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A protocol for a systematic review of economic evaluations conducted on gender-transformative interventions aimed at preventing unintended pregnancy and promoting sexual health in adolescents

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ABSTRACT

Introduction

Gender-transformative approaches aim to help communities understand and challenge the social norms that perpetuate inequalities between men and women and improve women's access to key services and contraceptive methods. The purpose of this systematic review is to synthesise the best available evidence on economic evaluations of gender transformative interventions targeted at preventing unintended pregnancy and promoting sexual health in adolescents, assess the methodological quality of the economic evaluation studies and identify gaps in the evidence.

Methods and Analysis

We will search the following bibliographic databases for economic evaluations that meet our selection criteria; PubMed, Cochrane, National Health Service EE database, EMBASE, SCOPUS, CINHALL, Web of Science and Paediatric EE Database. We will additionally conduct a grey literature search. Two independent reviewers will conduct the screening, data extraction and quality assessment. We will consider the following outcomes from economic evaluations; relative resource use, cost, and Incremental Cost Effectiveness Ratio (ICER), Incremental Net Benefit Ratio (NBR) or Net Present Value (NPV). Quality assessment will be conducted using the consolidated health economic evaluation reporting standards (CHEERS) statement, Consensus on Health Economic Criteria (CHEC) checklist and Philips checklist. Results will be reported using summary tables and narratively. Attempts will be made to use the Joanna Briggs Institute (JBI) three by three dominance ranking matrix tool to compare relevant cost effectiveness studies.

Ethics and dissemination

Ethics approval is not required because the review will not use individual patient data, instead publicly available economic evaluation research studies will be used. However, an ethics exemption was obtained from the Stellenbosch University Health Research Ethics Committee (HREC), Reference No:

X21/05/012. The results of the systematic review will be published in a peer reviewed journal and presented at a relevant scientific conference.

PROSPERO Registration number CRD42021264698

Key words: health economics, pregnancy, sexual health

Strengths and limitations of the study

- The study includes both partial and full economic evaluations from all settings which will make the findings relevant to most decision makers
- Standard methods and guidelines for systematic reviews and tools for quality assessment will be used which will produce a high-quality review
- A comprehensive search strategy which includes all the SRHR domains will be conducted to obtain all available evidence of gender transformative interventions to prevent unintended pregnancies and improve sexual health of adolescents
- The restriction of language to English publications only may be a source of bias in the study.
- Focusing on adolescents only may produce results that are not applicable to children and the adult population

INTRODUCTION

The World Health Organization defines gender-transformative approaches (GTA) as interventions that 'address the root causes of gender-based health inequities through challenging and redressing harmful and unequal gender norms, roles, and unequal power relations that privilege men over women'. [1] Gender is recognised as a social determinant of health globally; this was decided at the International Conference on Population and Development (ICPD) in 1994. [2] Gender-transformative interventions mainly target adolescents aged 10-19 and have a focus on sexual and reproductive health, HIV and violence. [3] Adolescence is the critical point where puberty reshapes male and female perceptions as well as social expectations. Romantic and sexual feelings emerge at this stage and gender roles play out as adolescents negotiate intimate relationships; early adolescence is therefore seen as the unique opportunity to address gender attitudes before they solidify. [4] GTAs help to fulfil the fifth goal of the United Nations 2030 Agenda for sustainable development which seeks to achieve gender equality and empower all women and girls. [5]

In the context of family planning and reproductive health, a gender-transformative approach involves helping communities understand and challenge the social norms that perpetuate inequalities between men and women, and improving women's access to key services and contraceptive methods. Gender transformative approaches also involve engaging men and boys in ways that address their reproductive health needs and that support women's and girls' family planning and reproductive health decision-making. [6]

An evidence gap map and systematic review of reviews aimed at interventions addressing men and gender equality in sexual and reproductive health rights observed that a minority of reviews (39 out of 462 reviews, 8.4%) included gender transformative interventions with men and boys. Thirty nine percent of these studies reported positive results whilst the rest had mixed or inconclusive results. [7] The evidence gap map and systematic review of reviews was followed up by a systematic review of primary studies that were selected from the 39 identified gender transformative intervention systematic reviews using an inclusion / exclusion criteria. The selected studies included 16 primary studies for interventions targeting healthy adolescence in the World Health Organisation (WHO) sexual and reproductive health and rights (SRHR) domains. Of these adolescence studies, five studies were on promoting sexual health and wellbeing, one was on preventing adolescence pregnancy, one was on health of pregnant women and girls and their new-born infants and the rest of the studies were on gender-based violence and dating violence. [8] The limitations of the systematic reviews were that they

only included randomised control trials and quasi-experimental studies therefore some relevant observational gender transformative intervention studies may have been excluded. Other primary studies that were excluded from the systematic reviews in the initial evidence gap map and systematic review of reviews were not considered. The systematic review did not include the cost effectiveness of the interventions therefore there is a gap in the evidence.

An economic evaluation is defined as the comparative analysis of alternative courses of actions in terms of both their costs and consequences. Partial or full economic evaluations may be conducted. Full economic evaluations have two or more competing alternatives and both the costs and consequences of the competing alternatives are considered. [9] There are three types of full economic evaluations, cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA). These economic evaluations differ in the way outcomes are measured. In cost effectiveness analyses, natural or disease specific outcomes for the interventions are used. The cost utility analysis uses generic outcome measures, for example the quality adjusted life years (QALYs) and disability adjusted life years (DALYs). Cost benefit analyses measure both costs and outcomes in monetary values. Partial economic evaluations consider costs and or consequences but there may not be comparison between alternative interventions or costs may not be related to benefits.[9] Five types of partial economic evaluations may be distinguished, outcome description, cost description, cost outcome description effectiveness evaluation and cost analyses. Full economic evaluations are usually the preferred type of economic evaluations for inclusion in systematic reviews. Inclusion of partial economic evaluations in systematic reviews of economic evaluations (SR-EEs) is justified when there is lack of knowledge on a decision topic.[9,10]

SR-EEs are important in synthesising and critically appraising primary economic evaluations to inform policy decisions and identify knowledge gaps. Some question the utility and value of systematic reviews of economic evaluation studies because of the limits in generalisability from the findings. This is due to variations in; resource use and costs across countries and time frames, context and populations and differences in the decision-making context.[11] However, there is a growing number of application of systematic reviews of economic evaluations because they are important for decision makers in identifying the range and quality of available studies for a particular resource use or cost effectiveness question, obtaining results for intervention choices or trade-offs they are considering and also they provide an enhanced understanding of the different conditions that promote effectiveness and

efficiency of different interventions.[9,12]To our knowledge, a few systematic reviews of economic evaluations targeting sexual and reproductive health have been published.

A systematic review to assess the costs and outcomes of control programmes for sexually transmitted infections (STIs) in young people aged 30 and below from the Organisation for Economic Co-operation and Development (OECD) countries was conducted by Bloch *et al*, 2021.[13]There were thirty-one studies that met the inclusion criteria and 25 of these studies were on chlamydia screening, 6 studies were on gonorrhoea and one on HIV screening. The publication period covered was 1999 to 2019. Modelling was the predominant study design (30 studies), there was significant heterogeneity in the methods applied which affected the comparability of the results. Most of the interventions included in the systematic review were cost-effective.[13] Since most of the economic evaluations that met the inclusion criteria were on chlamydia, the focus of the study was limited. There were no studies on behavioural interventions or equity in access to screening interventions which limited applicability of the study by decision makers. Limiting studies to OECD countries restricted applicability of findings to some settings.

In another systematic review conducted by Shepherd *et al*, 2010 to determine the effectiveness and cost-effectiveness of behavioural interventions for the prevention of sexually transmitted infections in adolescents aged 13-19 years old, 5 economic evaluation studies met their inclusion criteria. All five studies were on cost effectiveness of HIV prevention interventions and only one of these studies included other sexually transmitted infections. The search period was for publications from 1990 to 2008. All included studies were modelling studies, there were differences in the assumptions and parameters used in the models leading to variability in the estimated cost-effectiveness of the interventions. The studies were all from the United States of America (USA) except one multi-country study that was from Sub-Saharan Africa and Southeast Asia. [14]The systematic review is not current and needs to be updated to include findings from more recent studies. The interventions in the systematic reviews of economic evaluations were not gender transformative and they did not cover all the WHO sexual and reproductive health and rights (SRHR) domains relevant for adolescents. There is therefore a gap in the available evidence. The purpose of this systematic review is to:

- synthesise the best available evidence on economic evaluations of gender transformative interventions targeted at preventing unintended pregnancy and promoting sexual health in adolescents.
- Assess the methodological quality of the economic evaluation studies.

- Identify the gaps in the economic evaluations evidence

METHODOLOGY

The Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRISMA-P 2015) was used to guide the development of this protocol (appendix 1).[15] We intend to register our protocol on the International Prospective Register of Systematic Reviews (PROSPERO). The systematic review will be conducted and reported following the PRISMA guidelines, 2020.[16]

Eligibility criteria

Studies will be selected according to the criteria stated below.

Inclusion criteria

Type of studies

Partial and full economic evaluations will be included in the systematic review. Partial economic evaluations eligible for inclusion include cost analyses, cost consequence studies, and cost minimisation analyses. The three types of full economic evaluations will be included: CEA, CUA and CBA. Both trials based and model-based studies will be included in the systematic review.

Where the economic evaluation of gender transformative approaches was done as part of a larger study, the study will only be included if the relevant results can be differentiated in terms of effects and costs of the gender transformative intervention. Publications from 1990 – 2021 will be included. We will restrict the search to articles from 1990 onwards because the studies from before 1990 will not be relevant due to changes in social norms and behaviours.[17] We will include articles published in the English language.

Population

The population of interest is adolescents aged between 10 to 19 years old from any country. Studies for either boys or girls or both sexes will be considered. If different population age groups were investigated, studies will only be included if results for the age 10-19 years old age group can be differentiated.

Intervention

Economic evaluations for interventions that are gender transformative will be eligible for inclusion in the review. Gender transformative components will be determined according to the definition published by WHO and applied in the study by Ruane-McAteer *et al*, 2020. These interventions target transforming harmful gender norms, or practices or gender-based inequalities at individual or group level AND transforming unequal gender norms, practices or gender based inequalities.[8]

The interventions are within the WHO sexual and reproductive health and rights (SRHR) domains for adolescents, and these include:

- Ensuring the health of pregnant girls and their infants
- Preventing unintended pregnancies and unsafe abortion
- Promoting sexual health and wellbeing (prevention of sexually transmitted infections and HIV)
- Promoting sexual reproductive health in disease outbreaks
- Preventing and responding to violence against girls and harmful practices like female genital mutilation, early and forced marriages [18,19]

The economic evaluations should compare different interventions or have a control which may be the standard of care or no intervention.

Setting

All types of healthcare or community settings from any country will be considered.

Outcome measures

The outcome measures from cost-effectiveness analyses will be relative resource use, cost and Incremental Cost Effectiveness Ratio (ICER). Outcome measures from cost benefit analyses will be relative resource use, costs and Incremental Net Benefit Ratio (NBR) or Net Present Value (NPV). For Cost-utility analyses outcome measures will be resource use; costs and Incremental Cost Effectiveness Ratio with costs expressed in monetary units and effects in QALYs or DALYs. Outcome measures from costing analysis and cost minimization analysis partial economic evaluations will be resource use and cost, for cost consequence analysis multiple outcomes indicated in the relevant studies will be considered.

Exclusion criteria

Studies will be excluded if they were done as part of a variety of interventions being compared and could not be differentiated in terms of effects and cost of interventions. Non-original studies will not be

included. Studies done in non-adolescent populations will not be considered. Studies that did not provide costing details will not be included. Commentaries, editorials, reviews, and protocols will be excluded. Posters, conference presentations or abstracts with no full articles will not be included in the systematic review.

Search methods for identification of studies

We will search the following public health and economic evaluations bibliographic databases for full economic evaluation studies that meet our selection criteria; PubMed, Cochrane, National Health Service EE database, EMBASE, SCOPUS, CINHAI, Web of Science and Paediatric EE Database. The search strategy will be tailored specifically for each database. We will scan reference lists of included economic evaluation studies of relevant reviews identified during the search to ensure literature saturation. A grey literature search for unpublished data will also be conducted. Databases that include MedNar or Google Scholar, ProQuest Dissertations, and the Online clinical trials registers will be searched for unpublished studies.

Search terms and draft search strategy for PubMed are appendix 2. Search terms for SRHR interventions were adopted from the evidence gap map and systematic review by Ruane-McAteer *et al*, 2019.[7]

Data management

Endnote X8 will be used to store all references selected for the systematic review from the different databases and to remove duplicate results. The screening and study selection will be done in Microsoft excel. All study data will be saved on a file on the computer and backed up on an external hard drive during the study period.

Study selection

The first reviewer (JN) and second reviewer (TA) will independently screen the titles and abstracts of the articles obtained from the search. Titles and abstracts rejected by both reviewers will not be included in the study. Full articles of the titles and abstracts that meet the study inclusion criteria will be sourced and reviewed for inclusion into the study. Where titles and abstracts are not clear, the reviewers will read the full article to determine eligibility. Any differences in the selection of articles by the two reviewers will be discussed and a consensus reached. Where the two reviewers fail to agree, the third author (LN) will be consulted to resolve the disagreement and reach a final resolution. The reviewers will

contact authors of original studies if they need clarification during the selection process. Fig 1 summarises the selection process flow.

Data extraction

A standardised data extraction form will be used to extract relevant information from the research articles. The first reviewer (JN) will extract the data and the data extraction forms and the second reviewer (TA) will verify the information to check for errors in the data extraction. The data extraction form will be piloted before use in the study. The data extracted will cover *descriptive data* about the

- (i) study population/participants, intervention, comparator(s) and outcomes
- (ii) study methods including evaluation design type, analytic viewpoint(s), source of effectiveness data, prices and currency used for costing, period of analysis, sensitivity testing, measures of resource use, cost and health effect/clinical and cost effectiveness
- (iii) study context (geographical, health care and broader service delivery setting and culture)[20]

Secondly, the data extraction form will also cover results for the resource use and/or cost and/or cost effectiveness measures; and lastly where possible author conclusions about factors that promote intervention cost effectiveness.[20] The draft data extraction form which will be piloted is in appendix 3.

Any disagreements in the data extraction will be resolved in a meeting between the two reviewers and the third reviewer LN. In the event of missing data required for the systematic review, the reviewers will contact the study authors by email to request for further information. A maximum of 3 attempts to reach the authors will be done. If missing information cannot be obtained, the authors will decide on how to handle the missing data. This will be documented. The data extraction form is in the appendix section.

Critical appraisal of methodological quality

There is a lack of universally recognised methodological evaluation standard for systematic reviews of economic evaluations. There are at least eleven checklists and guidelines for the appraising of the quality of economic evaluation studies included in systematic reviews.[21] The most widely used tools for assessing the methodological quality of both trial based and model based economic evaluations in systematic reviews include the Drummond checklist (2005)[9], BMJ checklist (1996)[22] Consensus on

Health Economic Criteria (CHEC) extended checklist[23,24]. [21,25] For this systematic review, we will use the CHEC extended checklist for trial and model based economic evaluations. The CHEC checklist was developed for economic evaluations conducted along effectiveness studies and had questions on 19 criteria.[23] An extended guideline was later published with an additional criterion on modelling studies.[24] The scoring system as applied by Wijnen *et al*, 2017 will be used where a score of 1 will be allocated for criterion fully met, 0.5 criterion partially met and 0 for criterion not fulfilled. All criteria will be equally weighted, and a percentage will be calculated for overall quality assessment.[26]The results of the quality assessment will also be described narratively. For modelling studies we will use the Philips checklist which was designed specifically for modelling studies.[27] The consolidated health economic evaluation reporting standards (CHEERS) statement[28] is a guideline for reporting standards for economic evaluations. It consists of 24 criteria on the minimum standards on reporting economic evaluations.[28] We will use the CHEERS statement checklist to assess reporting quality of the economic evaluations. The scoring system similar to the one proposed for the CHEC checklist was applied to the CHEERS statement checklist by Mangham-Jefferies *et al*, 2014.[29] We will use this scoring system for the CHEERS quality assessment where a score of 1 will be allocated for criterion fully met, 0.5 criterion partially met and 0 for criterion not fulfilled. All criteria will be equally weighted, and a percentage will be calculated for overall quality assessment of each included economic evaluation. Furthermore, the scores will be ranked as $\geq 75\%$ high quality, 50 -74% moderate quality and $< 50\%$ poor quality to determine an overall assessment for each study.[29] There are criteria that overlap between the CHEC and CHEERS checklists but complete assessments will be conducted for each checklists to determine overall outcomes for each type of assessment.

Two reviewers (JN and TA) will appraise the articles independently and disagreements will be resolved through discussion or by consulting the third reviewer (LN).

Data analysis and synthesis of findings

All studies that met the inclusion criteria will be included in the data analysis and synthesis regardless of outcome from the quality assessment. A Prisma flow chart diagram will be used to show the search results and the number of articles selected for the systematic review. A narrative summary and tables will be used to present the results from the included studies. We will attempt to structure the narrative summary where data is available around the type of SRHR interventions, gender transformative components of each intervention, type of economic evaluation, methodological features around the economic evaluations, categorisation of outcomes, perspectives, and locations where the studies

originate. Attempts will be made to use the Joanna Briggs Institute (JBI) three by three dominance ranking matrix tool to compare relevant cost effectiveness studies if applicable. [20]

Patient consent and public involvement

Patients and the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

DISCUSSION

The systematic review will provide evidence on economic evaluations across all settings using a standard and reproducible method based on the PRISMA guidelines for systematic reviews. The inclusion and exclusion criteria were clearly stated and explained in detail. Although there are some systematic reviews of economic evaluations aimed at sexual and reproductive health issues, to our knowledge this is the first systematic review targeting the gender transformative elements of the interventions and conducting a comprehensive review of all relevant elements of the WHO SRHR. Our broad context and inclusion of all types of economic evaluations (partial and full) will be useful for decision makers from different environments. The systematic review will report on resource use data from the economic evaluations which will also be useful for improving the transferability of the review findings to different settings. It also helps different health systems identify future resource priorities. The data is useful for decision makers who are involved in the development of clinical practice guidelines. The quality assessment will help the researchers in the field identify areas of weaknesses which they can improve on in future research. Identifying gaps in the evidence helps on the mapping of future research priorities.

We restricted our search to publications in English due to lack of resources and time which will be a source of bias in the study because relevant non-English publications may be excluded. Although there are stated benefits in targeting adolescents for sexual and reproductive health gender transformative interventions in this study, the generalisability of the findings to other age groups is reduced. Scarcity of evidence to include in the systematic review is a potential risk of the study.

ETHICS AND DISSEMINATION PLAN

Ethics approval is not required because the review will not use individual patient data, instead publicly available economic evaluation research studies will be used. However, an ethics exemption was

obtained from the Stellenbosch University Health Research Ethics Committee (HREC), Reference No: X21/05/012. The results of the systematic review will be published in a peer reviewed article and presented at a relevant scientific conference or workshop.

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Authors' contributions

LN conceptualised the study. All authors (JN, TA and LN) participated in the design of the systematic review. JN drafted the study protocol which was critically reviewed by TA and LN who provided technical expertise for the systematic review. All authors reviewed and approved the final version of the protocol. LN is the the guarantor for the research study.

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Competing interests

None declared.

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Figure Legend

Figure 1. PRISMA flow diagram for study selection.

For peer review only

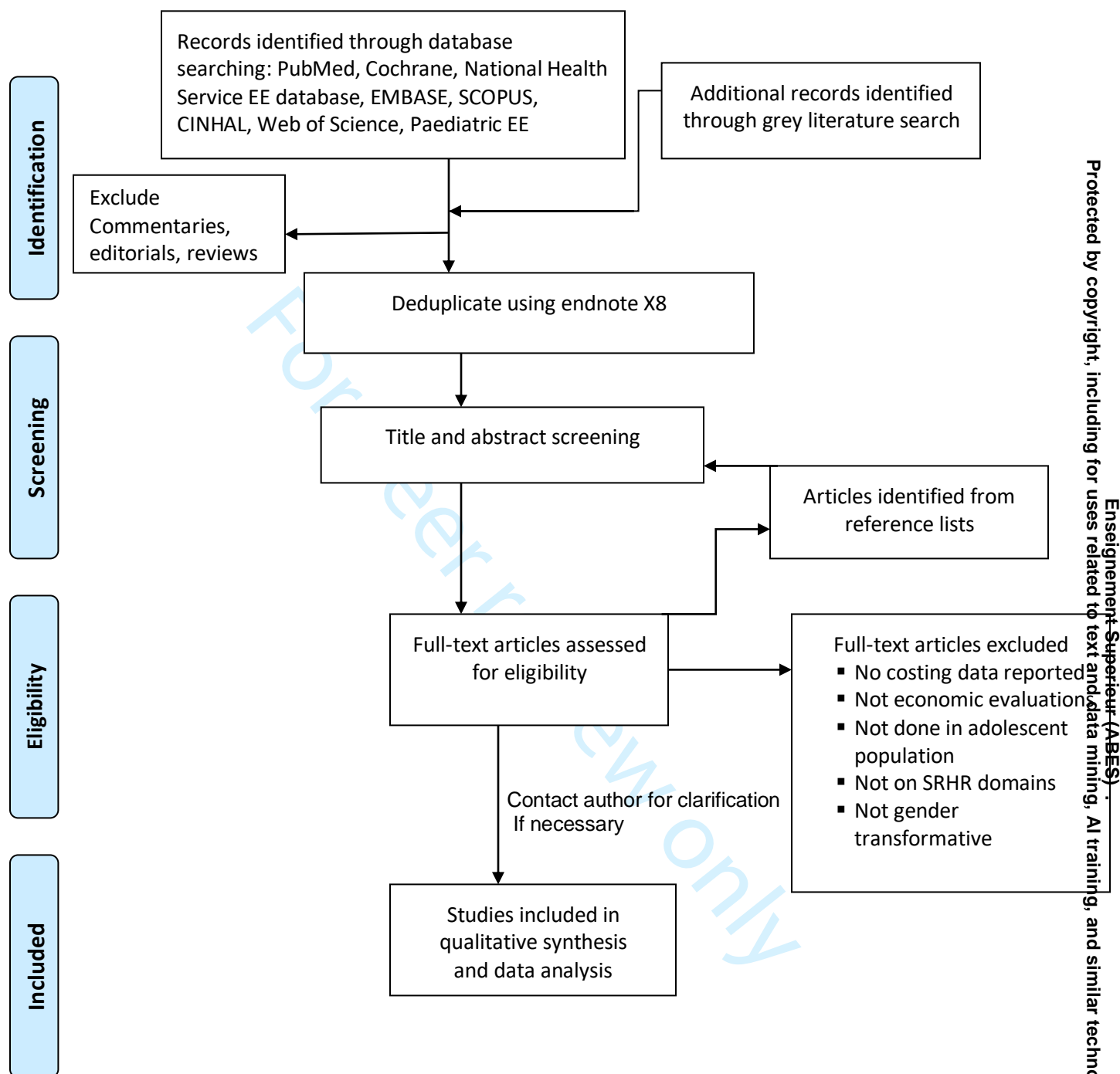


Figure 1. Selection process flow diagram

APPENDIX 1

PRISMA-P 2015 Checklist

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	√	<input type="checkbox"/>	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	√	<input type="checkbox"/>	Registration still pending
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	√	<input type="checkbox"/>	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	√	<input type="checkbox"/>	16
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Support					
Sources	5a	Indicate sources of financial or other support for the review	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Sponsor	5b	Provide name for the review funder and/or sponsor	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input type="checkbox"/>	<input type="checkbox"/>	n/a
INTRODUCTION					

Rationale	6	Describe the rationale for the review in the context of what is already known	√	<input type="checkbox"/>	4-6
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	√	<input type="checkbox"/>	6-7
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	√	<input type="checkbox"/>	7-9
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	√	<input type="checkbox"/>	9
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	√	<input type="checkbox"/>	Supplemental file – appendix 2
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	√	<input type="checkbox"/>	9
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	√	<input type="checkbox"/>	9-10
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	√	<input type="checkbox"/>	9-10
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	√	<input type="checkbox"/>	7-8
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	√	<input type="checkbox"/>	8

Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	√	<input type="checkbox"/>	10-11
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	<input type="checkbox"/>	<input type="checkbox"/>	n/a
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	<input type="checkbox"/>	<input type="checkbox"/>	n/a
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input type="checkbox"/>	<input type="checkbox"/>	n/a
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	√	<input type="checkbox"/>	11-12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input type="checkbox"/>	√	

APPENDIX 2

Research Question

In adolescents aged 10 -19years old, what are the cost-effectiveness of gender-transformative interventions on preventing unintended pregnancy and promoting sexual health?

PICO Format

P -adolescents (13 -19years old) , boys and girls

I – Gender transformative interventions addressing the WHO Sexual Reproductive Health Rights outcomes (SRHR) domains.

- Ensuring the health of pregnant girls and their infants
- Preventing unintended pregnancies and unsafe abortion
- Promoting sexual health and wellbeing (prevention of sexually transmitted infections and HIV)
- Promoting sexual reproductive health in disease outbreaks
- Preventing and responding to violence against girls and harmful practices like female genital mutilation, early and forced marriages

O – economic evaluations

- Cost effectiveness
- Cost utility
- Cost benefit
- Cost minimization analysis
- Costing analysis
- Cost consequence analysis
- Decision analysis

Search Strategy – PUBMED

a. MeSH Terms

Concepts #1 Adolescents	Mesh terms: "Adolescent"[Mesh] Search Terms/ key words : Adolescents or Adolescence or Teens or Teen or Teenagers or Teenager or Youth or Youths or Female Adolescent, or Female Adolescents or Male Adolescent or Male Adolescents or minor or minors
#2 SRHR	MeSH terms: "Reproductive Health"[Mesh] OR "Reproductive Health Services"[Mesh] OR "Sexual Health"[Mesh] OR "Pregnancy"[Mesh] OR "Pregnancy, Unplanned"[Mesh] OR "Sex Offenses"[Mesh] OR "Abortion, Criminal"[Mesh] OR "Abortion, Legal"[Mesh] OR "Abortion, Induced"[Mesh] OR "Condoms"[Mesh] OR "Condoms, Female"[Mesh] OR "Gender-Based Violence"[Mesh] OR "Sexually Transmitted Diseases"[Mesh] Search terms: sexual health or reproductive health or maternal health or maternal welfare or maternal mortality or neonatal health or perinatal care or perinatal health or prenatal

	<p>care or prenatal health or antenatal health or ante-natal health or postnatal health or postnatal health or post-part* or post part* or newborn health or family planning or contracepti* or condoms or condom or pregnan* or abortion or pregnancy termination or induced abortion or</p> <p>abort* or birth or miscarriage or spontaneous abortion or stillb* or Minimum Initial Service Package or obstetric* or gynecology or gynaecology or safe motherhood or safe delivery or or sexually transmitted infection* or sexually transmitted disease* or HIV or Human immunodeficiency virus or AIDS or acquired immune deficiency syndrome or PMTCT</p> <p>gender based violence or partner violence or family violence or violence against women or domestic violence or sexual abuse or sex crime or sexual crime or or sexual violence or rape or intimate partner violence or partner violence or partner abuse or sexual assault or sexual harassment or sexual coercion or forced sex or sexual exploitation or coercive control or or female genital mutilation or FGM or female genital cutting or FGMC or female circumcis* or (early and marriage) or (child and marriage) or (forced and marriage) or (arranged and marriage) or (abduction and marriage)</p>
# 3 Economic evaluation	<p>MeSH terms "Cost-Benefit Analysis"[Mesh] OR "Decision Support Techniques"[Mesh]</p> <p>Key words: Cost-Benefit or Cost-Benefit Analyses or Cost Benefit Analys* or Cost Effectiveness or Cost-Benefit Data or Cost Benefit Data or Data, Cost-Benefit or Cost-Utility Analysis or Analyses, Cost-Utility Analysis, Cost-Utility or Cost Utility Analys* or Economic Evaluation* or Economic Evaluations or</p> <p>Marginal Analysis or Analyses, Marginal or Analysis, Marginal or Marginal Analyses or Cost Benefit or Costs and Benefits or Benefits and Costs or Cost-Effectiveness Analysis or Analysis, Cost-Effectiveness or Cost Effectiveness Analysis or Costing analys* or cost minimization analys* or cost minimisation analys* or cost consequence analys*</p>

Search will be conducted using MeSH terms and free text from the listed terms using advanced search options on PubMed.

1 “gender transformative intervention*”

2 “gender transformative approach*”

3 1 OR 2

4 “reproductive health” or “Reproductive Health”[MESH] or “Reproductive Health Services”[MESH]

5 “sexual health” or “Sexual Health”[MESH]

6 “sexual reproductive health”

7 “sexually transmitted infection*”

8 “sexually transmitted disease*” or “Sexually Transmitted Diseases”[MESH]

9 “HIV”

10 “Human immunodeficiency virus”

11 “AIDS”

12 “Acquired immun* deficiency syndrome”

13 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12

14 “family planning”

15 “contracept*”

16 “condom*” or “Condoms”[Mesh]

17 “condom use”

18 “pregnan*” or “Pregnancy”[Mesh]

19 “unintended pregnan*” or “Pregnancy, Unplanned”[MESH]

20 “abort*”

21 “unsafe abort*”

22 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21

23 “gender based violence”

24 “domestic violence”

25 “partner violence”

26 “violence against girls”

27 “sexual abuse”

28 "sex crime"

29 "sexual crime"

30 "intimate partner violence" or "Intimate Partner Violence"[MESH]

31 "sexual assault" or "Sex Offenses"[MESH]

32 "coercive control"

33 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32

34 "female genital mutilation"

35 "FGM"

36 "female genital cutting"

37 "FGC"

38 34 or 35 or 36 or 37

39 "early marriage"

40 "arranged marriage"

41 "child marriage"

42 38 or 39 or 40

43 "economic evaluation"

44 "cost benefit analys*" or "cost benefit" or "Cost-Benefit Analysis"[MESH]

45 "cost effectiveness" or "cost effectiveness analys*"

46 "cost utility" or "cost utility analys*"

47 "cost analys*"

48 "cost consequence analys*" or "cost consequence"

49 "cost minimization" OR "cost minimization analysis"

50 "cost minimisation" OR "cost minimisation analysis"

51 "decision modelling"

52 "decision analysis"

53 "decision analytic modelling"

54 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53

55 3 or 13 or 22 or 33 or 38 or 42

56 "Adolescen*" or "teen*" or "youth*" or "girl*" or "boy*" or "male adolescen*" or "female adolescen*" or "Adolescent"[MESH]

57 “adolescent boy” or “adolescent girl*” or “adolescent boys and girls”

58 56 or 57

59 54 AND 55

60 59 AND 58

Limits for the search are Human studies and publication years 1990 -2021

For peer review only

APPENDIX 3
Draft data extraction form

Date form completed:
Name of reviewer extracting data:
Study details
Study Title:
Author and publication year:
Author contact details:
Study context: <ul style="list-style-type: none">- Healthcare, service delivery, social context- Country
Study objectives:
Source of funding:
Conflict of interest :
Methods
Type of study <ul style="list-style-type: none">(i) For effectiveness data(ii) Economic evaluation study design
Participants / population:
Types of Intervention(s):
Types of outcome measure
Decision: <ul style="list-style-type: none">- If excluded, give reason for exclusion
DO NOT PROCEED IF STUDY IS EXCLUDED FROM THE REVIEW
Perspective:
Primary cost / consequences / outcome measures:
Comparators:
Time horizon:
Discounting (if discounting was used, list the discount rates):
Currency:
Data sources for costs:
Data sources for clinical data:
Data sources for utility data:
Was modelling used? If yes, state type of modelling:
Results
Costs / resources:
Outcomes / benefits:
Incremental cost effectiveness:
Analysis of uncertainty:
Author's conclusions:

For peer review only

BMJ Open

A protocol for a systematic review of economic evaluations conducted on gender-transformative interventions aimed at preventing unintended pregnancy and promoting sexual health in adolescents

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Primary Subject Heading:	Health economics
Secondary Subject Heading:	Public health
Keywords:	HEALTH ECONOMICS, PUBLIC HEALTH, REPRODUCTIVE MEDICINE

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Manuscripts

Title	A protocol for a systematic review of economic evaluations conducted on gender-transformative interventions aimed at preventing unintended pregnancy and promoting sexual health in adolescents
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ABSTRACT

Introduction

In the context of family planning and reproductive health, a gender-transformative approach involves helping communities understand and challenge the social norms that perpetuate inequalities between men and women, and improving women's access to key services.

The purpose of this systematic review is to synthesise the best available evidence on economic evaluations of gender transformative interventions targeted at preventing unintended pregnancy and promoting sexual health in adolescents, assess the methodological quality of the economic evaluation studies and identify gaps in the evidence.

Methods and Analysis

We will search the following bibliographic databases for economic evaluations that meet our selection criteria; PubMed, Cochrane, National Health Service EE database, SCOPUS, CINHALL, Web of Science and Paediatric EE Database. We will additionally conduct a grey literature search. The search will be conducted for the period 1 January 1990 to 31 December 2021. Two independent reviewers will conduct the screening, data extraction and quality assessment. We will consider the following outcomes from economic evaluations; relative resource use, cost, and Incremental Cost Effectiveness Ratio (ICER), Incremental Net Benefit Ratio (NBR) or Net Present Value (NPV), Quality Adjusted Life Years (QALYs) and Disability Adjusted Life Years (DALYs). Quality assessment will be conducted using the consolidated health economic evaluation reporting standards (CHEERS) statement and the Consensus on Health Economic Criteria (CHEC) checklist. Results will be reported using summary tables and narratively. Attempts will be made to use the Joanna Briggs Institute (JBI) three by three dominance ranking matrix tool to compare relevant cost effectiveness studies.

Ethics and dissemination

Ethics approval is not required because the review will not use individual patient data, instead publicly available economic evaluation research studies will be used. However, an ethics exemption was obtained from the Stellenbosch University Health Research Ethics Committee (HREC), Reference No: X21/05/012. The results of the systematic review will be published in a peer reviewed journal and presented at a relevant scientific conference.

PROSPERO Registration number CRD42021264698

Key words: health economics, pregnancy, sexual health

Strengths and limitations of the study

- The study includes both partial and full economic evaluations from all settings which will make the findings relevant to most decision makers
- Standard methods and guidelines for systematic reviews and tools for quality assessment will be used which will produce a high-quality review
- A comprehensive search strategy which includes all the SRHR domains will be conducted to obtain all available evidence of gender transformative interventions to prevent unintended pregnancies and improve sexual health of adolescents
- The restriction of language to English publications only may be a source of bias in the study.
- Focusing on adolescents only may produce results that are not applicable to children and the adult population

INTRODUCTION

The World Health Organization defines gender-transformative approaches (GTA) as interventions that 'address the root causes of gender-based health inequities through challenging and redressing harmful and unequal gender norms, roles, and unequal power relations that privilege men over women'. [1]

Gender is recognised as a social determinant of health globally; this was decided at the International Conference on Population and Development (ICPD) in 1994. [2] Adolescence is the critical point where puberty reshapes male and female perceptions as well as social expectations. Romantic and sexual feelings emerge at this stage and gender roles play out adolescents negotiate intimate relationships; early adolescence is therefore seen as the unique opportunity to address gender attitudes before they solidify. [3] In a systematic review, gender-transformative interventions that specifically target adolescents aged 10-19 were found to mainly focus on sexual and reproductive health, HIV and violence. [4] GTAs help to fulfil the fifth goal of the United Nations 2030 Agenda for sustainable development which seeks to achieve gender equality and empower all women and girls. [5]

In the context of family planning and reproductive health, a gender-transformative approach involves helping communities understand and challenge the social norms that perpetuate inequalities between men and women, and improving women's access to key services and contraceptive methods. Gender transformative approaches also involve engaging men and boys in ways that address their reproductive health needs and that support women's and girls' family planning and reproductive health decision-making. [6]

An evidence gap map and systematic review of reviews aimed at interventions addressing men and gender equality in sexual and reproductive health rights observed that a minority of reviews (39 out of 462 reviews, 8.4%) included gender transformative interventions with men and boys. Thirty nine percent of these studies reported positive results whilst the rest had mixed or inconclusive results. [7] The evidence gap map and systematic review of reviews was followed up by a systematic review of primary studies that were selected from the 39 identified gender transformative intervention systematic reviews using an inclusion / exclusion criteria. The selected studies included 16 primary studies for interventions targeting healthy adolescence in the World Health Organisation (WHO) sexual and reproductive health and rights (SRHR) domains. Of these adolescence studies, five studies were on promoting sexual health and wellbeing, one was on preventing adolescence pregnancy, one was on health of pregnant women and girls and their new-born infants and the rest of the studies were on gender-based violence and dating violence. [8] The limitations of the systematic reviews were that they

only included randomised control trials and quasi-experimental studies therefore some relevant observational gender transformative intervention studies may have been excluded. Other primary studies that were excluded from the systematic reviews in the initial evidence gap map and systematic review of reviews were not considered. The systematic review did not include the cost effectiveness of the interventions therefore there is a gap in the evidence.

An economic evaluation is defined as the comparative analysis of alternative courses of actions in terms of both their costs and consequences. Partial or full economic evaluations may be conducted. Full economic evaluations have two or more competing alternatives and both the costs and consequences of the competing alternatives are considered. [9] There are three types of full economic evaluations, cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA). These economic evaluations differ in the way outcomes are measured. In cost effectiveness analyses, natural or disease specific outcomes for the interventions are used. The cost utility analysis uses generic outcome measures, for example the quality adjusted life years (QALYs) and disability adjusted life years (DALYs). Cost benefit analyses measure both costs and outcomes in monetary values. Partial economic evaluations consider costs and or consequences but there may not be comparison between alternative interventions or costs may not be related to benefits.[9] Five types of partial economic evaluations may be distinguished, outcome description, cost description, cost outcome description effectiveness evaluation and cost analyses.[9]

Economic evaluations theoretical underpinnings are in welfare economics. *Welfare economics* is a branch of economics concerned with maximising social welfare. It assumes rational individuals who maximise their utilities and that the overall welfare of society is a function of individual utilities. Economic evaluations that apply *welfare economics* to health care are concerned with individual utility. Whereas, Economic evaluations *that apply extra-welfarist* economics are concerned with maximising health, including individual and social preferences. *Extra-welfarist* economics builds on but goes beyond the individualist focus in welfare economics.[9]

Full economic evaluations are usually the preferred type of economic evaluations for inclusion in systematic reviews. Inclusion of partial economic evaluations in systematic reviews of economic evaluations is justified when there is lack of knowledge on a decision topic.[9,10] Systematic reviews of economic evaluations are important in synthesising and critically appraising primary economic evaluations to inform policy decisions and identify knowledge gaps. Some question the utility and value of systematic reviews of economic evaluation studies because of the limits in generalisability from the

findings. This is due to variations in; resource use and costs across countries and time frames, context and populations and differences in the decision-making context.[11] However, there is a growing number of application of systematic reviews of economic evaluations because they are important for decision makers in identifying the range and quality of available studies for a particular resource use or cost effectiveness question, obtaining results for intervention choices or trade-offs they are considering and also they provide an enhanced understanding of the different conditions that promote effectiveness and efficiency of different interventions.[9,12]

To our knowledge, few systematic reviews of economic evaluations targeting sexual and reproductive health have been published.

A systematic review to assess the costs and outcomes of control programmes for sexually transmitted infections (STIs) in young people aged 30 and below from the Organisation for Economic Co-operation and Development (OECD) countries was conducted by Bloch *et al*, 2021.[13] There were thirty-one studies that met the inclusion criteria and 25 of these studies were on chlamydia screening, 6 studies were on gonorrhoea and one on HIV screening. The publication period covered was 1999 to 2019. Modelling was the predominant study design (30 studies), there was significant heterogeneity in the methods applied which affected the comparability of the results. Most of the interventions included in the systematic review were cost-effective.[13] Since most of the economic evaluations that met the inclusion criteria were on chlamydia, the focus of the study was limited. There were no studies on behavioural interventions or equity in access to screening interventions which limited applicability of the study by decision makers. Limiting studies to OECD countries restricted applicability of findings to some settings.

In another systematic review conducted by Shepherd *et al*, 2010 to determine the effectiveness and cost-effectiveness of behavioural interventions for the prevention of sexually transmitted infections in adolescents aged 13-19 years old, 5 economic evaluation studies met their inclusion criteria. All five studies were on cost effectiveness of HIV prevention interventions and only one of these studies included other sexually transmitted infections. The search period was for publications from 1990 to 2008. All included studies were modelling studies, there were differences in the assumptions and parameters used in the models leading to variability in the estimated cost-effectiveness of the interventions. The studies were all from the United States of America (USA) except one multi-country study that was from Sub-Saharan Africa and Southeast Asia. [14] The systematic review is not current and needs to be updated to include findings from more recent studies. The interventions in the

systematic reviews of economic evaluations were not gender transformative and they did not cover all the WHO sexual and reproductive health and rights (SRHR) domains relevant for adolescents. There is therefore a gap in the available evidence. The purpose of this systematic review is to:

- synthesise the best available evidence on economic evaluations of gender transformative interventions targeted at preventing unintended pregnancy and promoting sexual health in adolescents.
- Assess the methodological quality of the economic evaluation studies.
- Identify the gaps in the economic evaluations evidence

METHODOLOGY

The Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRISMA-P 2015) was used to guide the development of this protocol (appendix 1).[15] The systematic review will be conducted and reported following the PRISMA guidelines, 2020.[16] We registered the protocol on the International Prospective Register of Systematic Reviews (PROSPERO), registration number CRD42021264698 (https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=264698).

Eligibility criteria

Studies will be selected according to the criteria stated below.

Inclusion criteria

Type of studies

Partial and full economic evaluations will be included in the systematic review. Partial economic evaluations eligible for inclusion include cost analyses, cost consequence studies, and cost minimisation analyses. The three types of full economic evaluations will be included: CEA, CUA and CBA. In addition, both trials based and model-based economic evaluation studies will be included in the systematic review. The economic evaluations should either compare different interventions or an intervention compared to a control which may be the standard of care or no intervention.

We will include qualitative evaluations with economic evaluation quantitative data of a single intervention, as well as economic evaluations alongside observational studies.

Where the economic evaluation of gender transformative approaches was done as part of a larger study, the study will only be included if the relevant results can be differentiated in terms of effects and costs of the gender transformative intervention. Publications from 1 January 1990 – 31 December 2021 will be included. We will restrict the search to articles from 1990 onwards because the studies from before 1990 will not be relevant due to changes in social norms and behaviours.[17] We will include articles published in the English language.

Population

The population of interest is adolescents aged between 10 to 19 years old from any country. Studies for either boys or girls or both sexes will be considered. Where there are studies with adolescents and children or adolescents and adult populations, we will include studies that have outcome measures stratified by age and outcomes for adolescents can be identified. If the outcome measures are not specified for different age groups, the study will be excluded.

Intervention

Economic evaluations for interventions that are gender transformative will be eligible for inclusion in the review. Gender transformative components will be determined according to the definition published by WHO and applied in the study by Ruane-McAteer *et al*, 2020. These interventions target transforming harmful gender norms, or practices or gender-based inequalities at individual or group level AND transforming unequal gender norms, practices or gender based inequalities.[8]

The interventions are within the WHO sexual and reproductive health and rights (SRHR) domains for adolescents, and these include:

- Ensuring the health of pregnant girls and their infants
- Preventing unintended pregnancies and unsafe abortion
- Promoting sexual health and wellbeing (prevention of sexually transmitted infections and HIV)
- Promoting sexual reproductive health in disease outbreaks
- Preventing and responding to violence against girls and harmful practices like female genital mutilation, early and forced marriages [18,19]

Setting

All types of healthcare or community settings from any country will be considered.

Outcome measures

The outcome measures from cost-effectiveness analyses will be relative resource use, cost and Incremental Cost Effectiveness Ratio (ICER). Outcome measures from cost benefit analyses will be relative resource use, costs and Incremental Net Benefit Ratio (NBR) or Net Present Value (NPV). For Cost-utility analyses outcome measures will be resource use; costs and Incremental Cost Effectiveness Ratio with costs expressed in monetary units and effects in QALYs or DALYs. Outcome measures from costing analysis and cost minimization analysis partial economic evaluations will be resource use and cost, for cost consequence analysis multiple outcomes indicated in the relevant studies will be considered.

Exclusion criteria

Studies will be excluded if they were done as part of a variety of interventions being compared and could not be differentiated in terms of effects and cost of interventions. Non-original studies will not be included. Studies done in non-adolescent populations will not be considered. Studies that did not provide costing details will not be included. Commentaries, editorials, reviews, and protocols will be excluded. Posters, conference presentations or abstracts with no full articles will not be included in the systematic review.

We will exclude systematic reviews of economic evaluations. However, we will scan search their reference list for primary economic evaluations studies and include those studies if they meet our inclusion criteria.

Search methods for identification of studies

We conducted a preliminary search on PROSPERO, Cochrane Library and PUBMED to determine if there were similar systematic reviews that are in process or had been published. The full title or key words to describe the population, intervention and outcomes were used in the search. Of the 11 review titles identified on PROSPERO, 2 reviews on Cochrane Library and 33 titles on PUBMED (appendix 2a), there were no completed or ongoing systematic reviews that matched all aspects of our proposed systematic review.

We will search the following public health and economic evaluations bibliographic databases for full economic evaluation studies that meet our selection criteria; PubMed, Cochrane, National Health Service EE database, SCOPUS, CINHAI, Web of Science and Paediatric EE Database. Not all relevant studies may be published in one database therefore we will search a variety of databases as stated to reduce bias in the study selection. The economic evaluation database, National Health Service EE

database has publications up until March 2015 and is no longer publishing, whereas Paediatric EE Database is updated annually therefore general databases are useful in finding more recent publications.[20,21] Minor adaptations of the search strategy will be done to meet the needs of each database when necessary. We will scan reference lists of included economic evaluation studies of relevant reviews identified during the search to ensure literature saturation. A grey literature search for unpublished data will also be conducted to ensure that an extensive search for articles has been conducted. Databases that include MedNar or Google Scholar, ProQuest Dissertations, and the Online clinical trials registers will be searched for unpublished studies. Key words derived from the title and listed in the search strategy will be used in the grey literature search.

Search terms and draft search strategy for PubMed are in appendix 2b. Search terms for SRHR interventions were adopted from the evidence gap map and systematic review by Ruane-McAteer *et al*, 2019.[7]

Data management

Endnote X8 will be used to store all references selected for the systematic review from the different databases and to remove duplicate results. The screening and study selection will be done in Microsoft excel. All study data will be saved on a file on the computer and backed up on an external hard drive during the study period.

Study selection

The first reviewer (JN) and second reviewer (TA) will independently screen the titles and abstracts of the articles obtained from the search. Titles and abstracts rejected by both reviewers will not be included in the study. Full articles of the titles and abstracts that meet the study inclusion criteria will be sourced and reviewed for inclusion into the study. Where titles and abstracts are not clear, the reviewers will read the full article to determine eligibility. Any differences in the selection of articles by the two reviewers will be discussed and a consensus reached. Where the two reviewers fail to agree, the third author (LN) will be consulted to resolve the disagreement and reach a final resolution. The reviewers will contact authors of original studies if they need clarification during the selection process. Fig 1 summarises the selection process flow.

Data extraction

A standardised data extraction form will be used to extract relevant information from the research articles. The first reviewer (JN) will extract the data and the data extraction forms and the second reviewer (TA) will verify the information to check for errors in the data extraction. The data extraction form will be piloted before use in the study. The data extracted will cover *descriptive data* about the

- (i) study population/participants, intervention, comparator(s) and outcomes
- (ii) study methods including evaluation design type, analytic viewpoint(s), source of effectiveness data, prices and currency used for costing, period of analysis, sensitivity testing, measures of resource use, cost and health effect/clinical and cost effectiveness
- (iii) study context (geographical, health care and broader service delivery setting and culture)[22]

Secondly, the data extraction form will also cover results for the resource use and/or cost and/or cost effectiveness measures; and lastly where possible author conclusions about factors that promote intervention cost effectiveness.[22] The draft data extraction form which will be piloted is in appendix 3.

Any disagreements in the data extraction will be resolved in a meeting between the two reviewers and the third reviewer LN. In the event of missing data required for the systematic review, the reviewers will contact the study authors by email to request for further information. A maximum of 3 attempts to reach the authors will be done. If missing information cannot be obtained, the authors will decide on how to handle the missing data. This will be documented. The data extraction form is in the appendix section.

Critical appraisal of methodological quality

There is a lack of universally recognised methodological evaluation standard for systematic reviews of economic evaluations. There are at least eleven checklists and guidelines for the appraising of the quality of economic evaluation studies included in systematic reviews.[23] The most widely used tools for assessing the methodological quality of both trial based and model based economic evaluations in systematic reviews include the Drummond checklist (2005)[9], BMJ checklist (1996)[24] Consensus on Health Economic Criteria (CHEC) extended checklist[25,26]. [23,27] For this systematic review, we will use the CHEC extended checklist for trial and model based economic evaluations. We will use the Consensus on Health Economic Criteria (CHEC) extended checklist to meet the second objective of our

systematic review which is to assess the methodological quality of the economic evaluation studies. The CHEC checklist was developed for economic evaluations conducted along effectiveness studies and had questions on 19 criteria.[25] An extended guideline was later published with an additional criterion on modelling studies.[26] The scoring system as applied by Wijnen *et al*, 2017 will be used where a score of 1 will be allocated for criterion fully met, 0.5 criterion partially met and 0 for criterion not fulfilled. All criteria will be equally weighted, and a percentage will be calculated for overall quality assessment.[28]The results of the quality assessment will also be described narratively. The consolidated health economic evaluation reporting standards (CHEERS) statement[29] is a guideline for reporting standards for economic evaluations. It consists of 24 criteria on the minimum standards on reporting economic evaluations.[29] We will use the CHEERS statement checklist to assess reporting quality of the economic evaluations. The scoring system similar to the one proposed for the CHEC checklist was applied to the CHEERS statement checklist by Mangham-Jefferies *et al*, 2014.[30] We will use this scoring system for the CHEERS quality assessment where a score of 1 will be allocated for criterion fully met, 0.5 criterion partially met and 0 for criterion not fulfilled. All criteria will be equally weighted, and a percentage will be calculated for overall quality assessment of each included economic evaluation. Furthermore, the scores will be ranked as $\geq 75\%$ high quality, 50 -74% moderate quality and $< 50\%$ poor quality to determine an overall assessment for each study.[30] There are criteria that overlap between the CHEC and CHEERS checklists, but we opted to use both guidelines in their entirety despite some overlapping questions because we would like to separately report on methodological quality and reporting standards assessments.

Two reviewers (JN and TA) will appraise the articles independently and disagreements will be resolved through discussion or by consulting the third reviewer (LN).

Data analysis and synthesis of findings

All studies that met the inclusion criteria will be included in the data analysis and synthesis regardless of outcome from the quality assessment. A Prisma flow chart diagram will be used to show the search results and the number of articles selected for the systematic review. A narrative summary and tables will be used to present the results from the included studies. We will attempt to structure the narrative summary where data is available around the type of SRHR interventions, gender transformative components of each intervention, type of economic evaluation, methodological features around the economic evaluations, categorisation of outcomes, perspectives, and locations where the studies originate. Attempts will be made to use the Joanna Briggs Institute (JBI) three by three dominance

ranking matrix tool to compare relevant cost effectiveness studies if applicable. A table of the main features of the studies will be included to show similarities and differences by population, intervention, comparator, and outcome. The JBI three-by-three matrix dominance will be used to classify the cost-effectiveness outcomes of each included study. Based on the costs and health effects outcomes between the intervention and the comparator, we will classify each study as one of nine options under strong dominance, weak dominance, or non-dominance for the intervention. [22]

Patient and public involvement

Patients and the public will not be involved in the design, conduct, reporting, or dissemination plans of this research.

DISCUSSION

The systematic review will provide evidence on economic evaluations across all settings using a standard and reproducible method based on the PRISMA guidelines for systematic reviews. The inclusion and exclusion criteria were clearly stated and explained in detail. Although there are some systematic reviews of economic evaluations aimed at sexual and reproductive health issues, to our knowledge this is the first systematic review targeting the gender transformative elements of the interventions and conducting a comprehensive review of all relevant elements of the WHO SRHR. Our broad context and inclusion of all types of economic evaluations (partial and full) will be useful for decision makers from different environments. The systematic review will report on resource use data from the economic evaluations which will also be useful for improving the transferability of the review findings to different settings. It also helps different health systems identify future resource priorities. The data is useful for decision makers who are involved in the development of clinical practice guidelines. The quality assessment will help the researchers in the field identify areas of weaknesses which they can improve on in future research. Identifying gaps in the evidence helps on the mapping of future research priorities.

We restricted our search to publications in English due to lack of resources and time which will be a source of bias in the study because relevant non-English publications may be excluded. Although there are stated benefits in targeting adolescents for sexual and reproductive health gender transformative interventions in this study, the generalisability of the findings to other age groups is reduced. Scarcity of evidence to include in the systematic review is a potential risk of the study.

ETHICS AND DISSEMINATION PLAN

Ethics approval is not required because the review will not use individual patient data, instead publicly available economic evaluation research studies will be used. However, an ethics exemption was obtained from the Stellenbosch University Health Research Ethics Committee (HREC), Reference No: X21/05/012. The results of the systematic review will be published in a peer reviewed article and presented at a relevant scientific conference or workshop.

ACKNOWLEDGMENTS

We thank the Stellenbosch University Library and information services for enabling us to access articles that are not freely available and the librarian, Pamela Nyokwana for assisting with improving the search strategy.

Authors' contributions

LN conceptualised the study. All authors (JN, TA and LN) participated in the design of the systematic review. JN drafted the study protocol which was critically reviewed by TA and LN who provided technical expertise for the systematic review. All authors reviewed and approved the final version of the protocol. LN is the guarantor for the research study.

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Competing interests

None declared.

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Figure Legend

Figure 1. PRISMA flow diagram for study selection.

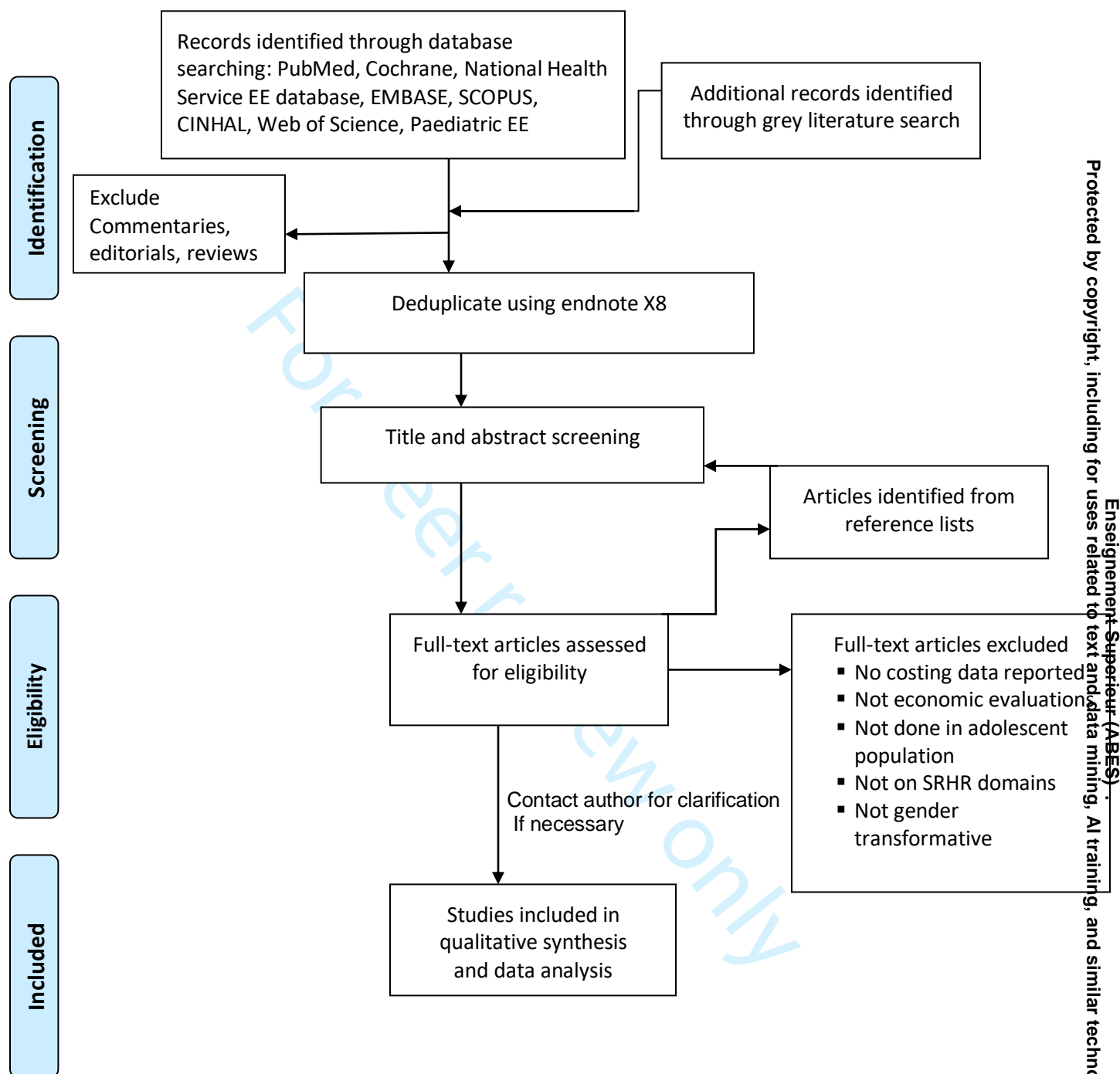


Figure 1. Selection process flow diagram

APPENDIX 1

PRISMA-P 2015 Checklist

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	√	<input type="checkbox"/>	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	√	<input type="checkbox"/>	PROSPERO Registration CRD42021264698
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	√	<input type="checkbox"/>	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	√	<input type="checkbox"/>	14
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Support					
Sources	5a	Indicate sources of financial or other support for the review	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Sponsor	5b	Provide name for the review funder and/or sponsor	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input type="checkbox"/>	<input type="checkbox"/>	n/a
INTRODUCTION					

Rationale	6	Describe the rationale for the review in the context of what is already known	√	<input type="checkbox"/>	4-7
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	√	<input type="checkbox"/>	7
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	√	<input type="checkbox"/>	7-9
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	√	<input type="checkbox"/>	9-10
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	√	<input type="checkbox"/>	Supplemental file – appendix 2b
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	√	<input type="checkbox"/>	10
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	√	<input type="checkbox"/>	10
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	√	<input type="checkbox"/>	11
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	√	<input type="checkbox"/>	7-8
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	√	<input type="checkbox"/>	9

Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	√	<input type="checkbox"/>	11-12
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	<input type="checkbox"/>	<input type="checkbox"/>	n/a
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	<input type="checkbox"/>	<input type="checkbox"/>	n/a
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input type="checkbox"/>	<input type="checkbox"/>	n/a
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	√	<input type="checkbox"/>	11-12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input type="checkbox"/>	√	

Preliminary scoping search for ongoing and published related systematic reviews

PROSPERO

#1 Adolescent* OR boys OR girls 14711

#2 unintended pregnancy OR reproductive health OR sexual health OR gender transformative intervention OR gender transformative approach 1215

#3 economic evaluation OR cost effectiveness analysis OR cost utility analysis or cost benefit analysis OR cost minimisation analysis OR costing analysis OR cost consequence analysis 2103

#4 #3 AND #2 AND #1 11

Of the 11 review titles, there was no completed or ongoing review that matched all aspects of our proposed systematic review.

COCHRANE

Advanced search

Adolescent* OR boys OR girls in Title Abstract Keyword AND "unintended pregnancy" OR "reproductive health" OR "sexual health" OR "gender transformative intervention" OR "gender transformative approach" in Title Abstract Keyword AND "economic evaluation" OR "cost effectiveness analysis" OR "cost utility analysis" OR "cost benefit analysis" OR "cost minimisation analysis" OR "costing analysis" OR "cost consequence analysis" in Title Abstract Keyword

2 Cochrane reviews and 0 protocols were obtained in the search results. The reviews were for effectiveness studies and did not match the objectives of our proposed systematic review.

PUBMED

#1 Adolescent*[Title/Abstract] OR boys[Title/Abstract] OR girls[Title/Abstract] - 387 821

#2 "unintended pregnancy"[Title/Abstract] OR "reproductive health"[Title/Abstract] OR "sexual health"[Title/Abstract] OR "gender transformative intervention"[Title/Abstract] OR "gender transformative approach"[Title/Abstract] - 31 170

#3 "economic evaluation" OR "cost effectiveness analysis" OR "cost utility analysis" OR "cost benefit analysis" OR "cost minimisation analysis" OR "costing analysis" OR "cost consequence analysis" - 99 231

#1 AND #2 AND #3 - 33

APPENDIX 2

Research Question

In adolescents aged 10 -19years old, what are the cost-effectiveness of gender-transformative interventions on preventing unintended pregnancy and promoting sexual health?

PICO Format

P -adolescents (10-19years old), boys and girls

I – Gender transformative interventions addressing the WHO Sexual Reproductive Health Rights outcomes (SRHR) domains.

- Ensuring the health of pregnant girls and their infants
- Preventing unintended pregnancies and unsafe abortion
- Promoting sexual health and wellbeing (prevention of sexually transmitted infections and HIV)
- Promoting sexual reproductive health in disease outbreaks
- Preventing and responding to violence against girls and harmful practices like female genital mutilation, early and forced marriages

O – economic evaluations

- Cost effectiveness
- Cost utility
- Cost benefit
- Cost minimization analysis
- Costing analysis
- Cost consequence analysis
- Decision analysis

Search Strategy – PUBMED

a. MeSH Terms

Concepts #1 Adolescents	Mesh terms: "Adolescent"[Mesh] Search Terms/ key words: Adolescents or Adolescence or Teens or Teen or Teenagers or Teenager or Youth or Youths or Female Adolescent, or Female Adolescents or Male Adolescent or Male Adolescents or minor or minors
#2 SRHR	MeSH terms: "Reproductive Health"[Mesh] OR "Reproductive Health Services"[Mesh] OR "Sexual Health"[Mesh] OR "Pregnancy"[Mesh] OR "Pregnancy, Unplanned"[Mesh] OR "Sex Offenses"[Mesh] OR "Abortion, Criminal"[Mesh] OR "Abortion, Legal"[Mesh] OR "Abortion, Induced"[Mesh] OR "Condoms"[Mesh] OR "Condoms, Female"[Mesh] OR "Gender-Based Violence"[Mesh] OR "Sexually Transmitted Diseases"[Mesh] Search terms: sexual health or reproductive health or maternal health or maternal welfare or maternal mortality or neonatal health or perinatal care or perinatal health or prenatal care or prenatal health or antenatal health or ante-natal health or postnatal health or postnatal health or post-part* or post part* or newborn health or family planning or

	<p>contracepti* or condoms or condom or pregnan* or abortion or pregnancy termination or induced abortion or</p> <p>abort* or birth or miscarriage or spontaneous abortion or stillb* or Minimum Initial Service Package or obstetric* or gynecology or gynaecology or safe motherhood or safe delivery or or sexually transmitted infection* or sexually transmitted disease* or HIV or Human immunodeficiency virus or AIDS or acquired immune deficiency syndrome or PMTCT</p> <p>gender based violence or partner violence or family violence or violence against women or domestic violence or sexual abuse or sex crime or sexual crime or or sexual violence or rape or intimate partner violence or partner violence or partner abuse or sexual assault or sexual harassment or sexual coercion or forced sex or sexual exploitation or coercive control or or female genital mutilation or FGM or female genital cutting or FGMC or female circumcis* or (early and marriage) or (child and marriage) or (forced and marriage) or (arranged and marriage) or (abduction and marriage)</p>
# 3 Economic evaluation	<p>MeSH terms "Cost-Benefit Analysis"[Mesh] OR "Decision Support Techniques"[Mesh]</p> <p>Key words: Cost-Benefit or Cost-Benefit Analyses or Cost Benefit Analys* or Cost Effectiveness or Cost-Benefit Data or Cost Benefit Data or Data, Cost-Benefit or Cost-Utility Analysis or Analyses, Cost-Utility Analysis, Cost-Utility or Cost Utility Analys* or Economic Evaluation* or Economic Evaluations or</p> <p>Marginal Analysis or Analyses, Marginal or Analysis, Marginal or Marginal Analyses or Cost Benefit or Costs and Benefits or Benefits and Costs or Cost-Effectiveness Analysis or Analysis, Cost-Effectiveness or Cost Effectiveness Analysis or Costing analys* or cost minimization analys* or cost minimisation analys* or cost consequence analys*</p>
#4 Gender transformative intervention	<p>Search terms: "gender transformative intervention*" OR "gender transformative approach"</p>

Search will be conducted using MeSH terms and free text from the listed terms using advanced search options on PubMed.

- 1 “gender transformative intervention*”
- 2 “gender transformative approach*”
- 3 1 OR 2
- 4 “reproductive health” or "Reproductive Health"[MESH] or "Reproductive Health Services"[MESH]
- 5 “sexual health” or "Sexual Health"[MESH]
- 6 “sexual reproductive health”
- 7 “sexually transmitted infection*”
- 8 “sexually transmitted disease*” or "Sexually Transmitted Diseases"[MESH]
- 9 “HIV”
- 10 “Human immunodeficiency virus”
- 11 “AIDS”
- 12 “Acquired immuno deficiency syndrome”
- 13 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
- 14 “family planning”
- 15 "contracept*"
- 16 “condom*” or "Condoms"[Mesh]
- 17 “condom use”
- 18 “pregnan*” or "Pregnancy"[Mesh]
- 19 “unintended pregnan*” or "Pregnancy, Unplanned"[MESH]
- 20 “abort*”
- 21 “unsafe abort*”
- 22 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
- 23 “gender based violence”
- 24 “domestic violence”
- 25 “partner violence”
- 26 “violence against girls”
- 27 “sexual abuse”
- 28 “sex crime”
- 29 “sexual crime”
- 30 “intimate partner violence” or "Intimate Partner Violence"[MESH]

31 "sexual assault" or "Sex Offenses"[MESH]
32 "coercive control"
33 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
34 "female genital mutilation"
35 "FGM"
36 "female genital cutting"
37 "FGC"
38 34 or 35 or 36 or 37
39 "early marriage"
40 "arranged marriage"
41 "child marriage"
42 38 or 39 or 40
43 "economic evaluation"
44 "cost benefit analys*" or "cost benefit" or "Cost-Benefit Analysis"[MESH]
45 "cost effectiveness" or "cost effectiveness analys*"
46 "cost utility" or "cost utility analys*"
47 "cost analys*"
48 "cost consequence analys*" or "cost consequence"
49 "cost minimization" OR "cost minimization analysis"
50 "cost minimisation" OR "cost minimisation analysis"
51 "decision modelling"
52 "decision analysis"
53 "decision analytic modelling"
54 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53
55 3 or 13 or 22 or 33 or 38 or 42
56 "Adolescen*" or "teen*" or "youth*" or "girl*" or "boy*" or "male adolescen*" or "female
adolescen*" or "Adolescent"[MESH]
57 "adolescent boy" or "adolescent girl*" or "adolescent boys and girls"
58 56 or 57
59 54 AND 55
60 59 AND 58

Limits for the search are Human studies and publication years 1990 -2021

APPENDIX 3
Draft data extraction form

Date form completed:
Name of reviewer extracting data:
Study details
Study Title:
Author and publication year:
Author contact details:
Study context: <ul style="list-style-type: none">- Healthcare, service delivery, social context- Country
Study objectives:
Source of funding:
Conflict of interest :
Methods
Type of study <ul style="list-style-type: none">(i) For effectiveness data(ii) Economic evaluation study design
Participants / population:
Types of Intervention(s):
Types of outcome measure
Decision: <ul style="list-style-type: none">- If excluded, give reason for exclusion
DO NOT PROCEED IF STUDY IS EXCLUDED FROM THE REVIEW
Perspective:
Primary cost / consequences / outcome measures:
Comparators:
Time horizon:
Discounting (if discounting was used, list the discount rates):
Currency:
Data sources for costs:
Data sources for clinical data:
Data sources for utility data:
Was modelling used? If yes, state type of modelling:
Results
Costs / resources:
Outcomes / benefits:
Incremental cost effectiveness:
Analysis of uncertainty:
Author's conclusions:

For peer review only