What approaches to peri-conception care for women with pre-existing medical conditions work, for whom, and in what circumstances? A protocol for a realist review

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Review question

The aim of this review is to use a theory-driven evidence synthesis to explore, amongst a group of women with pre-existing medical conditions, what form of peri-conception care works for whom, how these approaches work, and in what circumstances. Following the initial literature search, we will conduct the review in two main phases: firstly, we will conduct systematic searches to develop initial program theories, and secondly, we will conduct targeted searches to test and refine these theories. The objectives of this two-phase review are listed below:

1. To develop theory relating to the main factors or mechanisms that are thought (both scientifically and experientially) to explain why women (and their partners) with pre-existing medical conditions a) seek or receive appropriate condition-specific peri-conception care or advice, and b) engage in recommended behaviour change prior to pregnancy (we are defining "engagement in recommended behaviour change" as engagement in at least one condition-specific behaviour change, which is known to reduce morbidity or mortality for either mother or baby prior to conception)
2. To identify types of peri-conception care that may be particularly beneficial and appropriate for different groups of people in different contexts

Searches

In line with realist review methodology, the purpose of the first phase of literature searching will be to develop program theories that will explicate underlying mechanisms explaining how approaches to peri-conception care are thought to work for different groups of people in different contexts. A "broad brush" approach will therefore be applied to the search in order to capture all types of peri-conception care, including all terminology that we identify as relating to this topic. Databases that we will search are MEDLINE, Embase, PsycINFO, Cochrane Library, British Nursing Database and CINAHL. We will include studies written in English (to avoid the need for translation), from the Organisation for Economic Co-operation and Development (OECD) member countries, to select those with similar approaches to healthcare and economic status. Initially, we will not limit the publication date of studies, as searches are not anticipated to result in high numbers of hits.

We will undertake supplementary searches of grey literature, using strategies including emailing authors of identified studies, conducting Google and Google Scholar searches, hand searching relevant journals and conference proceedings, backwards and forward citation chasing, and searching for theses and dissertations on the British Library EThOS online service. We will also search additional websites for data, including the Department of Health and relevant condition-specific third sector websites such as those belonging to Diabetes UK, the British Heart Foundation and Epilepsy Action.

Having developed initial program theories in phase one of the review, the second phase will involve searching for empirical evidence that can be used to test and refine these theories; "testing" in this case will constitute adjudicating between 2 rival theories, or more where applicable. Searching will be purposive (based on the theoretical framework) and iterative as the review evolves; searching will stop when saturation is reached. Search terms for

database searches in this second stage will depend on results from the first phase and will be discussed within the review team and wider stakeholder advisory group for sense checking and completeness.

Types of study to be included

We will include evidence that provides descriptions of peri-conception care using a broad variety of methods. This will include both qualitative and quantitative studies as well as non-empirical studies. We will therefore include any studies that provide a detailed account of a peri-conception care intervention as outlined above. If numerous studies are identified, these will be prioritized based on relevance and rigor (see below).

Condition or domain being studied

This review concerns peri-conception care. The period before and during very early pregnancy is referred to as "peri-conception". The precise period used is dependent on the perspective from which this concept is viewed, which may be biological (4 weeks either side of conception), individual (from the point at which a couple decide they want to have a baby) or population level (from adolescence through to the end of the reproductive life stage). For the purpose of this review, a combination of all three will be included, to address the issues of both planned and un-planned pregnancy, and in recognition of the fact that some conditions (such as raised obesity) may take several months or even years of behaviour change to address.
Care during the peri-conception period is particularly important for women with pre-existing medical conditions; these include diabetes, epilepsy, cardiac conditions, hypertension, hypothyroidism and severe mental health problems. This is due to the increased risk of morbidity and mortality for both mothers and babies in these groups. This is demonstrated in the most recent report on maternal mortality in the United Kingdom (UK), which highlighted that two thirds of women who died in 2013-15, during or up to six weeks after giving birth or the end of pregnancy had pre-existing physical or mental health problems. The report stated that forward planning could have prevented many of these deaths. These findings emphasize the importance of this area of care, which has been somewhat neglected to date in terms of both research and policy, hence the focus of our proposed review upon peri-conception care for women with pre-existing medical (including physical and mental health) conditions.

Participants/population

The population inclusion criteria will be women of reproductive age, and / or their partners, who have any type of pre-existing medical (including physical and mental health) condition, and who are seeking or receiving peri-conception care. This may be part of routine primary or secondary care related to their condition, or specifically because they are considering planning a pregnancy. Some women in this group may have previously experienced pregnancy, and some may have previously experienced a pregnancy loss, complicated pregnancy, or neonatal loss; others will not have experienced any of these events. We will not initially restrict evidence to any particular medical or mental health condition, but we may iteratively focus on one or more specific conditions in response to findings from our initial search phase. Interventions that will be excluded, include any aimed specifically at

women experiencing fertility problems, seeking advice regarding contraception or delaying pregnancy, women seeking termination of pregnancy or pre-pregnancy screening.

Intervention(s), exposure(s)

We will include evidence concerning a range of peri-conception care packages aimed specifically at women with pre-existing medical conditions. Some of these will target all women of reproductive age, and others will target women who are planning, or considering planning, a pregnancy. Although the evidence is likely to be scarce, our search will include care offered to men, as well as women, and include care offered to same-sex couples. Any form of peri-conception intervention will be included in the first phase; this may include face-to face clinics, telephone advice, video recordings or internet-based resources including web and mobile applications (apps). Intervention inclusion in the second phase is likely to focus on face-to-face clinics and mobile apps, but we may iteratively focus on another area in response to initially identified evidence, resulting in a shift or expansion in scope.

Comparator(s)/control

Since the testing of programme theories will involve a range of study designs, including evaluations and qualitative research, comparator criteria in both phases will mainly be applied to comparative effectiveness studies. In these studies, comparator criteria will be women with pre-existing medical conditions who have not received any peri-conception care. Comparator criteria may also be applied to studies involving similar types of care where access or engagement may differ resulting in significant differences in outcome.

Context

Main outcome(s)

We anticipate that the outcomes will be context specific, and may emerge during both phases of the review process. However, the likely outcomes relating to peri-conception care for this population group include, but are not limited to, the following:
1. Health care professionals' awareness and delivery of appropriate peri-conception care
2. Health care professionals' awareness of and referral to appropriate peri-conception care
3. Women's (and/or their partners') recollection of peri-conception advice as part of normal primary or secondary care related to their medical condition
4. Women's (and/or their partners') initial attendance at a peri-conception clinic
5. Women (and/or their partners) downloading or accessing specific peri-conception advice / mobile app
6. Women's (and/or their partners') engagement in appropriate health behaviour change
Appropriate health behaviour change will be dependent on the individual woman's circumstances or "context" related to her pre-existing medical condition. However, in this review we are interested in how the context may influence the firing of particular mechanisms, rather than the effectiveness of the intervention (peri-conception care), which, in many cases, has been explored elsewhere.

Additional outcome(s)

Since this is a realist review, there may be unintended outcomes of peri-conception care that the authors will be interested in, but are unaware of at this stage.

Data extraction (selection and coding)

The first phase of this review will use the realist approach of "engaging with" the data, rather than formal data extraction; this involves note taking, annotation and conceptualisation. Specifically, we will examine a variety of types of peri-conception care and factors contributing to identified intended and un-intended outcomes. The process will be continually refined based on discussion, with the aim of developing programme theory for further refinement in phase two.
Data extraction in phase two of this review will involve annotation of papers, collation of evidence using a bespoke data extraction form (based on the theoretical framework identified at the end of phase one), and reportage, which involves the use of extracts of evidence to identify the basis of inferences used for synthesis. Data will be extracted by one reviewer and checked by another. The data will be used to clarify and explain the mechanisms and refine programme theory, and as such, data will not simply be classified, but used to develop a line of argument that feeds into the final synthesis stage.

Risk of bias (quality) assessment

In line with requirements for realist review, we will assess the quality of data based on relevance (to the programme theory) and rigour (credibility and trustworthiness of the methods used). This will be achieved in the first phase of the review by using a hybrid classification tool, which classifies sources as "conceptually-rich" or "thin". This enables focus on stronger sources without exclusion of weaker ones.
Standard quality assessment tools will also be used in the review. This includes the Cochrane Collaboration's tool for assessing risk of bias in studies of effectiveness, and the Wallace criteria for appraisal of qualitative studies. Appraisal of studies during both phases will be undertaken by two reviewers independently, with any disagreement being resolved through discussion and, where necessary, a third reviewer.

Strategy for data synthesis

We aim to develop an understanding of how different approaches to peri-conception care might work for women with pre-existing medical conditions by identifying how specific outcomes are generated by relevant mechanisms, which are triggered in particular contexts. We will seek recurring patterns across the data. A similar strategy will be used for both phases, following realist methodology, which may involve some of the following tools:
1. juxtaposition of sources of evidence, for example when evidence about implementation in one source enables insights into evidence about outcomes in another source
2. reconciling of sources of evidence, when results differ in apparently similar circumstances, further investigation is appropriate in order to find explanations for why these different results occurred
3. adjudication of sources of evidence, on the basis of methodological strengths or weaknesses
4. consolidation of sources of evidence, when evidence about mechanisms and outcomes is complementary and enables a multi-faceted explanation to be built

5. situating sources of evidence, when outcomes differ in particular contexts, an explanation can be constructed of how and why these outcomes occur differently
Transparency will be achieved by documenting the reasoning processes used and applied during synthesis as outlined above. In phase one we will organise studies according mechanisms and contextual factors, such as type of pre-existing medical condition and demographics. We will tabulate the data to explore combinations of contexts, mechanisms and outcomes, and develop a series of "if, then" statements around mechanisms, which we will refine through discussion. The resulting theoretical explanatory model, including CMO configurations, will be used as a theoretical framework for phase two of the review. Synthesis during phase two will follow the strategy outlined in phase one above; with the purpose of refining programme theory developed during phase one in the light of evidence and analysis of findings from phase two.

Analysis of subgroups or subsets

The purpose of this realist review is to explore what works for who and how. The exploration of different types of participants, interventions and settings is therefore an integral part of the review, and will be addressed when analysing context, mechanism and outcome configurations.