Injectable: 302 COC: 482 Condom: 707 *Total costs:*	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Implant: £667,275 IUS: £603,534 IUD: £534,555 Injectable: £760,600 COC: £899,697 Condom: £993,769 *Incremental cost-effectiveness ratio:* Implant vs IUD: £7,574/pregnancy averted, extended dominance Implants vs IUS: £4,598/pregnancy averted IUS vs IUD: £18,845/pregnancy averted Injectable: Dominated by implant, IUD, IUS COC: Dominated by all LARC methods Condom: Dominated by all LARC methods ***10 years of use:*** *Total pregnancy:* Implant: 483	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				IUS:522 IUD: 551 Injectable: 635 COC: 932 Condom: 1291 *Total costs:* Implant: £1,210,419 IUS: £1,119,079 IUD: £1,050,425 Injectable: £1,401,818 COC: £1,632,762 Condom: 1,830,496 *Incremental cost-effectiveness ratio:* Implant vs IUD: £2,342/pregnancy averted/ extended dominance Implant vs IUS: £2,339/pregnancy averted IUS vs IUD: £2,346/pregnancy averted Injectable: Dominated by implant, IUD, IUS	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				COC: Dominated by all LARC methods Condom: Dominated by all LARC methods ***15 years of use:*** *Total pregnancy:* Implant: 719 IUS: 778 IUD: 828 Injectable: 948 COC: 1330 Condom: 1788 *Total costs:* Implant: £1,622,769 IUS: £1,563,548 IUD: £1,469,754 Injectable: £1,965,220 COC: £2,260,880 Condom: £2,534,998 *Incremental cost-effectiveness ratio:*	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Implant vs IUD: £1,403/pregnancy averted/ extended dominance Implant vs IUS: £999/pregnancy averted IUS vs IUD: £1,884/pregnancy averted Injectable: Dominated by implant, IUD, IUS COC: Dominated by all LARC methods Condom: Dominated by all LARC methods **Secondary analysis: Comparison of LARC methods with non-reversible contraceptive methods:** ***1 year of use:*** *Total pregnancies:* Male sterilisation: 7 Female sterilisation: 19 Implant: 719 IUS: 778 IUD: 828	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Injectable: 948 *Total costs:* Male sterilisation: £466,776 Female sterilisation: £750,191 Implant: £1,622,769 IUS: £1,563,548 IUD: £1,469,754 Injectable: £1,965,220 *Incremental cost-effectiveness ratio:* Implant: Dominated by male and female sterilisation IUS: Dominated by male and female sterilisation IUD: Dominated by male and female sterilisation Injectable: Dominated by male and female sterilisation **Sensitivity analysis:** *Comparison across reversible contraceptive methods: LARC methods, COC, male condom:* - Varying the failure rates of COC and male condom by	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				±10%: no impact in the base-case results - Varying the failure rates of LARC methods by ±10%: no impact no impact in the cost-effectiveness of the base-case results relative to the COC and male condom. No impact in the ranking of LARC methods in terms of effectiveness or the case dominance across LARC methods - Varying the failure rate of IUD: moderate impact on the ICERs of the implant versus IUD only for short periods of contraceptive use (3-4 years) *Comparison of LARC methods with non-reversible contraceptive methods:* - Varying the failure rates of female and male sterilisation by ±10%: no impact in the base-case results	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- Varying the failure rates of LARC methods by ±10%: no impact in the cost-effectiveness results	
Pilgrim et al. (2010) **Aim of study:** To assess the cost-effectiveness of a range of interventions to encourage young people, especially socially disadvantaged young people, to use contraceptives or contraceptive services **Type of economic analysis:** Cost-effectiveness	**Source populations:** 1. Young people aged 14-16 years who have not previously been a parent (but who may or may not have been pregnant without carrying to term) within secondary school 2. Young mothers within a secondary school 3. Young people aged 15–19 years who are sexually active **Setting:** UK **Data sources:** *Probability of abortion and birth:*	**Intervention description:** 1. School-based dispensing of hormonal contraceptives within the school (DH); school-based dispensing of condoms (DC) 2. Intensive case management to prevent repeat pregnancy (includes a culturally matched school-based social worker [including home visits], weekly school-based peer education support and comprehensive medical care including contraception) (ICM)	**Primary outcomes:** Cost per pregnancy averted, cost per abortion averted **Secondary outcomes:** Cost of the intervention and additional contraception required as a result of the intervention; cost of maternity care; cost of abortion; cost of miscarriage/ ectopic pregnancy/ stillbirth; cost of treatment for low birth weight babies; cost of treatment of sexually transmitted infections (STIs); cost of	**Primary analysis:** ***Model 1: Deterministic results (discounted)*** *Total cost (billions):* - ND: £1,527 - DC: £1,519 - DH: £1,417 *Cost per abortion averted:* - DC: £815 - DH: £1,514 (compared with DC) *Cost per pregnancy averted (excluding benefits):* - DC: £32 - DH: £441 (compared with DC) *Cost per pregnancy averted (including benefits):* - DN: dominated by DC	**Limitations identified by author:** - A lack of data on the long-term employment and education impacts of teenage pregnancy meant that this could not be included in the analysis. If negative impacts on future productivity were included the intervention might appear more cost-effective - Only primary transmission of STIs is considered in the model. Consideration of additional infections averted could improve the cost-effectiveness ratio - The long-term implications of the interventions are not well known. For example, it is not clear if teenage

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Economic perspective: Public sector **Quality score:** Medium **Applicability:** Partly applicable	National government statistics for England and Wales *Probability of miscarriage and ectopic pregnancy:* Hospital Episode Statistics (HES); a Denmark study was used to parameterise the miscarriage rates *Long term of a teenage birth:* Literature review including only UK papers and elicitation technique with programme development group (PDG) at NICE *Sexually transmitted infection (STI) outcomes:* NICE Sex and Relationship Education (SRE)	3. Advance provision of emergency hormonal contraception (AP) **Comparator/control description:** 1. School nurse only (ND) 2. No follow-up following first pregnancy 3. No advance provision of EHC (No AP) **Sample sizes:** Simulated cohort of 100,00 young individuals	government-funded benefits **Time horizon:** Lifetime **Costing year(s) and currency:** 2007-2008 GBP **Discount rates:** 3.5% **Perspective:** Public sector **Measures of uncertainty:** One-way and probabilistic sensitivity analysis **Modelling method:** Cost-effectiveness modelling study with a hypothetical cohort over a lifetime from the age at which the intervention is provided; the following scenarios were modelled: 1. School-based interventions for	- DC: dominated by DH - DH: dominates DC and ND ***Model 2: Deterministic results (discounted)*** *Total costs (millions):* - No follow-up: £655,572 - ICM: £705,730 *Cost per repeat teenage pregnancy averted (excluding benefits):* ICM: £15,155 *Cost per repeat teenage pregnancy averted (including benefits):* ICM: £4,031 ***Model 3: Deterministic results (Discounted)*** *Total cost (billions):* - No AP: £1,524 - AP: £1,447 *Cost per abortion averted:* AP: £2,795 Cost per age pregnancy averted: AP (excluding benefits): £310	pregnancies are averted or delayed - Available evidence on contraceptive effectiveness in teenagers has been generated based on 6-12 months of follow-up - Outcomes are not reported in terms of QALYs gained, limiting the extent to which they can be compared with other interventions using this outcome - Variability in baseline health and risk factors is not captured in the model - The comparison within Model 1 is highly dependent upon the true effectiveness of each of the methods of contraception - Research comparing the cost-effectiveness of different methods of contraception in terms of both STIs and contraception is sparse due to

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
	public health guidance *Effectiveness:* National statistics and assumptions *Benefits:* Office for National Statistics (ONS, 2009), previous published studies, assumptions *Costs:* British National Formulary (BNF 58, 2009), NICE assessment of Long-Acting Reversible Contraception, health economic model developed for the NICE Sex and Relationship Education (SRE) public health guidance, NHS reference costs		nulliparous young people 2. School-based interventions to prevent repeat pregnancy 3. Interventions to encourage the use of emergency hormonal contraception following unprotected sex	*Cost per age pregnancy averted:* AP (including benefits) dominates **Secondary analysis:** ***Model 1: Expected results (discounted)*** *Total cost (billions):* - DN: £1,524 - DC: £1,517 - DH: £1,515 *Cost per abortion averted:* - DC: £822 - DH: £1,495 (compared with DC) *Cost per pregnancy averted (excluding benefits):* - DC: £38 - DH: £443 (compared with DC) *Cost per pregnancy averted (including benefits):* - DN: dominated by DC - DC: dominated by DH	the limitations around which outcome measure can reasonably capture both effects - The cost of maternity services may differ for teenage mothers compared with older mothers **Limitations identified by review team:** Authors stated that no preterm births were assessed, which may be more common amongst young people; however, this statement seems odd since multiples and low birth weight are included - unless low-birth weight is the same as preterm. Other adverse events associated with teen pregnancy, such as fistula, were not mentioned **Evidence gaps and/or recommendations for future research:** Modelling was based on previous model

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- DH: dominates DC and ND ***Model 1: Expected results (undiscounted)*** *Total cost (billions):* - DN: £2,307 - DC: £2,297 - DH: £2,295 *Cost per abortion averted:* - DC: £848 - DH: £1,535 (compared with DC) *Cost per pregnancy averted (excluding benefits):* - DC: £92 - DH: £488 (compared with DC) *Cost per pregnancy averted (including benefits):* - DN: dominated by DC - DC: dominated by DH - DH: dominates DC and ND ***Model 2: Expected results (discounted)***	(NICE), but no discussion of model calibration has been provided **Source of funding:** Not declared

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Total cost (millions): - No follow-up: £654,756 - ICM: £705,164 *Cost per repeat teenage pregnancy averted (excluding benefits):* ICM: £15,175 *Cost per repeat teenage pregnancy averted (including benefits):* ICM: £4,052 ***Model 2: Expected results* (undiscounted)** *Total cost (millions):* - No follow-up: £825,978 - ICM: £866,883 *Cost per repeat teenage pregnancy averted (excluding benefits):* ICM: £15,186 *Cost per repeat teenage pregnancy averted (including benefits):* ICM: £2,935 ***Model 3: Expected results (discounted)*** *Total cost (billions):* - No AP: £1,522	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- AP: £1,445 *Cost per abortion averted:* AP: £2,803 *Cost per age pregnancy averted:* AP (excluding benefits): £314 *Cost per age pregnancy averted:* AP (including benefits) dominates ***Model 3: Expected results (undiscounted)*** *Total cost (billions):* - No AP: £2,303 - AP: £2,198 *Cost per abortion averted:* AP: £2,948 *Cost per age pregnancy averted:* AP (excluding benefits): £395 *Cost per age pregnancy averted:* AP (including benefits) dominates **Sensitivity analysis:** ***Model 1:***	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				PSA: The analysis shows very little difference in both costs and effectiveness between dispensing condoms within schools and dispensing hormonal contraceptives within schools. There is the possibility that either one could be more effective and/or more costly than the other *One-way:* -Delay in births averted (14-16 years to 17-19 years): (1) DC would remain cost saving compared with ND for the cost per age 14–16 pregnancy averted including government-funded benefits; (2) DH would remain cost saving compared with DC within schools for this outcome - Pregnancies averted at ages 14–16 years would have been	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				additional: cost-effectiveness ratio for the cost per abortion averted decreases - Probability of condom failure is doubled: DC results in greater net costs than DH - Doubled risk of miscarriage: DC is estimated to result in net cost savings compared with ND - Increase in medical abortions: net cost savings of DC compared with ND - Increase in relative risk of both interventions: higher cost-effectiveness ratios than the base case analysis **Model 2:** *PSA:* - ICM is unlikely to result in net cost savings when excluding benefit payments - 20% probability that ICM will result in net cost savings (with government-funded	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				benefits) compared with no follow-up after first teenage pregnancy *One-way:* - Reducing cost of intervention: cost per repeat teenage pregnancy averted (excluding benefits) of £6,844 - Including benefits: ICM will dominate no follow-up after a teenage birth - Other variations do not have substantial impact upon the model results **Model 3:** *PSA:* - AP is unlikely to result in net cost savings using the cost per abortion averted outcome - 24% probability AP will result in net cost savings when using the cost per age 15–19 pregnancy averted outcome (excluding benefit payments)	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- AP is likely to be cost saving using a cost per age 15–19 pregnancy averted outcome (including Benefit payments) *One-way:* - Increasing the baseline usage of EHC following unprotected sex: AP dominates, including and excluding government-funded benefit payments; estimated cost per abortion averted associated with AP decreases to £688 - Other variations do not have substantial impact upon the model results	
Rodriguez et al. (2010a) **Aim of study:** To estimate the costs of expanding Emergency Medicaid coverage to	**Source populations:** Latina immigrant women in 10 states with a high proportion of immigrants, who have been in the United States for fewer than 5 years	**Intervention description:** Expanded Emergency Medicaid coverage to include postpartum contraception: - IUD - female surgical sterilisation	**Main outcome:** -Number of pregnancies averted -Net savings **Time horizon:** 5 years **Costing year(s) and currency:** 2002 USD **Discount rates:** 3%	**Primary analysis:** *benefits:* -In the 4 years following delivery, 18.5% of EM patients had a subsequent admission at OHSU for an obstetrical diagnosis -In the absence of a postpartum IUD programme,	**Limitations identified by author:** -Modelling limited by the imprecision of healthcare cost estimates - The study considered Medicaid payments and costs in only one state

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
include postpartum contraception **Type of economic analysis:** Cost-benefit analysis **Economic perspective:** Three perspectives: the hospital, state Medicaid programmes and society **Quality score:** Low **Applicability:** Partly applicable	and have just given birth **Setting:** US **Data sources:** Study database (all women with EM who delivered at the Oregon Health and Science University – OHSU – in 2002); trial conducted by the World Health Organization, literature	- DMPA - oral contraceptives - condoms **Comparator/control description:** Status quo. **Sample sizes:** Total: 1,037 women Unclear how they divided the groups for comparison	**Perspective:** Hospital, state Medicaid programmes and society **Measures of uncertainty:** Univariate sensitivity analysis **Modelling method:** Cost-benefit analysis	266 women per 1,000 EM patients will have a repeat pregnancy within 4 years at OHSU -For every 1,000 women who receive an IUD, 122 pregnancies were expected due to discontinuation or expulsion and 18 pregnancies due to IUD method failure -It was estimated that 126 pregnancies would be averted from a postpartum IUD programme *Costs (4 years' analysis):* -IUD insertion and removal for 1000 women estimated at £215,824 ($328,000) -For EM at hospital a cost of £140,812 ($214,000) (without IUD) and £78,302 ($119,000) was estimated with an IUD programme in place *Cost-benefit analysis:* -From the hospital perspective, the hospital	- The additional benefits that family planning provides was not taken into account in the analysis -The study assumed normal, term pregnancies. However, some of these pregnancies would lead to preterm births, which are more expensive to all three payer perspectives -Limited ability to predict the effect that free postpartum contraception would have on uptake **Limitations identified by review team:** Authors identified main limitation related to the model in question **Evidence gaps and/or recommendations for future research:** Further research into interstate migratory patterns and probabilities should be conducted to assess the economic value of a

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				would lose £0.46 per £1 (70 cents per dollar) spent on a postpartum IUD programme or a benefit–cost ratio of 0.30 -From the state's perspective, the state would save £1.93 ($2.94) in costs for repeat obstetrical care for every state dollar spent on an IUD programme **Secondary analysis:** -Varying the discontinuation rates and expulsion rates did not affect the positive savings to the state of financing postpartum IUD provision -The programme remains cost-effective for the state unless first-year discontinuation rate becomes as high as 90%, significantly higher than the expected postpartum IUD expulsion rate of 12% -Programme costs for the state would break even with	federal mandate for preventive coverage of new immigrants **Source of funding:** Funded by an anonymous donor. Dr Caughey is supported in part by a grant under the Robert Wood Johnson Foundation Physician Faculty Scholars Programme. The authors report no conflict of interest.

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				costs of subsequent care if the IUD expulsion rate exceeded 70% -IUD costs would need to exceed £6,909 ($10,500) per woman before the programme would begin to cost the state more than future pregnancy costs	
Rodriguez et al. (2010b) **Aim of study:** To examine the hospital and state costs of offering the option of a postpartum intrauterine device (IUD) to an underinsured population of recent immigrants to the United States with Emergency	**Source populations:** Women with EM who delivered at Oregon Health and Science University (OHSU) in July 2001 and December 2006 **Setting:** OHSU, USA **Data sources:** *Annual rates of pregnancy in the absence of the programme:* Hospital records *Mean pregnancy costs and revenue and probability of*	**Intervention description:** Long-acting method of contraception postpartum to women with EM: hospital provision of IUDs postpartum and state funding of IUDs postpartum **Comparator/control description:** Hospital's current policy of covering only the obstetrical delivery **Sample sizes:** Simulated cohort of	**Outcomes:** *Cost:* Mean charges and mean net revenue for each pregnancy outcome type *Benefit:* Number of pregnancies that would be averted by offering a postpartum IUD to EM patients **Time horizon:** 4 years **Costing year(s) and currency:** 2008 USD **Discount rates:** Annual rate of 3%	**Primary analysis:** ***State perspective*** *Absence of a postpartum IUD programme:* Pregnancies: 226 Total costs: £1,371,300 ($2.1 million) *Postpartum IUD programme:* Benefit: 126 pregnancies averted Total cost of the programme: £99,885 ($152,964) Costs of pregnancies expected: £653,000 (~$1 million)	**Limitations identified by author:** - The model underestimates the total costs of unintended pregnancy because the hospital does not cover elective, uncomplicated abortions - Data from a single hospital, thus the results are specific to this hospital and do not capture repeat pregnancies seen at other area hospitals - Conservative estimate of cost savings because repeat pregnancy was calculated from a single institution

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Medicaid (EM) insurance coverage only **Type of economic analysis:** Cost-benefit analysis **Economic perspective:** Hospital and the state **Quality score:** Low **Applicability:** Partly applicable	*repeat pregnancy and pregnancy outcome:* Institution's department-specific cost-to-charge ratio, hospital billing records *Probability of IUD uptake and continuation:* Hospital records and literature *IDU baseline expulsion rates:* Trial conducted by the World Health Organization *Pregnancy outcomes:* Hospital records	individuals derived from multiple estimates	**Perspective:** Hospital and the state **Measures of uncertainty:** Sensitivity analyses to assess how a decreased and increased expulsion rate would affect the cost outcome from both perspectives **Modelling method:** Not reported	Net saving for the state: 2003: £3,244 ($4,968) 2004: £211,722 ($324,229) 2005: £168,408 ($257,899) 2006: £147,437 ($225,784) The state would save £1.92 ($2.94) in costs for repeat obstetrical care for every state dollar spent on an IUD programme ***Hospital perspective*** - Programme costs for an IUD, insertion and removal: £214,184 ($328,000) - Cost of repeat pregnancy without the programme: £139,742 ($214,000) - Cost of repeat pregnancy with the programme: £77,707 ($119,000) - Benefit-cost ratio of 0.30 **Secondary analysis:** N/A **Sensitivity analysis:** Cost-effectiveness of a postpartum	- The study only considers women who had repeat pregnancies in their first 5 years in the US and did not capture women who had a birth on EM, then became eligible for Standard Medicaid (SM) during a repeat obstetrical admission - The model includes direct costs associated with admission for an obstetrical diagnosis and does not consider that an infant born to a woman with EM can be eligible for a full array of public services - The study underestimates new-born costs because this assumes that all new-borns are healthy **Limitations identified by review team:** Details of the modelling method were not provided by the authors

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				IUD programme is robust and varying the discontinuation and expulsion rates did not affect the positive savings to the state of financing postpartum IUD provision. The programme remains cost-effective for the state unless first-year discontinuation rate becomes as high as 90%, significantly higher than the expected postpartum IUD expulsion rate of 12%. Programme costs for the state would break even with costs of subsequent care if the IUD expulsion rate exceeded 70%. IUD costs would need to exceed $10,500 per woman before the programme would begin to cost the state more than future pregnancy costs.	**Evidence gaps and/or recommendations for future research:** The extension of the study to include complications would give a better scenario about IUD programmes **Source of funding:** Study funded by an anonymous donor
Salcedo et al. (2010) **Aim of study:** To evaluate the	**Source populations:** Low-income women **Setting:** USA, California	**Intervention description:** Immediate post-abortion IUD insertion	**Outcomes:** Public programme costs, rates of unintended pregnancy	**Including costs of only direct medical care of IUD insertion:** 1 year: £75 ($111)	**Limitations identified by author:** - Future pregnancies for women who breastfeed may

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
potential cost savings associated with a policy of immediate post-abortion IUD insertion, compared to planned IUD insertion at the time of abortion follow-up **Type of economic analysis:** Cost saving **Economic perspective:** Public payer **Quality score:** Medium **Applicability:** Partly applicable	**Data sources:** *Model probabilities:* Literature *Contraception uptake rates:* California Family Planning, Access, Care, and Treatment (PACT) female client population *Cost inputs:* California Medicaid and Family PACT	**Comparator/control description:** Planned IUD insertion at the time of abortion follow-up **Sample sizes:** Simulated cohort of individuals derived from multiple estimates	**Time horizon:** 1 year and 5 years **Costing year(s) and currency:** 2011 USD **Discount rates:** 3% per year **Perspective:** Public payer **Measures of uncertainty:** Univariated (triangular distribution) and bivariated sensitivity analysis and Monte Carlo simulation with 10,000 trials **Modelling method:** Decision analytic, Markov model	5 years: £548 ($810) **Including public health insurance and social programme costs**: 1 year: £1,324 ($1,956) 5 years £2,908 ($4,296) **Secondary analysis:** Over 5 years, for every 1,000 low-income women who undergo immediate post-abortion IUD placement, more than 400 pregnancies, 180 deliveries and 160 abortions will be averted **Sensitivity analysis:** Sensitivity analyses demonstrate that results are robust over a wide range of model inputs *Input variations for a no cost saving programme:* - Over 1 year: increasing 25% of the IDU price and considering only direct costs	be overestimated because the model assumes that women who became pregnant maintained the same chance of pregnancy in the following cycle - There is no difference between pregnancies that are avoided and those that are delayed as a result of public funding for contraception. Thus, when a woman delays pregnancy for the duration of the model and becomes pregnant later, public spending is only deferred. The study estimates that half of all pregnancies in the model are truly averted. Therefore, the savings would be reduced by less than 50% **Limitations identified by review team:** Model is heavily based on secondary data and authors should have discussed better

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- Over 5 years following the abortion: increasing the costs of the IUD to £2,332 ($3,444) or £4,595 ($6,787), considering public health insurance and social programme costs respectively - Expulsion rates for immediate post-abortion IUDs surpassing 30% - Planned IUD placement at abortion follow-up occurring more than 89% of the time for immediate post-abortion IUD placement *Monte Carlo simulations:* Results were consistent with those of the univariate sensitivity analyses *Considering costs of contraception and pregnancy-related care:* - Over 1 year: the programme was cost saving in 61% of scenarios	the applicability of parameters and implications of extension of conclusions to the population implications were only partly included in the model (no STIs for example) **Evidence gaps and/or recommendations for future research:** The inclusion of complications would express the full benefits of interventions to society **Source of funding:** Society of Family Planning Research Fund

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				- Over 5 years: the programme was cost saving in 84% of scenarios *Including public health insurance and social programme costs:* - Over 5 years: the programme was cost saving in 89% and 90% of trials respectively	
Thomas (2012) **Aim of study:** Stated as 'to assess the fiscal impact of three national-level policies designed to prevent unintended pregnancy'. In practice, the author wanted to assess the financial benefit of implementing interventions to	**Source populations:** 10,000 individuals aged 15-44 whose demographic characteristics were nationally representative (of USA) **Setting:** United States **Data sources:** The General Social Survey and the National Survey of Family Growth; the Guttmacher	**Intervention description:** 1. Mass media campaign 2. Evidence-based teen pregnancy prevention programme 3. Expanded access to Medicaid Family Planning **Comparator/control description:** N/A **Sample sizes:** Total N = 10,000 simulation cohort	**Outcomes (linked to unattained pregnancies):** *Main:* Benefit-cost ratio *Others:* % reduction in abortion; % reduction in births; % reduction in number of children born into poverty; programme costs, public savings, fiscal savings **Time horizon:** 5 years	**Primary analysis:** ***Benefits:*** -% reduction in abortion: Mass media (3.9%); evidence-based teen pregnancy prevention programme (1.4%); expanded access to Medicaid Family Planning (3.5%) - % reduction in births: Mass media (1.0%); evidence-based teen pregnancy prevention programme (0.6%); expanded access to Medicaid Family Planning (1.4%) - % reduction in number children born into poverty:	**Limitations identified by author:** Does not account for: - spending on children over the age of 5 - private costs of unintended pregnancy (e.g. lower earnings of mother) - other potentially important societal costs Does not consider likely effect on spread of STIs Scale-up of small interventions may be less effective than assumed

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
prevent unintended pregnancies using a cost-benefit analysis **Type of economic analysis:** Cost-benefit **Economic perspective:** Government and social **Quality score:** Medium **Applicability:** Partly applicable	Institute, the National Vital Statistics System; data from the Current Population Survey were used to parameterise the model that assigns a poverty status to each newborn child; meta-analysis for behaviour effects; Truth, VERB, and National Youth Anti-Drug Media (NYADMC) campaigns (costs); literature for both benefits and costs		**Costing year(s) and currency:** 2008 USD **Discount rates:** 3% **Perspective:** Social and public sector (government) **Measures of uncertainty:** One-way sensitivity analysis **Modelling method:** Cost-benefit analysis	Mass media (2.2%); evidence-based teen pregnancy prevention programme (1.4%); expanded access to Medicaid Family Planning (1.8%) ***Costs:*** -Programme costs (millions): mass media: £65.3 ($100); evidence-based teen pregnancy prevention programme: £94,685 ($145); expanded access to Medicaid Family Planning: £153,455 ($235) ***Public savings:*** *For pregnancy care alone:* -Mass media: £24,164,437 ($37,005,263); benefit-cost ratio: £0.24 ($0.37) -Evidence-based teen pregnancy prevention programme: £241,597,209 ($369,980,412); benefit-cost ratio: £0.17 ($0.26)	Assumption of effectiveness of national media campaign may be incorrect Programme costs and baseline parameters were uncertain **Limitations identified by review team:** Author has identified main limitations **Evidence gaps and/or recommendations for future research:** Short and long term complication to be taken into account. **Source of funding:** The William and Flora Hewlett Foundation

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				-Expanded access to Medicaid Family Planning: £79,455,150 ($121,677,106); benefit-cost ratio: £0.59 ($0.62) *Pregnancy care plus infant medical:* -Mass media: £58,929,344 ($90,244,018); benefit-cost ratio: £0.59 ($0.90) -Evidence-based teen pregnancy prevention programme: £51,856,523 ($79,412,746); benefit-cost ratio: £0.36 ($0.55) -Expanded access to Medicaid Family Planning: £186,002,878 ($284,843,611); benefit-cost ratio: £0.79 ($1.21) *Pregnancy care plus children benefits:* -Mass media: £281,383,852 ($430,909,421); benefit-cost ratio: £2.81 ($4.31) -Evidence-based teen pregnancy prevention	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				programme: £232,562,922 ($356,145,363); benefit-cost ratio: £1.61 ($2.46) -Expanded access to Medicaid Family Planning: £862,217,932 ($1,320,394,996); benefit-cost ratio: £3.67 ($5.62) **Secondary analysis:** Findings were relatively insensitive to large changes in the assumptions underlying the analysis, e.g. results of the preferred specifications suggest that, even if the cost of the Medicaid expansion were twice as high as it was assumed to be — or if the benefits of the teen pregnancy prevention programme were twice what they were estimated to be — the benefit-cost ratios for the former would still be at least as large as for the latter.	

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Conversely, the results from the preferred specifications that account for spending on children through age 5 suggest that, even if these programmes were half as effective (or twice as expensive) as they were assumed to be, all of them would have benefit-cost ratios of greater than 1	
Thomas and Cameron (2013) **Aim of study:** To calculate the cost of an unintended pregnancy in 2011 and use this cost in a cost-effectiveness model comparing ulipristal acetate (UPA) with levonorgestrel (LNG) for emergency	**Source populations:** Women in England presenting in primary care for EHC within 24 to 72 hrs of unprotected sexual intercourse **Setting:** English primary care **Data sources:** *Health outcome:* Probabilities of unintended pregnancies from clinical trials of EHC,	**Intervention description:** Ulipristal acetate (UPA) 30 mg indicated for EC within 120 hrs of unprotected sexual intercourse (UPSI) **Comparator/control description:** Levonorgestrel (LNG) 1.5 mg, which is indicated for EC if taken within 72 hrs of UPSI	**Primary outcome:** Number of unintended pregnancies and direct and indirect costs of unintended pregnancy **Secondary outcome:** Consequence of unintended pregnancy (miscarriage, abortion, ectopic pregnancy, stillbirth or live birth) **Time horizon:** One year **Costing year(s) and currency:** 2011 GBP	**Primary analysis:** *Direct health costs of a pregnancy:* -£3.9 billion (average cost: £3,903) -Cost per event: Miscarriage: £554; abortion: £714; ectopic pregnancy: £1,228; stillbirth: £3,765; live birth: £5,337 *Indirect health costs*: Government expenditure on maternal health benefits: £2.3 billion plus £34 billion in tax credits and child benefits *Overall analysis:*	**Limitations identified by author:** -Post-natal care costs for the mother were not included in the analysis -Cost estimates are based on average pregnancy costs, which may be different from the costs associated with an unintended pregnancy **Limitations identified by review team:** No additional limitations identified for this type of analysis

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
hormonal contraception (EHC) **Type of economic analysis:** Cost-effectiveness analysis **Economic perspective:** Healthcare only or health plus social care **Quality score:** Low **Applicability:** Partially applicable	published data sources and studies conducted on pregnancy intention in women in UK. Measure of effectiveness was number needed to treat *Costs:* Records from the NHS hospitals; NHS national Schedule of Reference Costs	**Sample sizes:** Simulated cohort of individuals derived from multiple estimates	**Discount rates:** Not applicable as time horizon is one year **Perspective:** Healthcare and societal **Measures of uncertainty:** Sensitivity analysis: failure rates of EHC and costs of unintended pregnancies **Modelling method:** N/A - not a modelling study	-Cost of treating woman with UPA instead of LGN: Healthcare cost: £1,469; health and societal costs: £1,469 (same) -Avoided costs (pregnancy averted): Healthcare costs: £1,663, health and societal costs: £2,992 -ICER (net benefit): Costs of treating minus avoided costs: Healthcare costs: −£194; Health and societal costs: −£1,453 **Secondary analysis:** None **Sensitivity analysis:** All main parameters were varied. The sensitivity analysis did not change the results and has produced negative ICERs for the main outcomes of analysis, indicating robustness of the cost-saving analysis	**Evidence gaps and/or recommendations for future research:** Long-term implications for the interventions could be explored in a modelling study **Source of funding:** HRA Pharma UK & Ireland Ltd, manufacturers of ellaOne (UPA) CT has worked as a consultant for HRA Pharma Ltd, the manufacturer of UPA. SC has received lecture fees from HRA Pharma Ltd and was the principal investigator for the clinical studies of UPA, which were also sponsored by HRA Pharma Ltd
Trussell et al. (2013)	**Source populations:** Women aged 15–44 years who are	**Intervention description:** Reversible contraceptive methods:	**Outcomes:** Cost impact of increased uptake of LARC	**Primary analysis: Impact of increased LARC utilisation (millions)**	**Limitations identified by author:**

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Aim of study: To estimate the cost to third-party payers associated with unintended pregnancies; to estimate the proportion of this cost attributable to imperfect contraceptive adherence; and to estimate cost savings that might be generated by women switching to LARC from other contraceptive methods **Type of economic analysis:** Costing study **Economic perspective:**	sexually active and of child-bearing age but who currently neither seek pregnancy nor wish to be permanently sterilised **Setting:** USA **Data sources:** *UP related events:* National Survey of Family Growth (NSFG), administrative claims database of US commercial health plans and assumptions *Costs of UP-related events:* Medicare Fee Schedule 2011 *Utilisation of contraceptive methods:* NSFG *Costs of contraceptives:* IMS	SARC - oral contraceptive pill (OC), male condom, patch, injectables and vaginal ring. LARC - implant, intrauterine device (IUD) and hormonal intrauterine system (IUS) **Comparator/control description:** No method **Sample sizes:** Simulated cohort of individuals derived from multiple estimates	methods according to three scenarios: 1. 10% of women aged 20–29 who are currently using OC switched to LARC 2. 10% of women aged 20–29 who are currently using any SARC method switched to LARC. 3. 10% of women aged 20–29 who are currently using either SARC or no method switched to LARC **Time horizon:** 1 year **Costing year(s) and currency:** 2011 USD **Discount rates:** Not applicable; time horizon of one year **Perspective:** Third-party payers	*Current practice:* Cost of UP: £1,639 ($2,421) Cost of contraception: £3,019 ($4,460) Total cost impact: £4,658 ($6,881) *Scenario 1:* -Cost of new contraceptive practice: Cost of UP: £1,604 ($2,370) Cost of contraception: £2,859 ($4,223) Total cost impact: £4,463 ($6,593) -Cost savings Cost of UP: £35 ($51) Cost of contraception: £160 ($237) Total cost impact: £195 ($288) *Scenario 2:* -Cost of new contraceptive practice: Cost of UP: £1,559 ($2,303)	- The model includes first-year failure rates for contraceptive methods, which may be higher than failure rates for subsequent years. Consequently, the estimated number of UPs may be overstated, as may cost savings generated from switching to LARC methods - For live births, the model includes only direct cost of delivery and omits pre-natal costs, long-term economic, social and health impacts of UP. Thus, the cost of UP is likely to be underestimated, as are cost savings when switching from SARC to LARC methods - Conservative assumption that 10% switch to LARC methods in the switching analysis. Potential cost savings arising from this switch may be underestimated

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Third-party healthcare payer perspective **Quality score:** Medium **Applicability:** Partly applicable	Multinational Integrated Data Analysis System (MIDAS), market share data used in conjunction with price data from the Medi-Span Master Drug Database, Medicare Fee Schedule, assumptions *UP due to imperfect adherence:* Research literature *Cost of pregnancy outcomes:* Medicare Physicians Fee Schedule, NSFG		**Measures of uncertainty:** Sensitivity analysis explored the impact of increased use of LARC on potential savings when costs of implant, IUD and IUS were not annualised. An additional sensitivity analysis estimated the duration of time that LARC methods would need to be used following a switch to achieve cost neutrality, defined as a zero net cost impact to the payer **Modelling method:** Cost model	Cost of contraception: £2,845 ($4,203) Total cost impact: £4,201 ($6,206) -Cost savings: Cost of UP: £79 ($117) Cost of contraception: £174 ($257) Total cost impact: £254 ($375) *Scenario 3:* -Cost of new contraceptive practice: Cost of UP: £1,494 ($2,207) Cost of contraception: £2,869 ($4,238) Total cost impact: £4,363 ($6,445) -Cost savings: Cost of UP: £145 ($214) Cost of contraception: £150 ($222) Total cost impact: £295 ($436)	- The prices Medicare used to calculate the cost of UP outcomes are likely to be lower than costs incurred by private third-party payers. Therefore, the cost of a UP, and the cost savings generated from switching to LARC, may be higher in a private-payer setting - The analysis did not consider the cost of side-effects and the impact of contraceptive method discontinuation and switching beyond a 1-year period - Wholesale acquisition costs for contraceptives used in the analysis may not reflect actual costs faced by third-party payers, who may obtain discounts or rebates **Limitations identified by review team:** Main limitations related to the model already identified by the authors

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Secondary analysis: *Estimated annual number of UPs:* 3.11 million: 1.44 million live births, 1.11 million induced abortions, 539,000 spontaneous abortions and 19,000 ectopic pregnancies *Cost for each UP in the US outcome:* -Hospital inpatient: Live birth: £3,202 ($4,729) Induced abortion: £2,386 ($3,524) Spontaneous abortion: £1,942 ($2,869) Ectopic pregnancy: £3,054 ($4,511) -Hospital outpatient: Induced abortion: £1,159 ($1,712) Spontaneous abortion: £1,195 ($1,765) -Non-hospital: Induced abortion: £205 ($303)	**Evidence gaps and/or recommendations for future research:** To include full range of complications (not only those related to delivery) in order to capture the full potential costs averted by society/public sector **Source of funding:** Anna Filonenko is a full-time employee of Bayer Pharma AG. Amy Law and Alexander Prezioso are full-time employees of Bayer Healthcare Pharmaceuticals Inc. Nathaniel Henry and Fareen Hassan are full-time employees of IMS Health and served as paid consultants to Bayer Healthcare Pharmaceuticals Inc. for the development of this study and manuscript. James Trussell is a full-time professor of economics and public affairs at Princeton University and received a consultancy fee

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				Spontaneous abortion: £247 ($365) *Annual cost of UP:* £3.11 billion ($4.6 billion) - Annual contraceptive costs ranged from £15 ($22) for condoms to more than £677 ($1,000) for the patch *Costs of perfect and imperfect adherence:* - All SARC and LARC methods considered are associated with UP rates of 2 or less per 100 women within the first year of perfect use (0.05-2) -Implication of imperfect adherence: 1.64 million UPs -Total cost of UP due to imperfect adherence: £167.22 billion ($2.47 billion) **Sensitivity analysis:** - When costs are not annualised, in the 20–29-year age group, switching from	from Bayer Pharma AG for his contribution to this work

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				non-LARC to LARC methods results in net cost increases - 10% of women switching to LARC from OCs, SARC, and no method results in net cost increases - Among women currently using OC, assuming a 10% switch to LARC, cost neutrality is achieved after 1.33 years in women aged 20-24 and after 1.39 years in women aged 25-29; among women currently using any SARC, cost neutrality is achieved after 1.62 years (aged 20-24) and 1.82 years (aged 25-29); among women currently using any SARC or using no method, cost neutrality is achieved after 1.63 years (aged 20-24) and 1.90 years (aged 25-29)	
Trussell et al. (2014)	**Source populations:** Young women requiring	**Intervention description:** LNG-IUS 13.5 mg	**Outcomes:** Cost per unintended pregnancy (UP) avoided, net	**Primary analysis:** *Effectiveness:* - SARC: 276 UP	**Limitations identified by author:**

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
Aim of study: To evaluate the cost-effectiveness of LNG-IUS 13.5 mg in comparison with short-acting reversible contraceptive (SARC) methods in a cohort of young women in the United States from a third-party payer's perspective **Type of economic analysis:** Cost-effectiveness analysis **Economic perspective:** Third-party payer's perspective, side-effect costs,	contraception in the United States, aged 20–29 years **Setting:** USA **Data sources:** *Failure and discontinuation probabilities:* Systematic review, assumptions *Contraceptive uptake:* Recent data from the National Survey of Family Growth *Costs:* Medi-Span Master Drug Database, current Procedural Terminology (CPT) 2008 Codebook derived from Healthcare Cost and Utilization Project data and the 2012 non-facility	**Comparator/control description:** Mixed market-weighted basket of SARC methods: branded and generic oral contraceptives (OC), ring, patch and injections; no method (chance) **Sample sizes:** Simulated cohort of individuals derived from multiple estimates	monetary benefit (NMB) **Time horizon:** 3 years and 1 year of cycle length **Costing year(s) and currency:** 2012 USD **Discount rates:** 3% in all costs **Perspective:** Third-party healthcare payer **Measures of uncertainty:** One-way and probabilistic sensitivity analysis and scenario analysis **Modelling method:** State transition model	- LNG-IUS 13.5 mg: 64 UP *Cost:* - UDC: £ 1,257,277 ($1,862,633) - LNG-IUS 13.5 mg: £ 866,348 ($1,283,479) * LNG-IUS 13.5 mg is a dominant intervention **Secondary analysis:** None **Sensitivity analysis:** - One-way sensitivity analysis show that the results were most sensitive to the probability of failure of OC, the probability of discontinuation associated with LNG-IUS 13.5 mg and the cost of live births - The base case probability of failure of OC is 0.090 (typical use) and varying the input between a lower bound set to the perfect use probability, and an upper bound set to 30% more than the base case	- The analysis considers 'Typical use' failure probabilities only for the first year of contraceptive use. However, failure rates are likely to be lower in the subsequent years. As a consequence, the cost impact of UP and the consequential incremental cost savings generated from UP avoided while on LNG-IUS 13.5 mg vs SARC may have been over-estimated in the model - Medicare prices are likely to be lower than those of private insurers. Therefore, the cost impact of UP may be underestimated - The model assumes that the subsequent year discontinuation was lower than discontinuation in the first year of use. However, the rate is likely to change

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
non-medical direct costs and indirect costs *not* considered **Quality score:** Low **Applicability:** Partly applicable	payments from the Medicare Reimbursement Fee Schedule; diagnosis-related group (DRG) 2008 Codebook, published data			input retains a positive NMB and preserves the cost-effectiveness of LNG-IUS 13.5 mg - When the base case probability of discontinuation associated with LNG-IUS 13.5 mg or the base case cost of live birth is varied by 30% NMB remains positive, preserving the cost-effectiveness of LNG-IUS 13.5 mg - PSA outputs demonstrated that 100% of model simulations fell in the southeast quadrant of the cost-effectiveness plane, indicating that the intervention was both cheaper and more effective than the SARC in all iterations - Scenario analysis assuming a 1-year time horizon found LNG-IUS 13.5 mg to be more	and it is unlikely to be the same across different methods - The absence of robust data on switching preferences necessitated a mixed market-weighted contraceptive 'basket' to act as a proxy for the subsequent method women would switch to once their initial method failed or when they chose to discontinue it. The mixed contraceptive 'basket' was a construct that approximated the average choices of women switching contraceptive method and was required as assumptions could not be made on the exact method to which women might switch **Limitations identified by review team:** Limited age group **Evidence gaps and/or recommendations for future research:** To include full

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
				effective but also more costly compared to the SARC - LNG-IUS 13.5 mg was therefore associated with an incremental cost of $2,760 USD per UP avoided. Assuming a 5-year time horizon resulted in higher effectiveness for LNG-IUS 13.5 mg compared to the SARC and lower total costs meaning that LNG-IUS 13.5 mg was considered dominant at 5 years - A scenario analysis in comparison to LNG-IUS 20 mcg/24h over a 3-year time horizon, showed that LNG-IUS 13.5 mg was less costly but also less effective - Over a 5-year time horizon, LNG-IUS 13.5 mg was more costly and less effective and dominated by LNG-IUS 20 mcg/24h	range of complications (not only those related to delivery) in order to capture the full potential costs averted by society/public sector **Source of funding:** Funded by Bayer Healthcare Pharmaceuticals Inc. This work was also supported in part by the Eunice Kennedy Shriver National Institute of Child Health and Human Development grant for Infrastructure for Population Research at Princeton University (Grant R24HD047879; to J.T.). Anna Filonenko is a full-time employee of Bayer Pharma AG. Jennifer Pocoski and Amy Law are full-time employees of Bayer Healthcare Pharmaceuticals Inc. Fareen Hassan and Nathaniel Henry are full-time employees of IMS Health and served as paid consultants to Bayer

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
					Healthcare Pharmaceuticals Inc. for the development of this study and manuscript. James Trussell is a full-time professor of economics and public affairs at Princeton University and received a consultancy fee from Bayer Pharma AG for his contribution to this work
Trussell et al. (2015) **Aim of study:** To estimate the average annual cost of available reversible contraceptive methods in the United States. and also quantify minimum duration of use required for LARC methods to achieve cost-neutrality	**Source populations:** Women aged 20–29 years (age group with the highest uptake of SARC methods) **Setting:** USA **Data sources:** *Weights assigned to each SARC method for the mixed-SARC basket:* Market share data from the most recent National Survey on Family Growth	**Intervention description:** Four short-acting reversible (SARC) methods – oral contraceptive, ring, patch and injection – and three LARC methods – implant, copper intrauterine device (IUD) and levonorgestrel intrauterine system (LNG-IUS) 20 mcg/24h (total content 52 mg)	**Outcomes:** Annual average cost per method and minimum duration of LARC method usage to achieve cost-savings compared to SARC methods **Time horizon:** 5 years **Costing year(s) and currency:** 2012 USD **Discount rates:** No discount rate applied; cost of each method was annualised for 5 years	**Primary analysis:** *Costs:* Despite high upfront costs associated with LARC methods, as duration of use increases, the average cost of LARC methods drops to become less expensive than the methods which have lower upfront costs. *Minimum duration of LARC method to reach cost-neutrality:* - Average LARC vs generic OC: 2.4 years - Average LARC vs ring: 0.4 years	**Limitations identified by author:** - The cost impact of UP may have been overestimated because the model take into account only the first year of 'typical-use' failure - The model assumes the same discontinuation rate across all methods due to a lack of robust literature on continuation of contraceptive methods beyond the first year of use - The absence of robust data on switching preferences

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
relative to other reversible contraceptive methods while taking into consideration discontinuation **Type of economic analysis:** Costing study **Economic perspective:** Public payer **Quality score:** Medium **Applicability:** Partly applicable	*First-year discontinuation rate:* Published studies *Subsequent-year discontinuation rate:* Assumption *Alternative discontinuation rate:* CHOICE study *Transition probabilities:* Systematic review *Costs of method acquisition:* Wholesale acquisition cost (WAC) price	**Comparator/control description:** No method (chance) **Sample sizes:** Simulated cohort of individuals derived from multiple estimates	**Perspective:** Public payer **Measures of uncertainty:** Scenario analysis **Modelling method:** State transition model	- Average LARC vs patch: 0.3 years - Average LARC vs injection: 2.6 years - Average LARC vs mixed SARC: 2.1 years - Average LARC vs condom: 3.0 years - Average LARC vs no method *(chance)*: 1.7 years **Secondary analysis:** None **Sensitivity analysis:** Scenario 1: The alternative discontinuation rates suggest that results are minimally sensitive to discontinuation assumptions. Scenario 2: conducting the analysis for a different population has an impact on results, but this impact is minimal	necessitated a mixed-market basket to act as a proxy for patients choosing to switch methods; however, this construct aimed to approximate the average choices of women switching contraceptive method - Medicare prices (used to calculate costs of unintended pregnancy) are expected to be lower than those of private insurers - This analysis was conducted from the public payer perspective, but wholesale acquisition costs (WACs) were used to estimate the acquisition cost of the various contraceptives. The results should support a similar conclusion under the private-payer perspective because WACs are similar to the costs that private payers pay would face

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis	Results	Notes
					Limitations identified by review team: Main limitations associated to the model already discussed by the authors **Evidence gaps and/or recommendations for future research:** To include full range of complications (not only those related to delivery) in order to capture the full potential costs averted by society/public sector **Source of funding:** This study and manuscript development were funded by Bayer Healthcare Pharmaceuticals Inc. and supported in part by the Eunice Kennedy Shriver National Institute of Child Health and Human development grant for Infrastructure for Population Research at Princeton University, grant R24HD047879 (J.T.)

Appendix 11: Structured summaries

Bayer LL, Edelman AB Caughey AB, Rodriguez MI (2013) The price of emergency contraception in the United States: what is the cost-effectiveness of ulipristal acetate versus single-dose levonorgestrel? *Contraception*, 87(3): 385-390.

This study aimed to examine the cost-efficacy of ulipristal acetate (UPA) compared to levonorgestrel (LNG) taken within 120 hours of unprotected intercourse, using a cost-effectiveness analysis and decision analytic model. Within the model, US women of reproductive age presenting in an unspecified location were given either type of emergency contraception within 120 hours of unprotected intercourse, and the primary outcomes – pregnancies averted, costs and quality-adjusted life years (QALYs) – were derived using a societal perspective. Sources of evidence to inform the model included meta-analysis, other research literature, state Medicaid payments and costs, and a national reproductive health survey. QALYs were calculated to measure the impact of an unintended pregnancy on a woman's quality of life, using an average life expectancy of 55 additional years after taking contraception. Cost-efficacy was tested using a threshold of $100,000 per QALY gained, calculating ICERs comparing both types of contraception. Sensitivity analyses were undertaken to test all inputs and also potential uncertainties around the threshold value, contraception failure and medication costs.

The results indicated that using UPA would result in 37,589 fewer unintended pregnancies per 4,176,572 estimated US annual emergency contraception episodes (UPA 54,295 pregnancies; LNG 91,884 pregnancies). The societal savings would be $116.3 million USD per year. A cost-effectiveness acceptability curve analysis indicated a 96% probability that UPA is more cost-effective at a willingness to pay $100,000 USD per QALY.

This economic evaluation rated low in terms of its methodological quality. The reviewers noted that the analysis was limited by a number of issues, including the fact that the authors did not state the perspective of the analysis, making it difficult to determine whether the results could be extrapolated to the entire society or whether the findings should be interpreted only from the perspective of Medicaid users. The reviewers also noticed that complications such as STIs were not included. We suggest that future research fully assess the benefits by accounting for these issues.

Burgos JL, Gaebler JA, Strathdee SA, Lozada R, Staines H, Patterson TL (2010) Cost-effectiveness of an intervention to reduce HIV/STI incidence and promote condom use among female sex workers in the Mexico-US border region. *PloS One*, 5(6): e11413.

An economic modelling study using a government healthcare payer perspective was undertaken in order to estimate the cost-effectiveness of a brief behavioural intervention of condom negotiation skills development to reduce HIV and STIs in 409 female sex workers in Tijuana and Ciudad Juarez, Mexico. Intervention participants were compared to 406 female sex workers who received a presentation on HIV and STI prevention of similar duration, assessing self-reported high-risk sex behaviour. The effectiveness of this intervention was evaluated using a randomised controlled trial, which rated medium in terms of methodological quality, due to issues of sample representativeness, objective outcome measurement, non-reporting of intention to treat analysis and questionable generalisability to the UK context. Using a Monte Carlo Markov model design, a hypothetical cohort of 1,000 women were followed over the course of their lifetime. Strategies were

compared in terms of HIV infections, quality-adjusted life expectancy (QALE) and QALYs, and annual or lifetime costs. Data were drawn from the randomised controlled trial (health outcomes and costs), government reports and published literature.

Analysis of the hypothetical cohort suggested that offering the intervention once only, 33 HIV infections would be prevented (95% CI: 30-37), increasing the QALE by 151 days per female sex worker (FSW) (95% CI 135-171), at a cost of $183 USD per QALY gained (95% CI $164-$206) to prevent each HIV case. If offered annually, the intervention model suggests an additional 29 new HIV cases prevented (95% CI 26-33), increasing the QALE by 132 days (95% CI $109-$149), at a cost per additional QALY gained of $1,075 USD (95% CI $931-$1259), at a cost of $13,413 USD (95% CI 11,697-$15,077) per HIV case averted. One-way, two-way and probabilistic sensitivity analyses were undertaken, including testing results with and without the uptake of HAART. In addition, the model was calibrated by comparing estimates of life expectancy, HIV incidence and median survival for women not in sex work, sourced from separate data sources. Major results from the sensitivity analysis showed that the *Mujer Segura* intervention would no longer be cost-effective with changes in incidence of HIV, syphilis, gonorrhoea and chlamydia.

This economic evaluation rated medium in terms of its methodological quality. The reviewers suggest that HIV complications should be explicitly modelled into the analysis, rather than just implicitly through the treatment of use or non-use of HAART by CD4 levels, in order to better understand the implications on costs and health outcomes in the long term.

Cooper K, Shepherd J, Picot J, Jones J, Kavanagh J, Harden A, Barnett-Page E, Clegg A, Hartwell D, Frampton G, Price A (2012) An economic model of school-based behavioral interventions to prevent sexually transmitted infections. *International Journal of Technology Assessment in Health Care*, 28(4), 407-414.

In order to assess the cost-effectiveness of teacher-led and peer-led school-based sexual health behavioural interventions compared to standard school health education in British schools, a Bernoulli probability model was developed, using a UK National Health Service and Personal Social Services perspective. The total number of HIV, chlamydia, gonorrhoea and genital warts cases averted, and consequent QALY gain, cost of the intervention and savings in medical costs for a hypothetical cohort of 1,000 males and 1,000 females aged 15 years were estimated for one year and cost-effectiveness was calculated. Data were sourced from multiple sources of evidence, including a systematic review with meta-analysis for the effectiveness of the programme, databases from the UK health authorities, surveys, published and unpublished studies and assumptions.

The results estimated that the teacher-led intervention would cost an additional €8,575, averting two STI cases, with a 0.35 QALY gain in comparison to standard sex education in British schools. This resulted in an ICER of €24,268 per QALY gained, with the largest STIs averted being chlamydia and the largest gains for females avoiding chlamydia infection. The peer-led intervention resulted in the same number of cases averted and QALYs gained. However, a higher ICER of €96,938 per QALY gained was incurred. The peer-led intervention is thus less cost-effective than the teacher-led intervention in comparison to standard sex education; most likely due to higher peer educator training costs. Sensitivity analyses were undertaken, varying the values of STIs, number of sex episodes per partner, the length of time the intervention effect lasted, and the difference in effectiveness if the

population were males aged 16 to 19 years. A series of sensitivity analysis were undertaken, including a probabilistic sensitivity analysis. Acceptability curves were generated to better understand the difference in effects for the interventions compared to the baseline (standard sex education in British schools). Several uncertainties were associated with the results, particularly regarding effectiveness. A scenario analysis was also undertaken to better explain the results, but some uncertainties remained due to a lack of reliable data.

This economic evaluation rated as high in terms of its methodological quality. The reviewers suggest that the model be repeated using empirical data to better define interventions that are cost-effective.

Crawford MJ, Sanatinia R, Barrett B, Byford S, Dean M, Green J, Jones R, Leurent B, Sweeting MJ, Touquet R, Greene L, Tyrer P, Ward H, Lingford-Hughes A (2015) The clinical and cost-effectiveness of brief advice for excessive alcohol consumption among people attending sexual health clinics: a randomised controlled trial. *Sexually Transmitted Infections*, 91(1): 37-43.

This trial aimed to examine the clinical and cost-effectiveness of brief advice for excessive alcohol consumption amongst people aged 19 years or older attending one of three sexual health clinics in London, England. The study design was a cost-effectiveness analysis based on an integrated parallel-arm, single-blind randomised controlled trial. The effects of a brief alcohol advice, a health information leaflet and an offer of an appointment with an alcohol assessment worker were compared with provision of a health information leaflet alone. The researchers measured a primary outcome of 90-day alcohol consumption, and secondary outcomes of three months of unprotected sex, health-related quality of life and costs up to six months post-intervention. QALYs were calculated based on EQ-5D ratings, and differences in mean costs per participant determined. An NHS and personal social service perspective was taken. Cost-effectiveness acceptability curves were derived to show the likelihood that the brief intervention is more cost-effective than the control treatment for different values that a decision maker is willing to pay for improvements in outcome.

The results suggested that no significant reductions in alcohol consumption or sexual behaviours occurred. While the costs were similar amongst intervention and control group participants (£311 and £319 respectively), and the additional cost of the intervention was low compared to the total cost of care provided (£12.57, standard deviation £6.59), the authors concluded that the intervention was not associated with clinically important improvements in alcohol consumption or sexual behaviour and did not provide a cost-effective use of resources.

The methodological quality of the integral trial was rated to be high, as the study design and parameters seemed to be appropriately explored and a sensitivity analysis was undertaken in which the authors tested the strength of the findings. In addition, 'bootstrap' techniques and non-hierarchical linear models were undertaken to assess missing data. The time horizon was very short to capture change in individual behaviour, leading the reviewers to suggest that a long time horizon be used to assess potential complications, such as STI transmission, in the long run.

Foster DG, Raine TR, Brindis C, Rostovtseva DP, Darney PD (2010) Should providers give women advance provision of emergency contraceptive pills? A cost-effectiveness analysis. *Women's Health Issues*, 20(4): 242-247.

In order to examine the effects and cost-effectiveness of different means of access to emergency contraception (EC) on unintended pregnancy rates in sexually active women, the authors utilised a Markov model. This compared the effects of advance provision or on-demand clinic or pharmacy provision against no use of EC on unintended pregnancies and costs in three hypothetical cohorts of one million sexually active women stratified by sexual behaviour risk. EC effectiveness data were derived from clinical trials and costs from the state Medicaid programme, utilising a societal perspective. Probabilities of taking contraception, conception and costs were calculated. Costs savings per dollar spent on each type of contraception for each risk group of women were reported.

The results indicated that advanced provision of ECP could potentially avert the same or more unintended pregnancies compared to on-demand provision, with largest reductions for low-risk women having advance provision. The number of dollars saved on averted pregnancy costs for each dollar spent on advance ECP is greater than one, suggesting a cost saving. The authors discussed the possible implications for the results when changes in effectiveness were observed, but the reviewers were unsure if their statement was based on sensitivity analysis as the authors did not report undertaking one.

This economic evaluation was judged to be of medium methodological quality. The reviewers noticed some limitations, for example that the authors only looked at savings from pregnancies averted for one year. If an ECP supply was kept for longer than this, the cost savings of advance provision would be underestimated. Further, the authors also assumed that unprotected acts of intercourse occurred randomly throughout the menstrual cycle; however, costs savings would likely be higher if women were more likely to use emergency contraceptive for acts that occurred in the week before ovulation. The authors also only modelled intercourse where no contraception was used. In this case, cost-effectiveness would be lower if EC was used in situations where the likelihood of conception was lower than with no contraception (e.g. missed pill). In addition, the authors only considered the medical costs of unintended pregnancy for up to two years after a birth: in fact, social, welfare and private costs are likely to be much higher. Reviewers suggest that authors model scenarios assessing the identified limitations for a longer period and include complications such as STIs in a long-term assessment of health benefits and costs.

Foster DG, Biggs MA, Malvin J, Bradsberry M, Darney P, Brindis CD (2013) Cost-savings from the provision of specific contraceptive methods in 2009. *Women's Health Issues*, 23(4): e265-271.

The authors conducted a cost-benefit analysis in order to determine the relative contribution of new contraceptive methods to averting unintended pregnancies. Health insurance claims data for contraception methods provided in 2009 to US women were used to construct a cohort of 1,058,381 women aged 15 to 44 years. No perspective was stated. Eleven types of contraception methods were included and compared: tubal ligation/ occlusion; copper IUD; hormonal IUS; implant; injectables; ring; patch; oral contraceptives; barriers; and emergency contraceptives. Contraceptive coverage and costs were estimated for a two-year time horizon, using claims data and a review of medical records. The health

outcomes estimated were pregnancies expected and pregnancies averted. The cost outcomes were those incurred in providing contraceptive services, including clinical and laboratory visits.

The authors asserted that all the contraceptive methods studied saved more in public expenditures for unintended pregnancy than the cost of provision. Contraceptive implants and copper IUD were estimated to have the highest rate of USD return at just over $5.00 USD in averted services. Hormonal IUS was estimated to save $4.89, followed by injectable methods at $4.00. Short-acting contraception including oral contraceptives ($3.37), ring ($2.20), patch ($2.12), barriers ($1.58) and emergency contraception ($2.56) ranged in cost savings. Tubal ligation and occlusion methods resulted in savings of $3.59 and $1.59 respectively. Two sensitivity analyses were undertaken: (1) cost outcome calculation without adjustment for months of protection for short-term methods, in order to test the possibility of women using all the methods dispensed; and (2) calculating the return of contraceptive provision by examining savings through delivery or termination rather than two years after birth.

This economic evaluation was judged to be of medium methodological quality. The main limitations associated with the study were identified by the authors, but the reviewers also suggest that future research should also incorporate the long-term benefits, in terms of costs and health outcomes, of the impact on complications such as HIV and other STIs.

Han L, Teal SB, Sheeder J, Tocce K (2014) Preventing repeat pregnancy in adolescents: is immediate postpartum insertion of the contraceptive implant cost-effective? ***American Journal of Obstetrics and Gynecology*****, 211(1): 24.e1-24e.7.**

This study aimed to determine the cost-effectiveness of a hypothetical state-funded programme to provide immediate postpartum implant (IPI) insertion for teenage mothers at 6, 12, 24 and 36 months postpartum. Data from women aged 13 to 22 years enrolled in an observational study of pregnancy and post-natal care were utilised. Reproductive outcomes for those adolescents who received IPI contraception prior to hospital discharge were compared to those choosing other types of contraception after delivery. Pregnancy outcomes were measured, including type of delivery, miscarriage and ectopic pregnancy. Costs were calculated using an unspecified perspective, but which appears to be health services, using Medicaid costs. The costs were then modelled by normalising them using a hypothesised cohort of 1,000 women in each group, where the costs for IPI insertion were estimated and total costs at 6, 12, 24 and 36 months were calculated. These included one year of well-baby care for delivered pregnancies.

The results at six months suggested that the costs of the IPI group were higher than the comparison group by $73,000. However, at 12, 24 and 36 months, publicly funded IPIs would result in a savings of more than $550,000, $2.5 million and $4.5 million respectively. The authors estimated that for every dollar spent on IPI, $0.79, $3.54, and $6.50 would be saved at 12, 24, and 36 months. Expenditures between the IPI and comparison groups would be equal if the comparison group pregnancy rate was 13.8%, 18.6% and 30.5% at 12, 24 and 36 months. Actual rates were 20.1%, 46.5% and 83.7%. Sensitivity analysis only varied the repeated pregnancy rates of the comparison group.

This economic evaluation was judged to be of low methodological quality: by assessing only one parameter in the study (rather than all), the robustness of the results might be

compromised. The reviewers also reported that discount rates were not reported. Further, benefits in terms of repeat pregnancy rates were not reported by type of complications, thus not capturing the full benefits generated by each outcome. It was suggested that for future research, these issues should be overcome and that discount rates should be reported.

Holtgrave DR, Maulsby C, Kharfen M, Jia Y, Wu C, Opoku J, West T, Pappas G (2012) Cost-utility analysis of a female condom promotion program in Washington, DC. *AIDS and Behavior*, 16(5): 1115-1120.

This study aimed to assess the affordability, performance standards and relative cost-effectiveness of a US-based intervention to provide female condoms and health education to the general population. This was done using a cost, threshold and cost-utility analysis modelling method. Female condom provision versus no provision was compared. Costs were based on service use over one year in Washington DC, using both societal and payer perspectives. Sources of evidence included data from the Female Health Company and MAC AIDS Fund for all cost elements, and Department of Health Washington DC, parameters from a previous model developed by the authors and literature, for health outcomes analysis.

The results indicated that distributing 200,000 female condoms and health education cost $414,186. From a societal perspective, 1.13 HIV infections would have to be averted for the program to be cost-saving; from a public sector payer perspective, 1.50 would need to be averted and a cost-effectiveness threshold of 0.46 HIV infections averted would be required. Modelling analyses suggested that the intervention averted approximately 23 HIV infections, demonstrating net cost savings.

The methodological quality of this study was determined to be high. When the model allowed for the use of male condoms by women, at a specific level, the cost-utility analysis was still cost-saving, as well as when allowing for the use of male condoms by females and female condoms were dropped as low as 7.04%; these results were shown in a sensitivity analysis. In addition to the limitations identified by the authors, the reviewers pointed out that the cost-effectiveness analysis and cost-utility analysis were not clearly stated in terms of the cost per outcome. The authors only presented net savings, which suggested that the alternative was dominant. Also, because the comparator was not clearly stated, it was not possible to fully understand what they were comparing. The reviewers suggest that future research clearly identify outcomes for a cost-effectiveness or utility analysis and that alternatives for dominance be fully described.

Holtgrave DR, Wolitski RJ, Pals SL, Aidala A, Kidder DP, Vos D (2013) Cost-utility analysis of the housing and health intervention for homeless and unstably housed persons living with HIV. *AIDS and Behavior*, 16: 1626-1631.

To understand the impact of providing supportive housing assistance for homeless and unstably housed persons living with HIV, a cost-utility analysis was conducted based on a trial undertaken in three major US cities. HIV viral load, emergency room use and perceived stress were examined in the treatment group receiving rental assistance and case management, compared to those who received customary housing services with case management. Neither a perspective of analysis or time horizon were reported. Costs included those for service provision, savings accrued through lowered emergency

department use, HIV transmissions averted and medical costs saved. QALYs saved due to improvements in perceived stress and HIV transmissions averted were also calculated.

The findings suggested that cost per QALY saved through the provision of rental assistance was $62,493 USD. A threshold analysis was conducted to assess uncertainties around the parameters used in the analysis. The authors concluded that the intervention would still be favourable compared to any other well-accepted medical and public health services even if the number of HIV transmissions was at the lowest level.

This economic evaluation rated low in terms of its methodological quality. The trial on which the economic evaluation was based was considered to have significant potential for bias, because the findings were based on 'as-treated' analyses rather than by intention to treat. Further, the model did not capture any complications associated with HIV, so none of the long-term benefits in terms of costs and health outcomes could be captured. In addition, the reviewers were unable to judge if the time horizon for the analysis was sufficient to capture changes in HIV transmission or behaviour, as this information was not reported.

Jackson LJ, Roberts TE, Fuller SS, Sutcliffe LJ, Saunders JM, Copas AJ, Mercer CH, Cassell JA, Estcourt CS (2015) Exploring the costs and outcomes of sexually transmitted infection (STI) screening interventions targeting men in football club settings: preliminary cost-consequence analysis of the SPORTSMART pilot randomised controlled trial. *Sexually Transmitted Infections*, 91(2): 100-105.

This pilot cluster randomised controlled trial aimed to compare the costs and outcomes of two STI screening interventions that were targeted at men aged 18 years and older in six English football club settings. The time horizon seemed to be one year, similar to the intervention, but it was not clearly stated. Cost data were collected prospectively within the trial. Two interventions were tested: a team captain-led and poster STI screening promotion or a sexual health adviser-led and poster STI screening promotion – compared to a poster-only STI screening promotion. Only start-up costs (i.e. the costs of the posters) were annuitised at a 3% rate for three years. Screening uptake for chlamydia and gonorrhoea testing and costs were measured and a cost-effectiveness analysis undertaken assessing costs per player tested, from a health systems perspective.

The results indicated a lower uptake of screening in the captain-led arm versus the health adviser-led arm and the poster-only condition, which were similar (50% versus 67% and 61% respectively). Costs per player screened were similar in all arms (£88.89 versus £88.33 versus £81.87 respectively), suggesting a need to further explore the acceptability of such interventions in non-clinical settings.

The economic evaluation was judged to be of medium methodological quality, due to lack of information on the parameters used in the analysis. Clearer reporting of the annuitisation of costs with posters and time horizon for the analysis is required: seemingly, the analysis was undertaken for a time horizon of one year and the costs with posters were considered for three years. If this was the case, the costs may be overestimated. Several sensitivity analyses were undertaken, including: additional preparation costs for captains, reduced club costs through higher organisational level support, additional incentive costs, different staff arrangements, different testing kit and processing costs, and increased uptake. However, not all parameters included in the model were assessed in a one-way

sensitivity analysis. The authors clearly stated that this analysis was conducted for the pilot phase, justifying the conduct of a cost-consequence analysis. A full cost-effectiveness analysis with an exploration of all parameters in sensitivity and probabilistic analyses will better indicate the parameters that bring the most uncertainty around the costs and health outcomes.

Kessler J, Myers JE, Nucifora KA, Mensah N, Kowalski A, Sweeney M, Toohey C, Khademi A, Shepard C, Cutler B, Braithwaite RS (2013) Averting HIV infections in New York City: a modelling approach estimating the future impact of additional behavioral and biomedical HIV prevention strategies. *PLoS One*, 8(9): e73269.

This study aimed to determine the cost-per-HIV infection averted for multiple intervention strategies, in order to determine the most cost-effective combination of interventions to provide in New York, USA. The economic evaluation design was reported as 'operations research modelling', a method which includes techniques such as Markov modelling. Different combinations of 16 HIV prevention interventions were compared over varying time horizons up to 20 years. Costs for each intervention were obtained from The Department of Health and Mental Hygiene of New York City and measures of benefits were collected from the literature and based on assumptions made by the authors. A hypothetical cohort of all people in New York City in 2009 aged 0 to 75 was created and divided into subgroups based on gender, sexual risk behaviour, sexual identity, infection status, treatment status and injection drug use, and the primary outcome was cost per infection averted. The perspective of the analysis was from the Department of Health and Mental Hygiene and the City of New York.

The results suggested that over a 20-year period, 58,632 new HIV cases would be detected. A total of 16,159 people were predicted to die as a result of AIDS-related conditions. A total of 10 unique interventions had the potential to be cost-saving: condom distribution; social marketing; community-based prevention; prioritised use of surveillance data (i.e., targeted use of HIV and STD surveillance data to prioritise risk reduction counselling and partner services for persons with previously diagnosed HIV infection with a new STD); cofactor risk reduction; screening, brief intervention and referral for treatment for unhealthy alcohol use (SBIRT); linkage to care; linkage to support services for HIV-positive persons; partner services (defined here as just partner notification and testing); and STD screening. Of these, implementation of evidence-based community-level interventions, STD screening for high-risk HIV infected persons, partner services and a linkage to support interventions were found to be most cost-saving and would prevent the most infections, resulting in a reduction of 20,211 new HIV infections per year at a cost per infection averted of $106,378 USD per year and cost savings over 20 years of $5 billion. Determining a package of interventions that were most effective (regardless of cost) resulted in included expanded provision of post-exposure prophylaxis for HIV-uninfected persons, linkage to support, social marketing for HIV-infected persons, evidence-based community-level interventions and enhanced HIV testing in clinical settings being found to be most effective. The authors estimated that 33,004 new HIV infections would be averted at an estimated cost per infection averted of nearly $9 million USD over twenty years. A 'test and treat only' package of interventions was estimated to result in 14,048 new infections over 20 years, with more than 80% of new infections averted and a cost per infection averted of over $360,000 USD. One-way and probabilistic sensitivity analysis were undertaken to test

for uncertainties around the parameters. Most interventions were still cost-effective or cost-saving even for an increase of 10% in effectiveness parameters.

This economic evaluation rated high in terms of its methodological quality, as the authors calibrated their model by using empirical figures. The authors also identified the main limitations of the study. The reviewers suggest that in future analysis, the treatment of HIV should be explicitly modelled by level of CD4 and that the time horizon be extended to a lifetime analysis, in order to better capture the long-term benefits of intervention strategies.

Lasry A, Sansom SL, Hicks KA, Uzunangelov V (2012) A model for allocating CDC's HIV prevention resources in the United States. *PLoS One*, 7: e37545.

This study aimed to create a model for the optimal allocation of HIV resources from the perspective of the Division of HIV/AIDS Prevention (DHAP) at the Centre for Disease Control and Prevention (CDC). The authors built two interrelated models, an epidemic dynamic compartmental model and an optimisation model, to assess HIV transmission and progression by different ethnic and HIV subgroups in the United States (men who have sex with men, injection drug users and heterosexuals) for a 5-year time horizon. The assessed interventions were those funded by the CDC: HIV testing, individual and group-level counselling and education. Sources of data include Cycle 6 (2002) of the National Survey of Family Growth (NSFG), DHAP data, other previously published studies and assumptions. The assessed scenarios for the projection of HIV infections over time were: 1) amounts to allocate each year towards interventions and population subgroups to minimise new infections for the general population, 2) per-person cost of testing based on the cost of opt-out testing in emergency department settings and the cost of a CDC-led expanded testing programme, also for the general population and 3) the cost of testing in STD clinic settings and the cost of testing in outreach settings by targeting the high-risk population.

The results showed that for a budget of $327 million USD, no allocation of resources would reduce 13% of new infections, and an optimised allocation would avert 31% of new infections. For an HIV scenario model and a $327 million USD budget, a non-optimal allocation by intervention (counselling plus testing) and by risk group, would reduce the proportion of new infections of the general population of US adults in 29%; by risk group it would be: 23% for mean who have sex with men (MSM),11% to injection drug users (IDU), and 36% to high risk heterosexuals (HRH). An optimal budget would reduce the risk in 51%, 11% and 38% of cases respectively for MSM, IDU and HRH. By ethnic group, the intervention (counselling plus test) would reduce new infections by 32% for blacks, 17% for Hispanics and 22% for others in a non-optimal allocation, and by 36% for blacks, 29% for Hispanics and 35% others in an optimal allocation. In a scenario of an intervention (counselling plus education) by serostatus, a non-optimal budget allocation would use 11% of the budget targeted for diagnosed positives and 89% for susceptibles, while in an optimised budget, 100% of the budget would target diagnosed positives. The authors stated that the current baseline and the optimal allocation of funds could be considered cost-saving when compared to the HIV lifetime treatment costs. In addition, the authors concluded that more funds should be allocated to testing and targeting MSM and IDU; that counselling and education ought to provide focus on HIV positive persons aware of their condition, and that interventions should target those with high risk of transmitting HIV. The univariate sensitivity analysis

showed robust results where only 9 out 100 scenarios with varying parameters changed the results.

The study was rated low in its methodological quality. The reviewers noted that the time horizon for the analysis was too short to account for all benefits generated by reductions in infection and recommended that a lifetime or a longer period for analysis be considered to capture the long-term benefits of the intervention, including an assessment of complications due to HIV.

Long EF, Mandalia R, Mandalia S, Alistar SS, Beck EJ, Brandeau ML (2014) Expanded HIV testing in low-prevalence, high-income countries: a cost-effectiveness analysis for the United Kingdom. *PLOS ONE*, 9(4): e95735.

This economic evaluation aimed to estimate the effectiveness and cost-effectiveness of expanded HIV testing in the UK. The authors modelled different HIV epidemic scenarios based on different interventions in a UK adult population aged 15 to 64 years, categorised by country of origin and risk status for 10-year HIV prevalence and incidence, and a lifetime horizon for the cost per QALY analysis. These included high-risk groups, including MSM, people who inject drugs (PWID), and men and women from HIV-endemic countries with high disease prevalence. Population groups were further subdivided by HIV infection and diagnosis status; antiretroviral therapy (ART) status if HIV positive; HIV serostatus; and male circumcision status. The interventions assessed were universal HIV testing, targeted HIV testing and expanded ART, compared to current HIV and treatment levels ('status quo').

The economic evaluation was a cost-utility analysis that took the perspective of society, healthcare and personal social services. The authors estimated HIV prevalence, incidence, QALYs and healthcare costs over ten years, and cost-effectiveness based on each intervention compared to the status quo. These were grouped according to gender, HIV serostatus and treatment status, injecting drug use status, including individual costs of voluntary counselling and testing (VCT) and ART. Costs were derived from the literature and health agencies in the UK and converted to 2012 GBP; all costs and QALYs were discounted at 3% annually.

The findings suggested that annual HIV testing of all adults could avert 5% of new infections, even with no behaviour change following HIV diagnosis because of earlier ART initiation, or up to 18% if risky behaviour was halved. This strategy costs £67,000–£106,000 per QALY gained. Providing annual testing only to MSM, PWID and people from HIV-endemic countries, and one-time testing for all other adults, would prevent 4–15% of infections, require one-fourth as many tests to diagnose each person with HIV, and cost £17,500 per QALY gained. Augmenting this programme with increased ART access could add 145,000 QALYs to the population over 10 years, at £26,800 per QALY gained. Modelled outcomes were compared to available UK Health Protection Agency data on HIV prevalence, incidence and diagnoses and were deemed similar. All modelled parameters were tested in a sensitivity analysis, but only those that brought more uncertainty to the results were highlighted; more prominent parameters were VCT and HIV transmission probabilities. The authors also argued that because the effectiveness evidence of HIV risk screening and ART treatment was uncertain, effectiveness could be built into sensitivity analysis of the resulting economic model.

The study rated as high in terms of its methodological quality. This was a landmark cost-effectiveness analysis of HIV screening in the UK because it was one of the first to use different sources of data to combine epidemiological, behaviour and CD4 bands into an assessment of complex HIV disease progress. The reviewers noted that in addition to the limitations identified by the authors, HIV treatment was not explicitly modelled; rather, it was assumed that upon diagnosis, individuals would have a long life expectancy. This was implicitly due to ART, where assumed reductions in HIV infection would be due to reduced viral load following initiation of ART. Future evaluations could explore the implications of early HIV screening on complications (costs and health outcomes). The reviewers also suggest that a 3.5% discount rate is applied for costs and 1.5% for health effects, rather than 3%. This is in line with NICE recommendations for evaluating the substantial treatment effects that are required to restore and maintain health over a long period of time (i.e. at least 30 years).

Marseille E, Shade SB, Myers J, Morin S (2011) The cost-effectiveness of HIV prevention interventions for HIV-infected patients seen in clinical settings. *Journal of Acquired Immune Deficiency Syndromes*, 56(3): e87-e94.

This is a cost-effectiveness analysis, using a computer-based epidemic HIV transmission model comparing three counselling-based interventions to standard care (no standard counselling): 1) a primary care provider-based (clinical provider) consisting of brief risk assessments administered by computer to patients in private while they waited for their medical appointments; 2) a social worker or peer educator-based (specialist), where the client receive a one-on-one session, group session, or a combination of both; and 3) a mix of primary care and specialist-based (mixed), where the intervention mixed both strategies, provider-delivered and specialist-delivered interventions. The outcomes of analysis were the unit costs for each of the intervention types, the average cost per dose-minute of service and HIV infections averted.

The analysis was conducted from the perspective of the health system for a three-year time horizon. Multiple sources of data were used and included a diverse range of providers in the USA – from university hospitals to health centres. In these institutions, data on all HIV-infected patients (including new and returning patients), male patients reporting sexual activity with other males in the last 6 months, all MSM patients, patients diagnosed with HIV for at least 3 months, patients older than age 45 years reporting unprotected sex in the last 12 months, patients reporting sexual activity or drug use in the last 3 and 6 months, female patients, patients reporting risk in the last 6 months, patients with sex or drug risk in the last 6 months.

The results showed that the total average costs were $146,075 USD, $337,881 and $268,911, for a clinical provider, specialist provider or mix of both respectively. The average costs per dose-minute of the service were $17.46, $7.37 and $13.78, for a clinical provider, specialist provider or a mix of both respectively, while the costs per HIV cases averted were $2.71, $1.11 and $3.02 for each outcome respectively. The cost-effectiveness analysis (cost per HIV case averted) compared to the baseline intervention (no standard intervention) estimated a ratio of $107,656 for the clinical provider and $535,782 for all sites combined. The clinical provider intervention dominated the specialist and the mix interventions. The multivariate sensitivity analysis for a threshold of $303,100 showed that

the clinical provider intervention would no longer be cost-effective for increases of 50% in the costs and if effectiveness was only 50%.

The study was rated as high for its methodological quality. The reviewers suggested that future research explore complications associated with HIV infections in the long term to better capture health and costs benefits of the intervention.

National Collaborating Centre for Women's and Children's Health (2013) ***Long acting reversible contraception: the effective and appropriate use of long acting reversible contraception*****. London: Royal College of Obstetricians and Gynaecologists Press.**

To inform national contraceptive guideline development, a decision-analytic Markov model was undertaken to evaluate the cost-effectiveness of LARC methods (copper IUDs, hormonal IUDs, injectables and implants), compared to each other and to combined oral contraceptives (COC), male condoms, and male and female sterilisation. This was based on a non-systematic review of relevant literature which did not specify its search strategy, inclusion criteria or methods of synthesis, resulting in an 'unsound' methodological quality rating. Using an NHS perspective, the model population was a hypothetical cohort of 1,000 sexually active women of reproductive age who took up a contraception method at the beginning of the first year, then were followed forward in time allowing for expected population rates of discontinuation of the method. The health outcome of contraceptive 'failure' was unintended pregnancy, via live birth, abortion, miscarriage and ectopic pregnancy. The costs estimated included: ingredient costs, healthcare resource use and costs resulting from any type of unintended pregnancy outcome. Sources of evidence included NHS reference costs, British National Formulary, Guidelines Development Group opinion and consensus, GP fee schedules, national statistics and literature. The results were analysed and presented as an annual event over a 15-year period, and economic outcomes were reported as the number of pregnancies averted by one contraceptive method compared to another. Costs and health outcomes were discount at 3.5% as recommended by NICE.

The findings suggested that all LARC methods averted more pregnancies in comparison to COC and the male condom for up to 15 years of use. For just one year of use, the IUD and the injectable were more effective and less costly than COC or the male condom. Where contraceptive use rose to two years or more, all LARC methods dominated COC and male condoms.

The methodological quality of this economic modelling study was rated as medium because many uncertainties were not fully described relating to the parameter and structure of the model. Sensitivity analyses were undertaken examining variation in: the duration of use; combined use with condoms; changes in ingredients and costs of health service comparisons; ideal use of condom and COC; and discount rates. All parameters should be assessed in a one-way sensitivity analysis to account for uncertainties related to them. Additionally, the model was adapted from previous studies, but no validation and/or calibration was reported. Validation and or calibration of the model outputs with empirical data would allow identification of the model parameter values that achieve a good fit.

Pilgrim H, Payne N, Chilcott J, Blank L, Guillaume L, Baxter S (2010) ***Modelling the cost-effectiveness of interventions to encourage young people, especially socially***

***disadvantaged young people, to use contraceptives and contraceptive services*. Sheffield: School of Health and Related Research.**

This study aimed to establish the cost-effectiveness of interventions to encourage young people in the UK aged up to 19 years, including those considered disadvantaged, to use contraception and contraceptive services. The alternatives compared were: the dispensing of condoms within schools, intensive case management to prevent repeated teenage pregnancies, advanced provision of emergency hormonal contraception provided to those young people who attended a clinic for contraceptive services. These alternatives were assessed against the baseline alternatives of 'current practice', where there was no standardised care (preventive or curative), and this was described as a school nurse service where there was no follow-up following first pregnancy and no advance provision of EHC. These alternatives were compared using a discrete decision analytical model. Health outcomes were the number of pregnancies averted for the age group relevant to the intervention, and STI infection was estimated by adapting an existing Bernoulli model for HIV transmission. Costs were estimated for: the intervention and additional contraception required as a result; maternity care; abortion; miscarriage, ectopic pregnancy or stillbirth; treatment for low birth weight infants; treatment for STIs; government-funded benefits. Appropriate sources of evidence were used to derive the costs and probabilities for health outcomes. Economic outcomes were determined to be the cost for each age-specific pregnancy averted and the cost for each abortion avoided.

The findings showed that the cost per abortion averted comparing school-based dispensing of hormonal contraceptives within the school to school-based dispensing of condoms was estimated at £1,514, when government-based benefits were excluded from the analysis, and at £441 when these benefits were included; different levels of dominance were observed when the different alternatives were compared. The cost per repeat teenage pregnancy averted for intensive case management compared to the current practice (baseline) was estimated at £15,155, excluding government-based benefits, and £4,031 when these benefits were included. Analyses for the advanced provision of EHC compared to the baseline showed that the cost per abortion averted was £2,975 and the cost per age pregnancy averted was £310, when government-based benefits were assessed; the advanced provision of EHC was dominated by the baseline regarding the cost per age pregnancy averted when government-based benefits were included.

The methodological quality of this economic modelling study was rated as medium because the parameters used in the model were not validated and calibrated using empirical data. A wide variety of sensitivity analyses were undertaken examining variations in both health outcomes and costs. The authors stated that no preterm births were assessed, which may be more common amongst young people. However, the reviewers noted a discrepancy in that multiples and low birth weight were included, suggesting that the authors incorrectly equated low-birth weight with preterm birth. Other adverse events associated with teen pregnancy, such as fistula, were not mentioned, and these should be taken into account in future cost-effectiveness analyses.

Roberts TE, Tsourapas A, Sutcliffe L, Cassell J, Estcourt C (2012) Is Accelerated Partner Therapy (APT) a cost-effective alternative to routine patient referral partner notification in the UK? Preliminary cost-consequence analysis of an exploratory trial. *Sexually Transmitted Infections*, 88:16-20.

This economic evaluation focused on adult clients aged 18 to 64 years old at two GUM clinics and six community pharmacies that were participating in an exploratory clinical trial in the UK. It aimed to assess two new models of partner notification, known as Accelerated Partner Therapy (APT) delivered via telephone or community pharmacy, as compared with routine patient referral partner notification, for sex partners of people with chlamydia, gonorrhoea and non-gonococcal urethritis. The time horizon for this analysis was not clearly stated, but appears to be for one year. Data on health, patient uptake and costs came from a trial, previous studies databases and government agencies. The primary health outcome was the proportion of sex partners for each partner notification intervention assumed treated within 4 to 6 weeks after index patient diagnosis. The effectiveness study on which the economic evaluation was based was considered to have a potential risk of bias because not all eligible clients were invited to participate in the study and analyses were based on patients who received treatment outside of their randomised groups; its methodological rating was thus low. The economic evaluation employed a cost consequence analysis, using an NHS perspective.

The findings suggested that the APT strategies were similar in cost per partner treated (hotline £54; pharmacy £53) and slightly more than routine partner notification (£46); in addition, the intervention strategies achieved the highest proportion of partners treated (35% and 34% respectively), compared to 11% of partners treated in the comparison condition.

This study rated medium on methods for its economic evaluation. The main limitations of the study are that, as an exploratory analysis, emphasis should be given to the assessment of key parameters used in the model to better understand sources of uncertainties. However, the authors stated that, because this was a preliminary economic analysis alongside a clinical trial, they did not undertake sensitivity analyses. The reviewers disagree with this statement and note that efforts should be made to better understand the impact of specific parameters on economic evaluations that informs policy makers, especially when effectiveness was considered to be affected by serious risk of bias.

Rodriguez MI, Caughey AB, Edelman A, Darney PD, Foster DG (2010a) Cost-benefit analysis of state- and hospital-funded postpartum intrauterine contraception at a university hospital for recent immigrants to the United States. *Contraception*, 81(4): 304-308.

A cost-benefit analysis was undertaken using a hospital and state perspective. Using a retrospective cohort study design, this study compared the hospital and state costs of post-natal IUD insertion for recent US immigrants with Emergency Medicaid insurance coverage for the delivery only. The population under study comprised all women who delivered at a university hospital in Portland, Oregon during 2002 and were followed for four years. Although further details of their socio-demographic characteristics are not clear, it is implied that they are recent immigrants to the US. The interventions being tested were the provision of usual care (delivery only) versus usual care plus post-natal IUD insertion. Drawing on hospital records, a previous trial and literature, the following were calculated: pregnancy costs and revenue, probabilities of repeat pregnancy and pregnancy outcome (vaginal delivery, caesarean section, vaginal delivery with sterilisation, ectopic pregnancy, spontaneous/threatened abortion, and probability of IUD uptake and continuation.

The results suggested that the post-natal IUD programme would not be cost beneficial from the hospital perspective, because it was estimated that for each dollar spent, 70 cents would be lost. In contrast, from the state perspective, a cost savings of $2.94 for each dollar spent would be expected from a state-financed programme. Sensitivity analyses were undertaken by varying the IUD discontinuation and expulsion rates and examining univariate costs from both perspectives. Model inputs were varied between one half and two times the baseline estimates. The main results for the sensitivity analysis showed that varying the discontinuation rates and expulsion rates did not affect the positive savings to the state of financing postpartum IUD provision and that the programme remained cost-effective for the state unless first-year discontinuation rate rose to 90%: this is significantly higher than the expected postpartum IUD expulsion rate of 12%. The results also suggested that the programme costs for the state would break even with costs of subsequent care if the IUD expulsion rate exceeded 70%, and that IUD costs would need to exceed $10,500 per woman before the programme would begin to cost the state more than future pregnancy costs.

This study rated low in terms of its methodological quality, as the reviewers noted that further research is necessary into interstate migratory patterns and their probabilities in order to better interpret the results. Complete details of the modelling methods were not provided, making it difficult to assess the model's structure and validity. The model would need to be extended to include complications for a better understanding of the benefits of IUD use.

Rodriguez MI, Jensen JT, Darney PD, Little SE, Caughey AB (2010b) The financial effects of expanding postpartum contraception for new immigrants. *Obstetrics and Gynecology*, 115(3): 552-558.

A Markov decision-analytic model was used to determine the cost benefits of expanding health insurance coverage to include post-natal contraception for Latina immigrant women in US states with a high proportion of new immigrants. Provision of family planning services versus no such service provision were compared, examining the probability of pregnancy and pregnancy outcomes of miscarriage, elective termination, ectopic and viable pregnancies. Data on health benefits and costs originated from the study database and a trial from the World Health Organization. The perspectives of the hospital, state funding programmes and society were examined.

The results suggested that over a five-year period, from a societal perspective $17,793 per woman could be saved, incurring a loss of $367 for hospitals and saving Medicaid $108 per woman. The authors reported the use of a Monte Carlo simulation to test uncertainty; further one-way and multi-way sensitivity analyses were undertaken around all inputs. From the hospital perspective, postpartum contraception was not cost-saving compared to the baseline policy, but it was from the state's perspective; from a society perspective, the intervention was cost-saving regardless the immigration status of the intervention population.

The study was rated low in terms of its methodological quality, and the reviewers suggested that further research into interstate migratory patterns and probabilities should be conducted to assess the economic value of a federal mandate for preventive coverage of new immigrants.

Ruger JP, Abdallah AB, Ng NY, Luekens C, Cottler L (2014) Cost-effectiveness of interventions to prevent HIV and STDs among women: a randomized controlled trial. *AIDS and Behavior*, 18: 1913-1923.

This study aimed to assess the cost-effectiveness of interventions to reduce risk-taking behaviours and HIV incidence in US intravenous drug-using women aged 18 or older who were identified as in need of treatment by outreach workers. Data were derived from a randomised controlled trial testing two interventions. In addition to standard HIV testing with pre- and post-test counselling, participants in one arm were offered a well-woman examination of history taking, and routine breast and pelvic examination with Pap smear; a second intervention evaluated both the standard HIV testing and well-woman examination with a four-session education intervention focused on health promotion, stress coping, health and nutrition, substance abuse and HIV/AIDS. Outcome measures included baseline and 12-month assessment for HIV, hepatitis C, syphilis, chlamydia and gonorrhoea. The RCT rated low in terms of methodological quality, as randomisation, allocation concealment and loss to follow-up were not well described. To conduct the economic evaluation, a combined cost-effectiveness and cost-utility analysis design was used, and societal and provider perspectives were adopted.

The findings from the trial suggested that the well-woman examination was more costly and less effective than the standard intervention for HIV; and that for the modelled outcomes (relative to the standard intervention), the well-woman examination cost £137,280 ($208,316, 2003 USD) per primary HIV infection averted. Results from modelling suggested that for hepatitis C infection rates, the well-woman examination was less costly and more effective compared to the four-education session at £72,034 (£109,308, 2007-2008 USD) per additional infection averted. Similarly, the well-woman examination was less costly and more effective than the four-session education intervention in reducing gonorrhoea rates (£706,949, $1,072,760, per additional QALY). However, for chlamydia rates, the four-education session was less costly and more effective than the well-woman examination at £2,273,217, $3,449,495) per additional QALY. One-way sensitivity analyses were undertaken for both the trial and the model, and bi- and multivariate analyses were conducted and acceptability curves calculated; the results were robust for most scenarios, the main exception being for hepatitis C, where the four education sessions were not cost-effective when the parameters changed.

This economic evaluation rated high in terms of its methodological quality. Assessing HIV complications by differences in CD4 level should be undertaken to foster understanding of the intervention's long term benefits.

Salcedo J, Sorenson A, Rodriguez MI (2013) Cost analysis of immediate postabortal IUD insertion compared to planned IUD insertion at the time of abortion follow up. *Contraception*, 87(4): 404-408.

In order to evaluate the potential cost savings possible in providing immediate post-abortion IUD insertion versus planned IUD insertion at abortion follow-up, a decision-analytic Markov model was conducted from a California state public payer perspective. A hypothetical cohort of low-income women who were seeking abortion was derived from the California Family Planning, Access, Care, and Treatment (PACT) programme, serving a low-income female client population. Public programme costs and unintended pregnancy rates were the primary and secondary outcomes respectively; costs were modelled with one- and

five-year time horizons. Costs included: medical care for contraception and pregnancy-related care, public health insurance and social programmes for which a woman and her dependent children would be eligible. Health outcomes included: pregnancy, delivery, abortion, miscarriage or an ectopic pregnancy. Sources of evidence included the PACT female client population, Medicaid and literature. Outcomes and costs were calculated over five years.

The results suggested that for each woman who had an immediate post-abortion IUD placement, public programmes would save $111 USD over one year compared to planned IUD insertion at abortion follow-up. This cost savings increased to $810 over five years. When public health insurance and programme costs were added in, savings increased to $1,956 and $4,296 over one and five years respectively. The authors asserted that for every 1,000 low-income women who underwent post-abortion IUD insertion, more than 400 pregnancies, 180 deliveries and 160 abortions would be avoided. Univariate and multivariate sensitivity analyses showed that the results were robust for a range of variation of parameters.

The methodological quality of this study was determined to be medium. The reviewers noted that the model was heavily based on secondary data and the authors should have discussed better the applicability of the parameters to the population. Further, the implications of extending these conclusions to the population should be considered, as the implications were only partly included in the model (for example, no STIs were included). For future research where secondary data is used, validation of the data should be undertaken by comparing the results to official figures and testing these figures within the model.

Schackman BR, Metsch LR, Colfax GN, Leff JA, Wong A, Scott CA, Feaster DJ, Gooden L, Matheson T, Haynes LF, Paltiel AD, Walensky RP (2013) The cost-effectiveness of rapid HIV testing in substance abuse treatment: results of a randomized trial. *Drug and Alcohol Dependence*, 28(1-2): 90-97.

In order to estimate the cost-effectiveness of HIV testing strategies to provide guidance to policy makers and substance abuse treatment programmes, the authors undertook a cost-effectiveness and cost-utility analysis by modelling findings from an intervention study targeting high-risk groups presenting at a substance use treatment clinic using a societal perspective. Here, on-site rapid HIV testing with information only or on-site rapid HIV testing with risk-reduction counselling were compared with off-site HIV testing and referral in terms of costs and sexual risk behaviour. Risk of bias assessment suggested that this trial was of medium quality, due to the lack of reporting of allocation concealment and questions about the sample's representativeness to the intended population. Data sources were varied: utilities for QALYs were derived from a SF-6D data from a national survey of HIV infected individuals; the National Drug Abuse Treatment Clinical Trials Network (CTN) HIV Rapid Testing and Counselling Study (CTN 0032), the Multicentre AIDS Cohort Study (MACS) and published literature for the population in substance abuse treatment, and the costs were estimated by using the medical service utilisation data from a national cohort and national costs.

The results from the modelling study indicated that on-site rapid testing and information only was found to dominate the other conditions, resulting in a cost-effectiveness ratio of £39,979 ($60,300, 2009 USD) per QALY. This exceeds the NICE cost-effectiveness threshold.

The on-site rapid testing with counselling cost £7 ($11) more per person but did not provide additional benefit. Varying prevalence of undiagnosed HIV and varying probability of testing were modelled and reported. The sensitivity analysis showed varied results: changing the prevalence of undiagnosed HIV, a higher cost-effectiveness ratio was observed for on-site testing plus information compared to no intervention; the cost-effectiveness ratio was $82,800/QALY, when varying the probability of testing. Other variations had little impact on cost-effectiveness ratios.

This economic evaluation rated high in terms of its methodological quality. The authors acknowledged the main limitations for their model and analysis and the reviewers did not have further suggestions.

Thomas A (2012) Three strategies to prevent unintended pregnancy. *Journal of Policy Analysis and Management*, 31(2): 280-311.

This multi-intervention modelling study used cost-benefit analysis methods to examine the fiscal impact of three national strategies to prevent unintended pregnancy in low-income US populations. These included a national media campaign encouraging condom use in unmarried men aged 15 to 44; a national school-based pregnancy prevention programme for high-risk low-income young women and men; and an expansion in Medicaid funding for family planning services for low-income women. A governmental perspective was employed (i.e. costs to the taxpayer for programme implementation and benefits of costs savings from reduced benefits payment) over a one-year and five-year time horizon. To parameterise the model (e.g. to assign a poverty status to each newborn child), data were used from a wide range of sources, including: the General Social Survey and the National Survey of Family Growth, the Guttmacher Institute, the National Vital Statistics System, and the Population Survey. Other data used to estimate benefits and costs included: a meta-analysis for behaviour effects and data from the Truth, VERB and National Youth Anti-Drug Media (NYADMC) campaigns. For ease of reading, each intervention and its resulting costs and benefits are presented separately below.

Model 1: Mass media campaign for condom use

In terms of benefits, the mass media intervention would potentially reduce abortion by 3.9%, births by 1% and number of children born into poverty by 2.2%; the programme would cost $100 million USD. The benefit-cost ratios would be $0.37 USD for pregnancy care alone, $0.90 USD for pregnancy care plus infant medical assistance and $4.31 USD for pregnancy care and children's benefits.

Model 2: Pregnancy prevention programme for unintended teenage pregnancy

For this intervention, reductions in abortion, births, and number of children born into poverty were estimated to be 1.4%, 0.6% and 1.4% respectively. The programme would cost $145 million USD. The benefit-cost ratios would be $0.26 USD for pregnancy care alone, $0.55 USD for pregnancy care plus infant medical assistance, and $2.46 USD for pregnancy care and children's benefits.

Model 3: Expansion in Medicaid funding for family planning services

The expansion in Medicaid would reduce abortion by 3.5%, births by 1.4% and number of children born into poverty by 1.8% in this analysis; The programme would cost $235 million

USD. The benefit-cost ratios would be $0.62 USD for pregnancy care alone, $1.21 USD for pregnancy care plus infant medical assistance, and $5.62 USD for pregnancy care and children's benefits.

Sensitivity analysis showed that that the results were robust and insensitive to a range of variations into the parameters. The study was rated as medium by the reviewers. The main limitations were discussed by the authors. Short- and long-term complications associated with unintended pregnancies (and unprotected sex) should be taken into account to further understand the interventions' benefits (in terms of health outcomes) and costs.

Thomas CM, Cameron S (2013) Can we reduce costs and prevent more unintended pregnancies? A cost of illness and cost-effectiveness study comparing two methods of EHC. *BMJ Open*, 3(12): e003815.

This study aimed to calculate the cost of an unintended pregnancy and use this cost to assess the comparative cost-effectiveness of ulipristal acetate (UPA) and levonorgestrel (LNG) for emergency hormonal contraception (EHC) within a one-year time horizon. Women in England in 2011 presenting in primary care for EHC within 24 to 72 hours of unprotected sexual intercourse were the population of interest. The primary outcome was the number of unintended pregnancies and the associated direct and indirect costs. Secondary outcomes included miscarriage, abortion, ectopic pregnancy, stillbirth or live birth. A health and health plus social care perspective was employed. Data were sourced from published studies of costs and outcomes, including a previous trial of these contraceptives on unintended pregnancy. The incremental cost-effectiveness ratio of UPA compared to LNG was calculated.

The findings suggested that one unintended pregnancy cost £1,663 in direct healthcare costs, rising to £2,922 when social costs were factored in; and costs were £194 less in direct health costs to prevent one more pregnancy with UPA than with LNG. When the social costs of pregnancy were added, this cost-saving potential was increased to £1,453 for each extra pregnancy avoided with UPA compared to with LNG.

The methodological quality of this economic modelling study was rated as low due to limitations in outcome measurement, model cycle, baseline estimates of health effect and resource use, and sensitivity analyses and model calibration, and unclear reporting of the time horizon and adverse events. Sensitivity analyses were undertaken examining the impact of changes in the cost of pregnancy and failure rate of either contraception method. The authors have identified major limitations associated with their analysis and the reviewers only recommended that for future analysis, complications associated with STIs are taken into account using a wider time horizon.

Trussell J, Henry N, Hassan F, Prezioso A, Law A, Filonenko A (2013) Burden of unintended pregnancy in the United States: potential savings with increased use of long-acting reversible contraception. *Contraception*, 87(2): 154-161.

This economic evaluation of cost savings aimed to evaluate the total costs of unintended pregnancy in the US and the impact of LARCs versus usual care on healthcare costs, using a third-party healthcare payer perspective. The population under study comprised all US childbearing women aged 15 to 44 years who were sexually active but also neither sought pregnancy nor wished sterilisation, i.e. in need of reversible contraceptive use. Ten

different types of short-acting and long-active reversible contraceptives were assessed, including no contraception. Individuals were separated into 5-year age groups and contraceptive use over one year was analysed. The health outcomes under study included live birth, induced abortion, spontaneous abortion and ectopic pregnancy. The health outcomes were obtained from a nationally representative survey of pregnancy, birth, parenting and health undertaken by the Centres for Disease Control and Prevention. The costs associated with contraceptive use and unintended pregnancy healthcare were calculated using the Medicaid Fee Schedule.

The estimated results suggested that unintended pregnancy costs $4.6 billion USD annually. Of this, 53% was estimated to be attributed to poor contraceptive adherence, with the highest number occurring in women aged 20 to 29 years. The authors suggested that $288 million yearly in unintended pregnancy healthcare costs could be saved if even 10% of all women aged 20 to 29 years took up LARC rather than oral contraceptives. Sensitivity analysis showed an increase in costs for changes in parameters, but cost neutrality was achieved when number of years was varied.

The study was determined to be of medium methodological quality. The authors have discussed the main limitations of their study, but the reviewers suggest that future research assume a longer-term assessment of complications associated with unintended pregnancies, in order to better inform policy makers about the benefits of interventions.

Trussell J, Hassan F, Henry N, Pocoski J, Law A, Filonenko A (2014) Cost-effectiveness analysis of levonorgestrel-releasing intrauterine system (LNG-IUS) 13.5 mg in contraception. *Contraception*, 89(5): 451-459.

A state transmission economic model was developed to evaluate the cost-effectiveness (i.e. cost per pregnancy avoided) of an initial method, unintended pregnancy and subsequent method of contraception over a three-year period of use, from a third-party payer perspective. The levonorgestrel-releasing intrauterine system 13.5 mg (LNG-IUS) was tested against short-acting reversible contraceptive methods (SARCs) in a cohort of 1,000 US women aged 20 to 29 years. Contraceptive rates, method failure and discontinuation rates were calculated from the National Survey of Family Growth, a systematic review and assumptions. Health outcomes included live birth, induced or spontaneous abortion or ectopic pregnancy. The costs of contraceptive method, administration of method and cost of method failure were calculated using the Medi-Span Master Drug Database, the Procedural Terminology (CPT) 2008 Codebook, Medicare, project and published data and the Diagnosis-Related Group (DRG) 2008 Codebook.

The results indicated that LNG-IUS resulted in 69 unintended pregnancies compared to 276 in those using SARCs. It was also less costly at initiation ($1.28 million USD versus $1.86 million). Lower drug acquisition ($650,320 vs $943,956) and method failure costs ($14,026 vs $299,784) were considered to be offset by the higher medical resources needed for insertion and removal ($415,810 vs $215,481). The costs associated with subsequent method use were lower in those choosing LNG-IUS over SARCs ($203,322 vs $403,412).

A one-way sensitivity analysis showed that many parameters were sensitive to changes. A probabilistic sensitivity analysis showed that the intervention was both cheaper and more effective than the SARC method for all iterations: analysis of LNG-IUS 20 mcg/24h over a three-year time horizon showed that LNG-IUS 13.5 mg was less costly but also less

effective. Similarly, in a five-year time horizon, LNG-IUS 13.5 mg was more costly and less effective and was therefore dominated by LNG-IUS 20 mcg/24h. The quality rating of this economic evaluation on assessment was low. The reviewers noted that a limited age group was explored in the analysis and that future results should assess the extent to which this influenced the study's outcomes. In addition, the modelling of complications associated with unintended pregnancies (including HIV and STIs) should be assessed in order to better capture the intervention's long-term benefits.

Trussell J, Hassan F, Lowin J, Law A, Filonenko A (2015) Achieving cost-neutrality with long-acting reversible contraceptive methods. *Contraception*, 91(1): 49-56.

In order to estimate the average annual costs of reversible contraceptives and to quantify the minimum duration of use required for LARC methods to achieve cost-neutrality, a three-state economic model was developed. Based on a third-party public payer model (i.e. considering direct medical costs only), this estimated and compared the relative costs of four SARC methods (oral contraception, ring, patch and injection), three LARC methods (implant, copper IUD, LNG-IUS) and no contraception, over a five-year time horizon. LARC was also compared with a weighted average of available SARCs only. The population cohort consisted of 1,000 US women aged 20 to 29 years. Health outcomes of interest included live birth, spontaneous or induced abortion and ectopic pregnancy. Cost data included contraceptive acquisition, administration and failure. Data on method-specific failure and discontinuation rates were obtained from the National Survey on Family Growth, the CHOICE study, a systematic literature review, published literature and assumptions. The authors stated that cost data were obtained from the wholesale acquisition cost (WAC) price; however, it was unclear which organisation provided this information.

For each woman per year, the findings suggested that copper IUD ($304) and LNG-IUS 20 mcg/24 hours ($308) were the least expensive methods in terms of direct medical costs. SARC methods were higher, ranging from injection to patch ($732) per woman, per year. No contraception cost an average of $509.60 per woman yearly. The authors estimated that any LARC would need to be used for a minimum of 2.1 years for the method to be cost-saving compared to SARC methods. Minimum impact was observed in the results when assumptions about discontinuation rate were changed.

This study rated medium in terms of methodological quality. The reviewers suggested the inclusion of long-term complications in the analysis to better understand the benefits of the interventions. It is possible that the costs of interventions may have been underestimated because only the price of wholesale acquisition were used, suggesting that a full-cost approach is needed for future cost-analysis.

Turner KM, Round J, Horner P, Macleod J, Goldenberg S, Deol A, Adams EJ (2014) An early evaluation of clinical and economic costs and benefits of implementing point of care NAAT tests for chlamydia trachomatis and neisseria gonorrhoea in genitourinary medicine clinics in England. *Sexually Transmitted Infections*, 90(2): 104-111.

The aim of this study was to estimate the costs and benefits of clinical pathways using a point of care nucleic acid amplification test (POC NAAT) for chlamydia and gonorrhoea in genitourinary medicine (GUM) clinics, compared with standard off-site laboratory testing. A one- to 28-day cycle length decision analytic model of cost-effectiveness and cost-utility analysis was used, based on a modelled cohort of 1.2 million index patients to simulate the

number of STI screening tests undertaken at GUM clinics in England. Data were derived from health agencies official figures, literature and assumptions. A societal, healthcare and personal social services perspective was used. The primary outcome was the incremental cost-effectiveness ratio of standard off-site laboratory testing compared to NAATs (total cost per QALY gained), with secondary outcomes comprising the number of inappropriate treatments, complications and transmissions averted.

The findings suggested that the POC NAAT was more effective and cheaper, costing £103.9 million compared with £115.6 million for standard care, and was associated with an increase of 46 QALYs. Further, it was suggested that same-day testing, diagnosis and treatment might prevent 189 cases of pelvic inflammatory disease and 17,561 onward transmissions per year.

This study was determined to be of high methodological quality by the reviewers, and the limitations were more associated with the availability of quality data to model the implications of POC NAAT testing on STIs. Sensitivity analyses were undertaken to examine differences in results by shorter time to treatment, no progression to pelvic inflammatory disease, lower baseline prevalence, higher POC test acquisition cost, and patient disutility whilst awaiting results. The authors have identified most of the studies' limitations, including that their assessment of complications was based only on pelvic inflammatory disease in women. This was justified by the absence of national data on early screening for other complications. The reviewers suggested that further analyses should be conducted to better understand changes in uptake over time, possibly by combining qualitative research on patient experiences of the impact of POC NAAT testing with quantitative research on the prevalence of complications. The resulting information could be generated as independent arms of a future model for evaluating the cost-benefit of POC NAAT.

Appendix 12: Costs and outcomes table: UK studies

Table A12.1: UK studies: STI screening/treatment

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Long et al. (2014) [CUA]	Current HIV testing and treatment (Baseline)	3,500 new infections per year 6,100 new diagnoses per year									
	Universal HIV testing every 1, 2 and 3 years versus current HIV testing and treatment	1-18% new infections averted over 1-3 years £67,000-106,000 per QALY gained (2012 GBP) over 10 years, depending on sexual partner reduction behaviour									✓
	Universal annual HIV testing versus current HIV testing and treatment (Baseline)	5-18% new infections averted £4.61 per test 57,400 QALYs gained		✓					✓		

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	Targeted annual HIV testing versus universal one-time HIV testing	4-15% of new infections averted ¼ as many tests to diagnose people living with HIV £0.75 per test; 42,900 QALYs gained £17,500 per QALY gained							✓		
	Targeted annual HIV testing and anti-retroviral treatment (ART) versus one-time universal HIV testing and current treatment	QALY: 145,300 £3.49 per test 145,000 QALYs added to population over 10 years £26,800 per QALY gained					✓			✓	
Turner et al. (2014) [CEA, CUA]	Standard care, off-site testing [C]	Cost £11.7 million (2012 GBP) QALY: 184,012									
		189 cases of pelvic inflammatory disease prevented per year									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	Point of care chlamydia/ gonorrhoea testing in GUM clinics versus standard off-site testing	17,561 onward transmissions prevented per year £11.7 million per 46 QALYs gained						✓			
Roberts et al. (2012) [CCA]	Accelerated Partner Therapy via telephone versus routine patient referral partner notification	35% of partners treated [I] versus 11% of partners [C] £54 per partner treated [I] versus £46 per partner [C] (2008 GBP)									
	Accelerated Partner Therapy via community pharmacy versus routine patient referral partner notification	34% of partners treated [I] versus 11% of partners [C] £53 per partner treated [I] versus £46 per partner [C]									
Jackson et al. (2015) [CEA]	Team captain-led STI screening promotion versus poster-only STI screening promotion	50% screening uptake [I] versus 61% screening uptake [C] £88.89 per participant screened [I] versus £81.87 per participants screened [C] (2012-2013 GBP)	✓								
	Sexual health adviser-led STI screening promotion versus poster-only STI screening promotion	67% screening uptake [I] versus 61% screening uptake [C] £88.33 per participant screened [I] versus £81.87 per participant screened [C]				✓					

[CBA]=cost-benefit analysis; [CCA]=cost-consequence analysis; [CEA]=cost-effectiveness analysis; [CSA]=cost saving analysis; [CUA]=cost utility analysis; [I]=intervention condition; [C]= comparison condition

Table A12.2: UK studies: Contraception

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Thomas and Cameron (2013) [CEA]	Cost-effectiveness comparison of ulipristal acetate (UPA) versus levonorgestrel (LNG) within 72 hours of unprotected sex	Primary: Number of unintended pregnancies estimated at 'almost 25%' Secondary: Miscarriage, abortion, ectopic, stillbirth, live birth Associated costs of unintended pregnancy £1,663 - £2,922 (depending on perspective)									
		UPA cost £194 - £1,453 less per avoided pregnancy than LNG (2011 GBP)						✓			
National Collaborating Centre (NCC) (2013) [CEA]	LARC methods (IUD, IUS, implant, injectable) versus UDCs (combined oral contraceptive (COC), male condom)	Over 15 years: All LARCs dominated COCs and condoms (see Evidence Tables for more detail)					✓				
		First three years: Implant dominated all other LARCs costing between £14,730 - £17,866 per pregnancy averted (2004-2005 GBP)					✓				

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Pilgrim et al. (2010) [CEA]	School nurse services only; no dispensing of condoms or contraceptives [C]	11,392 abortions / 2,186 pregnancies Total costs £1,527,318,794 (2007-2008 GBP)									
	School-based condom provision versus school nurse services only	11,153 estimated abortions 1,778 estimated pregnancies Total estimated costs £1,517,225,105 Estimated cost outcomes: £38 for each pregnancy averted £822 for each abortion avoided					✓				
	School-based hormonal contraceptive provision to sexually active nulliparous 14-	11,103 estimated abortions 1,693 estimated pregnancies Total estimated costs £1,515,641,998									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	16 year olds versus condom provision and school nurse	Estimated cost outcomes: £443 for each averted pregnancy (2007-2008 GBP) £1,453 for each abortion avoided					✓				
	School-based peer education and social work case management to prevent repeat pregnancy in teen mothers attending school versus no follow-up after first pregnancy	No follow-up [C]: 31,464 repeat pregnancies Total cost £655,572,463 Case management follow-up [I]: 19,022 repeat pregnancies Total cost £705,730,087 Estimated cost outcomes: £4,031 - £15,155 per repeat pregnancy averted (2007-2008 GBP)					✓				

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	Advance provision of EHC to sexually active high risk teens aged 15-19 years versus no advance provision of EHC	No advance provision [C]: 11,241 abortions / 11,363 pregnancies Total costs: £1,524,674,862 Advance provision [I]: 11,241 abortions / 11,363 pregnancies Total costs: £1,447,599,721									
		Estimated cost outcomes: £310 per pregnancy averted £2,795 per abortion avoided (2007-2008 GBP)					✓				

[CBA]=cost-benefit analysis; [CCA]=cost-consequence analysis; [CEA]=cost-effectiveness analysis; [CSA]=cost saving analysis; [CUA]=cost utility analysis; [I]=intervention condition; [C]= comparison condition

Table A12.3: UK studies: Health promotion

Study	Intervention	Outcomes	Cost-effectiveness						NICE Rating		
			More costly, less effective	Less costly, less effective	More costly, more	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Cooper et al. (2012) [CEA]	1. Teacher-led 20 session STI prevention intervention or 2. Peer-led three session STI prevention intervention versus standard sexual health education [C]	Compared to standard sex education [C], teacher-led intervention would have net additional cost £6,375 (€8,575) and avoid two extra STI cases for 0.35 increase in QALY Incremental cost-effectiveness ratio: £18,041 (€24,268) per QALY gained (2011-2012 Euro) Peer-led intervention cost £12,050 (€16,210) per case avoided Incremental cost-effectiveness ratio: £72,062 (€96,938) per QALY gained							✓		✓

Study	Intervention	Outcomes	Cost-effectiveness						NICE Rating		
			More costly, less effective	Less costly, less effective	More costly, more	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Crawford et al. (2015) [CEA] Cost year(s) and currency: 2010-2011 GBP	Brief alcohol advice, health information leaflet and referral offer versus health information leaflet only	No significant reductions in: 90-day alcohol consumption or Rates of unprotected sex in past 3 months £311 per person intervention £319 per person control				✓					
		Additional cost of intervention £12.57, SD £6.59 QALYs 0.007 lower in brief intervention group and costs £8.41 higher ICER: −£1,200 per QALY (2010-2011 GBP)									✓
Jackson et al. (2015) [CCA]	Team captain-led STI screening promotion versus poster-only STI screening promotion	50% screening uptake [I] versus 61% screening uptake [C] £88.89 per player screened [I] versus £81.87 per player screened [C] (2012-2013 GBP)	✓								

Study	Intervention	Outcomes	Cost-effectiveness						NICE Rating		
			More costly, less effective	Less costly, less effective	More costly, more	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	Sexual health adviser-led STI screening promotion v. poster-only STI screening promotion	67% screening uptake versus 61% screening uptake [C] £88.33 per player screened [I] versus £81.87 per player screened [C]				✓					
Pilgrim et al. (2010) [CEA]	School nurse services only; no dispensing of condoms or contraceptives [C]	11,392 abortions 2,186 pregnancies Total costs £1,527,318,794 (2007-2008 GBP)									
	School-based condom provision versus school nurse services only	11,153 estimated abortions 1,778 estimated pregnancies Total estimated costs £1,517,225,105 Estimated cost £38 for each pregnancy averted Estimated cost £822 for each abortion avoided					✓				
	School-based hormonal contraceptive provision to sexually active nulliparous 14-16 year olds	11,103 estimated abortions 1,693 estimated pregnancies									

Study	Intervention	Outcomes	Cost-effectiveness						NICE Rating		
			More costly, less effective	Less costly, less effective	More costly, more	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	versus condom provision and school nurse	Total estimated costs £1,515,641,998 (2007-2008 GBP) Estimated cost outcome £443 for each averted pregnancy Estimated cost outcome £1453 for each abortion avoided					↘				
	School-based peer education and social work case management to prevent repeat pregnancy in teen mothers attending school versus no follow-up after first pregnancy	No follow-up [C]: 31,464 repeat pregnancies Total cost £655,572,463 Case management follow-up [I]: 19,022 repeat pregnancies Total cost £705,730,087 Estimated cost £4,031 - £15,155 per repeat pregnancy averted					✓				

Study	Intervention	Outcomes	Cost-effectiveness						NICE Rating		
			More costly, less effective	Less costly, less effective	More costly, more	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	Advance provision of EHC to sexually active high risk teens aged 15-19 years versus no advance provision of EHC	No advance provision [C]: 11,241 abortions / 11,363 pregnancies Total costs: £1,524,674,862 Advance provision [I]: 11,241 abortions / 11,363 pregnancies Total costs: £1,447,599,721									
		Cost £310 per pregnancy averted Cost £2,795 per abortion avoided (2007-2008 GBP)					✓				

[CBA]=cost-benefit analysis; [CCA]=cost-consequence analysis; [CEA]=cost-effectiveness analysis; [CSA]=cost saving analysis; [CUA]=cost utility analysis; [I]=intervention condition; [C]= comparison condition

Appendix 13: Costs and Outcomes table: Contraception interventions

Table A13.1: Emergency hormonal contraception

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Foster et al. (2010) [CBA]	Advance EC provision versus no access/use of EC On-demand clinic and pharmacy provision of EC versus no access/use of EC	For high- and low-frequency use, advance and on-demand provision both result in a lower pregnancy rate than no access For high- and low-frequency use, cost-savings ratio higher in advance provision than on-demand provision but both still greater than 1.00 (i.e. no. of $ saved on averting pregnancy is greater than no. of $ spent on EC) (2005 USD) Pharmacy-dispensed advance provision: £0.83 ($1.28) - £1.41 ($2.17) saved for each $ spent (2005 USD) Clinic-dispensed advance provision: £0.66 ($1.01) - £1.14 ($1.75) saved for each $ spent						✓ ✓ ✓			

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		Clinic-dispensed on-demand provision: £0.65 ($1.00) - £1.01 ($1.56) saved for each $ spent						✓			
		Pharmacy-dispensed on-demand provision: £1.04 ($1.61) - £1.62 ($2.49) saved for each $ spent						✓			
Bayer et al. (2013) [CEA]	Oral ulipristal acetate at 120 hours versus oral levonorgestrel at 120 hours	*UPA:* 54,295 unintended pregnancies £270,251,630 ($399.19 million) (2011 USD) *LNG:* 91,884 unintended pregnancies £348,959,650 ($515.45 million) *UPA v. LNG:* 37,589 pregnancies averted £78,735,100 ($116 million) saved for 8,053 QALYs gained UPA was dominant intervention						✓			

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Thomas and Cameron (2013) [CEA]	Cost-effectiveness comparison of ulipristal acetate (UPA) versus levonorgestrel (LNG) within 72 hours of unprotected sex	Primary: Number of unintended pregnancies estimated at 'almost 25%' Secondary: Miscarriage, abortion, ectopic, stillbirth, live birth Associated costs of unintended pregnancy £1,663-2,922 (depending on perspective) UPA cost £194-1,453 less per avoided pregnancy than LNG (2011 GBP)						✓			

[CBA]=cost-benefit analysis; [CCA]=cost-consequence analysis; [CEA]=cost-effectiveness analysis; [CSA]=cost saving analysis; [CUA]=cost utility analysis

Table A13.2: Long-acting reversible contraception

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Foster et al. (2013) [CBA]	All contraceptive methods provided versus no care provision	Averted pregnancies: Oral contraceptives: 102,000 Injectables: 26,000 IUC: 24,000 Barrier: 18,000 Patch: 9,000 Implants: 3,000 Operative: 2,100 Copper intrauterine contraception (IUC): £3.36 ($5.07) (2009 USD) saved for each $ spent Hormonal IUC: £3.24 ($4.89) saved for each $ spent Implant: £3.24 ($4.89) saved for each $ spent Injectable: £2.65 ($4.00) saved for each $ spent						✓ ✓ ✓ ✓ ✓			

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		Interval tubal ligation: £2.38 ($3.59) saved for each $ spent						✓			
		Oral contraceptives: £2.23 ($3.37) saved for each $ spent						✓			
		Emergency contraceptives: £1.70 ($2.56) saved for each $ spent						✓			
		Ring: £1.46 ($2.20) saved for each $ spent						✓			
		Patch: £1.41 ($2.12) saved for each $ spent						✓			
		Tubal occlusion: £1.05 ($1.59) saved for each $ spent						✓			
		Barrier methods: £1.05 ($1.58) saved for each $ spent						✓			
Trussell et al. (2015) [Cost study]	LARCs (implant, copper IUD, LNG-IUS) versus no method LARCs versus UDCs (OC, ring, patch, injectables)	Minimum duration of LARC method to reach cost-neutrality: Average LARC vs generic OC: 2.4 years Average LARC vs ring: 0.4 years Average LARC vs patch: 0.3 years Average LARC vs injection: 2.6 years Average LARC vs mixed SARC: 2.1 years									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		Average LARC vs condom: 3.0 years Average LARC vs no method (chance): 1.7 years 2.1 years of LARCs would result in cost savings compared to UDCs						✓			
NCC (2013) [CEA]	LARC methods (IUD, IUS, implant, injectable) versus UDCs (combined oral contraceptive (COC), male condom)	Number of pregnancies averted Costs for intervention and additional care (See Evidence Tables for more details) First three years: Implant dominated all other LARCs costing between £14,730 - £17,866 per pregnancy averted (2004-2005 GBP) Over 15 years: All LARCs dominated COCs and condoms					✓ ✓				
Trussell et al. (2014) [CEA]	Levonorgestrel (LNG) IUS versus UDCs (OC, ring, patch, injectables, implant, condom)	*UDC:* 276 unintended pregnancies Costs £ 1,257,277 ($1,862,633) (2012 USD)									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		LNG-IUS: 64 unintended pregnancies Costs £ 866,348 ($1,283,479)									
		LNG-IUS cost-effective ('dominates') in comparison to SARCs					✓				
Trussell et al. (2013) [CSA]	Three scenarios of switching to LARCs (implant, IUD, IUS) 1. 10% of women aged 20–29 who are currently using OC switched to LARC 2. 10% of women aged 20–29 who are currently using any UDC method (OCs, condoms, patch, injectables, vaginal ring) switched to LARC	Current practice Cost of UP: £1,639 ($2,421) (2011 USD) Cost of contraception: £3,019 ($4,460) Total cost impact: £4,658 ($6,881) Scenario 1 cost savings: Cost of unplanned pregnancy (UP): £35 ($51) Cost of contraception: £160 ($237) Total cost impact: £195 ($288) Scenario 2 cost savings:									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	3. 10% of women aged 20–29 who are currently using either UDC or no method switched to LARC	Cost of UP: £79 ($117) Cost of contraception: £174 ($257) Total cost impact: £254 ($375) Scenario 3 cost savings: Cost of UP: £145 ($214) Cost of contraception: £150 ($222) Total cost impact: £295 ($436) Higher LARC uptake generates cost savings in: Women switching from OCs to LARCs Women switching from no method to LARCs Cost neutrality achieved (all age groups): used at least two years						✓ ✓			
Han et al. (2014) [CEA,CSA]	Post-natal implant insertion to adolescent mothers versus	Intervention: £475,083 ($699,680) (6 months) (2013 USD) £672,006 ($989,700) (12 months)									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	standard contraceptive initiation	£1,004,920 ($1.48 million) (24 months) £1,575,280 ($2.32 million) (36 months) Comparison: £425,783 ($627,073) (6 months) £1,045,660 ($1.54 million) (12 months) £2,675,260 ($3.94 million) (24 months) £4,651,150 ($6.85 million) (36 months) £0.53 ($0.79) saved for each $1 spent on programme (12m) £2.40 ($3.54) saved for each $1 spent on programme (24m) £4.41 ($6.50) saved for each $1 spent on programme (36 m)						✓ ✓			
Rodriguez et al. (2010a) [CBA]	Expanded Medicaid (EM) coverage for post-natal contraception versus regular coverage for recent immigrants	Estimated 126 pregnancies avoided through EM coverage £140,812 ($214,000) without EM programme (2002 USD) £78,302 ($119,000) with EM IUD programme						✓			

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		Hospital perspective: Hospital would lose £0.46 per £1 (70 cents per dollar) spent on a postpartum IUD programme State perspective: state would save £1.92 ($2.94) in costs for repeat obstetrical care for every state dollar spent on an IUD programme									
Rodriguez et al. (2010b) [CBA]	Post-natal IUD insertion versus routine post-natal care (no IUD)	Routine post-natal care [C]: Pregnancies: 226 Total costs: £1,371,300 ($2.1 million) (2008 USD) Cost of repeat pregnancy without the programme: £139,742 ($214,000)									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		Cost of repeat pregnancy with the programme: £77,707 ($119,000) Hospital perspective: Programme costs for an IUD, insertion and removal: £214,184 ($328,000) State perspective: £1.92 ($2.94) saved per $1.00 spent on IUD insertion Benefit–cost ratio of 0.30						✓			
Salcedo et al. (2013) [CSA]	Immediate post-abortion IUD placement versus IUD placement at post-abortion follow-up visit	At 5 years: 400 pregnancies avoided 180 deliveries avoided 160 abortions avoided Immediate post-abortion insertion saves £75-548 ($111-810) (at 1 and 5 years) per woman in direct costs compared to insertion at follow-up visit (2011 USD)						✓			

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		With societal costs included, this increases to savings of £1,324-2,908 ($1,956-4,296) per woman compared to insertion at follow-up visit						✓			

[CBA]=cost-benefit analysis; [CCA]=cost-consequence analysis; [CEA]=cost-effectiveness analysis; [CSA]=cost saving analysis; [CUA]=cost utility analysis; [C]= comparison condition

Table A13.3: General contraceptive services

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Thomas (2012) [CBA]	Mass media campaign to promote condom use to unmarried males aged 15 to 44 years old v. no programme	Benefits: Pregnancy: 1.7% reduction Abortions: 3.9% reduction Births: 1.0% reduction Births into poverty: 2.2% reduction Costs: £65.3 million ($100 million) (2008 USD) £2.81 ($4.31) saved for each $1 spent						✓			
	Teen pregnancy prevention programmes to unmarried low SES youth v. no programme	Benefits: Pregnancy: 0.8% reduction Abortions: 1.4% reduction Births: 0.6% reduction Births into poverty: 1.4% reduction									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		Costs: £94,685 million ($145 million) £1.61 ($2.46) saved for each $1 spent						✓			
	Expanded Medicaid for contraception to unmarried low SES youth v. no programme	Benefits: Pregnancy: 1.9% reduction Abortions: 3.5% reduction Births: 1.4% reduction Births into poverty: 1.8% reduction Costs: £153,455 million ($235 million) £3.67 ($5.62) saved for each $1 spent						✓			
Pilgrim et al. (2010)	School nurse services only; no dispensing of condoms or contraceptives [C]	11,392 abortions / 2,186 pregnancies Total costs £1,527,318,794 (2007-2008 GBP)									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
[CEA]	School-based condom provision versus school nurse services only	11,153 estimated abortions 1,778 estimated pregnancies Total estimated costs £1,517,225,105 Estimated cost £38 for each pregnancy averted Estimated cost £822 for each abortion avoided (2007-2008 GBP)					✓				
	School-based hormonal contraceptive provision to sexually active nulliparous 14-16 year olds versus condom provision and school nurse	11,103 estimated abortions 1,693 estimated pregnancies Total estimated costs £1,515,641,998 Estimated cost outcome £443 for each averted pregnancy (2007-2008 GBP) Estimated cost outcome £1,453 for each abortion avoided					✓				
	School-based intensive peer education and social work case management to prevent repeat pregnancy in teen mothers	No follow-up [C]: 31,464 repeat pregnancies Total cost £655,572,463									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	attending school versus no follow-up after first pregnancy	Case management follow-up [I]: 19,022 repeat pregnancies Total cost £705,730,087 Estimated cost £4,031-15,155 per repeat pregnancy averted (2007-2008 GBP)					✓				
	Advance provision of EHC to sexually active high risk teens aged 15-19 years versus no advance provision of EHC	No advance provision [C]: 11,241 abortions / 11,363 pregnancies Total costs: £1,524,674,862 Advance provision [I]: 11,241 abortions / 11,363 pregnancies Total costs: £1,447,599,721 Cost £310 per pregnancy averted Cost £2,795 per abortion avoided (2007-2008 GBP)					✓				

[CBA]=cost-benefit analysis; [CCA]=cost-consequence analysis; [CEA]=cost-effectiveness analysis; [CSA]=cost saving analysis; [CUA]=cost utility analysis; [I]=intervention condition; [C]= comparison condition

Appendix 14: Costs and outcomes table: Health promotion interventions

Table A14.1: Health promotion: HIV prevention

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Burgos et al. (2010) [CEA	Brief behavioural condom negotiation skills intervention to reduce STI and HIV among female sex workers versus time-equivalent didactic STI and HIV prevention session [C]	No intervention: - Cost: £12,730 ($19,200) - QALYs gained: 21,863 Without universal HAART access: Comparing one session of intervention to [C]: 33 HIV infections averted for 151 days of QALE, costing £121 ($183) per QALY and £1,571 ($2,370) to prevent each HIV case (2009 USD)							✓		

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		Considering universal HAART access: Comparing annual sessions of intervention to once-only session and comparative condition [C]: An additional 29 new HIV cases would be prevented, at a cost per QALY gained of £713 ($1,075) and £8,893 ($13,413) per HIV case averted							✓		
Holtgrave et al. (2012) [CEA, CUA]	Female condom distribution and HIV prevention education programme targeting general population (men and women) versus no intervention [C]	200,000 condoms distributed and education services provided at a cost of £279,575 ($414,186) (2012 USD) Cost £2.15 ($3.19) per product used (incl. education services) Cost saving: 1.13 infections averted (societal perspective) 1.50 infections averted (public payer perspective) Cost-effectiveness threshold of HIV infections averted = 0.46; intervention averted estimated 23 HIV infections per intervention provided						✓			

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Holtgrave et al. (2013) [CUA]	Rental assistance for homeless and unstably housed HIV-infected persons versus no intervention [C]	0.01567 HIV transmissions averted £63 ($97) per client emergency room use savings (2005 USD) 0.0324 QALYs gained in improved perceived stress Cost per QALY saved by intervention £40,558 ($62,493)									✓
Marseille et al. (2011) [CEA]	Three interventions targeting HIV-infected individuals: 1. Primary care clinical provider-based brief computer-based risk assessment and individual counselling for HIV transmission	Estimated HIV cases prevented and costs over 3 years: Clinical provider 2.71 cases costing £98,601 ($146,075) (2010 USD) Peer educator 1.11 cases costing £228,070 ($337,881) Mixed services 3.02 cases costing £181,515 ($268,911)									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	prevention; 2. Peer educator-based individual or group counselling; 3. Mixed primary care provide and peer-educator based counselling for HIV prevention versus standard care (risk assessment without specific counselling) [C]	Compared to no intervention, clinical provider intervention was most cost-effective at £72,668 ($107,656) per HIV case averted (this dominated peer educator and mixed services interventions)					✓				
Ruger et al. (2014) [CEA, CUA]	1. Well-woman examination (WWE) plus standard care or 2. Four HIV prevention educational sessions (4ES) plus well-woman examination plus standard care versus standard care alone [C] targeted to women who inject drugs	HIV outcomes: Four-session education (4ES) intervention was cost saving in relation to well-woman examination (WWE) intervention						✓			

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Sanders et al. (2010) [CEA]	1. Nurse-initiated routine screening with traditional HIV testing and counselling or 2. Nurse-initiated routine screening with rapid HIV testing and streamlined counselling versus traditional HIV testing and counselling [C]	Traditional HIV testing and counselling: per patient lifetime discounted costs of: £31,379 ($48,650) and benefits of 16.271 QALYs (2007 USD)									
		Nurse-initiated routine screening with traditional HIV testing and counselling: increased lifetime costs by £34 ($53) and benefits by 0.0013 QALYs (corresponding to 0.48 quality-adjusted life days)			✓						
		Nurse-initiated routine screening with rapid HIV testing and streamlined counselling: cost £42 ($66) more than traditional screening with an increase of 0.0018 QALYs (0.66 quality-adjusted life days). Incremental cost-effectiveness of £6,876 ($10,660) per QALY relative to traditional testing and counselling							✓		
		Nurse-initiated routine screening with rapid HIV testing and streamlined counselling, without benefits to partners from reduced HIV transmission: Incremental cost-effectiveness of								✓	

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		£23,472 ($36,390) per QALY compared to traditional testing and counselling									
Schackman et al. (2013) [CEA]	During community-based substance abuse treatment: 1. On-site rapid HIV testing with information only or 2. On-site rapid HIV testing with risk reduction counselling versus off-site HIV testing and referral [C]	Offer of off-site test: Cost-effectiveness ratio (cost per QALY): dominated On-site test + information: Cost-effectiveness ratio (cost per QALY): £39,979 ($60,300) (2009 USD)	✓								✓
		On-site test + counselling: Cost-effectiveness ratio (cost per QALY): dominated On-site rapid testing with counselling costs $36 more per person but without added benefit	✓								
Kessler et al. (2013)	Individual and optimal combinations of multiple HIV prevention programmes: clinical and non-	Model predicted: 58,632 new cases of HIV infection over a 20-year period, during which 16,159 persons were predicted to have died of AIDS-related conditions									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
[CSA]	clinical testing; condom distribution; post-exposure prophylaxis; linkage to care, care coordination; STI screening; partner services; risk-reduction education; linkage to support; social marketing; community-based interventions; prioritised surveillance data; social services; brief screening and intervention; and screening for co-morbidity factors versus no intervention	2,932 new HIV infections per year 808 HIV-related deaths per year **All cost saving:** Cost per infection averted: Condom distribution (all risk groups): £126,368 ($187,212) (2010 USD) Social marketing (all): £55,709 ($82,532) Community-based prevention (all): £4,482 ($7,173) Prioritised use of surveillance data (HIV-infected): £18,673 ($27,663) Cofactor risk reduction (HIV-infected, high risk): £21,130 ($31,304) Brief intervention and referral for alcohol use (HIV-infected, high risk): £24,821 ($36,772) Linkage to care (HIV-infected): £257,112 ($380,906)						✓			

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		Linkage to support services (HIV-infected) £83,896 ($124,291) Partner services (HIV infected and partners): £133,821 ($198,253) STI screening (HIV infected high risk): £228,843 ($339,026) **All not cost-saving:** STI screening (HIV uninfected only): £322,639 ($477,984) Risk reduction (HIV infected only): £518,016 ($767,431) Social services (HIV uninfected high risk): £706,311 ($1,046,387) Care coordination (HIV infected on ART): £781,784 ($1,158,199) Testing – clinical (HIV uninfected) £1,190,066 ($1,763,061) Testing – non-clinical (HIV uninfected): £2,099,507 ($3,110,381) Cofactors (HIV uninfected high risk): £2,451,098 ($3,631,257)	✓								

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		Brief screening and alcohol intervention (HIV uninfected, high risk): £2,629,434 ($3,895,458) Pre-exposure prophylaxis (HIV uninfected high risk): £6.075 million ($9,803,449) STI screening (HIV uninfected high risk): £7,698,044 ($11,404,509) Pre-exposure prophylaxis (HIV uninfected only: £9,812,825 ($14,537,519) STD screening (all): £11,907,321 ($17,640,475)									
Lasry et al. (2012) [CSA]	1. Current national provision of HIV testing and individual and group-level counselling and education interventions or 2. An optimised scenario in which funding is reallocated to provide:	Model predicts (over 5 years): 252,000 new HIV infections (versus no funding) Current £216.8 million ($327 million) budget (2009 USD): 223,000 new HIV infections (baseline scenario) 13% of new infections averted and £37,334 ($56,311) per infection averted (current versus no funding)						✓			

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	targeted testing for MSM and IVDU, targeted counselling and education for HIV-infected individuals, and targeted interventions to high-risk rather than general population, versus no funding	Optimised £216.8 million ($327) million budget: 192,000 new HIV infections 31% of new infections averted and £17,985 ($27,128) per infection averted (optimised versus no funding)						✓			

[CBA]=cost-benefit analysis; [CCA]=cost-consequence analysis; [CEA]=cost-effectiveness analysis; [CSA]=cost saving analysis; [CUA]=cost utility analysis; [I]=intervention condition; [C]= comparison condition

Table A14.2: Health promotion: STI prevention

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Cooper et al. (2012) [CEA]	Universally targeted: 1. Teacher-led 20 session STI prevention intervention or 2. Peer-led three session STI prevention intervention versus standard sexual health education [C]	Compared to standard sex education [C], teacher-led intervention would have net additional cost £6,375 (€8,575) and avoid two extra STI cases for 0.35 increase in QALY (2011-2012 Euro) Incremental cost-effectiveness ratio: £18,041 (€24,268) per QALY gained Compared to the teacher-led intervention, peer-led intervention cost £12,050 (€16,210) per case avoided Incremental cost-effectiveness ratio: £72,062 (€96,938) per QALY gained							✓		✓

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Crawford et al. (2015) [CUA]	Brief alcohol advice, health information leaflet and referral offer versus health information leaflet only	No significant reductions in: 90-day alcohol consumption or Rates of unprotected sex in past 3 months £311 per person intervention £319 per person control Additional cost of intervention £12.57, SD £6.59 QALYs 0.007 lower in brief intervention group and costs £8.41 higher ICER: −£1,200 per QALY				✓			✓		
Jackson et al. (2015) [CCA]	Team captain-led STI screening promotion versus poster-only STI screening promotion	50% screening uptake [I] versus 61% screening uptake [C] £88.89 per participant screened [I] versus £81.87 per participants screened [C]	✓								
	Sexual health adviser-led STI screening promotion versus poster-only STI screening promotion	67% screening uptake [I] versus 61% screening uptake [C]				✓					

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		£88.33 per participant screened [I] versus £81.87 per participant screened [C]									
Pilgrim et al. (2010) [CEA]	School nurse services only; no dispensing of condoms or contraceptives [C]	11,392 abortions 2,186 pregnancies Total costs £1,527,318,794 (2007-2008 GBP)									
	School-based condom provision versus school nurse services only	11,153 estimated abortions 1,778 estimated pregnancies Total estimated costs £1,517,225,105 Estimated cost £38 for each pregnancy averted					✓				
	School-based hormonal contraceptive provision to sexually active nulliparous 14-16 year olds versus condom provision and school nurse	11,103 estimated abortions 1,693 estimated pregnancies Total estimated costs £1,515,641,998 Estimated cost outcome £443 for each averted pregnancy Estimated cost outcome £1453 for each abortion avoided					✓				

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	School-based peer education and social work case management to prevent repeat pregnancy in teen mothers attending school versus no follow-up after first pregnancy	No follow-up [C]: 31,464 repeat pregnancies Total cost £655,572,463									
		Case management follow-up [I]: 19,022 repeat pregnancies Total cost £705,730,087 Estimated cost £4,031-15,155 per repeat pregnancy averted					✓				
	Advance provision of EHC to sexually active high risk teens aged 15-19 years versus no advance provision of EHC	No advance provision [C]: 11,241 abortions / 11,363 pregnancies Total costs: £1,524,674,862 (2007-2008 GBP) Advance provision [I]: 11,241 abortions / 11,363 pregnancies Total costs: £1,447,599,721 Estimated cost £310 per pregnancy averted					✓				

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
		Estimated cost £2,795 per abortion avoided									
Ruger et al. (2014) [CEA, CUA]	1. Well-woman examination (WWE) plus standard care or 2. Four HIV prevention educational sessions (4ES) plus well-woman examination plus standard care versus standard care alone [C] targeted to women who inject drugs	Modelling results: Hepatitis C: WWE was less costly and more effective compared to 4ES: £72,034 ($109,308) per additional infection averted (£27,996 ($42,482) QALYs gained) Chlamydia: 4ES was less costly than WWE: £2,273,217 ($3,449,495) per additional QALY Gonorrhoea: WWE was less costly than 4ES: £706,949 ($1,072,760) per additional QALY					✓ ✓ ✓				
Thomas (2012) [CBA]	Mass media campaign to promote condom use to unmarried males 15-44 years old versus no programme	Benefits: Pregnancy: 1.7% reduction									

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
Thomas (2012) cont'd.		Abortions: 3.9% reduction Births: 1.0% reduction Births into poverty: 2.2% reduction Costs: £65.3 million ($100 million) (2008 USD) £2.81 ($4.31) saved for each $1 spent						✓			
	Teen pregnancy prevention programmes to unmarried low SES youth versus no programme	Benefits: Pregnancy: 0.8% reduction Abortions: 1.4% reduction Births: 0.6% reduction Births into poverty: 1.4% reduction Costs: £94,685 million ($145 million) £1.61 ($2.46) saved for each $1 spent						✓			

Study	Intervention	Outcomes	Cost-effectiveness						NICE rating		
			More costly, less effective	Less costly, less effective	More costly, more effective	Similar cost, similar effect	Less costly, more effective	Cost saving	<£20,000 per QALY	£20-30,000 per QALY	>£30,000 per QALY
	Expanded Medicaid for contraception to unmarried low SES youth versus no programme	Benefits: Pregnancy: 1.9% reduction Abortions: 3.5% reduction Births: 1.4% reduction Births into poverty: 1.8% reduction Costs: £153,455 million ($235 million) £3.67 ($5.62) saved for each $1 spent						✓			

[CBA]=cost-benefit analysis; [CCA]=cost-consequence analysis; [CEA]=cost-effectiveness analysis; [CSA]=cost saving analysis; [CUA]=cost utility analysis; [I]=intervention condition; [C]= comparison condition

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Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre)
Social Science Research Unit
UCL Institute of Education, University College London
18 Woburn Square
London WC1H 0NR

Tel: +44 (0)20 7612 6397

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Please contact the UCL Institute of Education for assistance:
telephone: +44 (0)20 7947 9556 email: info@ioe.ac.uk