A Systematic Review of Clinical Guidelines for Preconception Care

Edwina Dorney, BAppSc, MBBS (Hons), MPH[1] Jacqueline A. Boyle, MBBS, FRANZCOG, MPH&TM, PhD[2] Ruth Walker, APD, BNutrDiet(Hons), BAppSc, DipEd, PhD[2] Karin Hammarberg, RN, BSc, PhD[3] Loretta Musgrave, RM, RN, Med[4] Danielle Schoenaker, BSc, MSc, PhD[5,6] Brian Jack, MD[7] Kirsten I. Black, MBBS, M.Med, FRANZCOG, MSRH, PhD, DDU[1]

[1] Faculty of Medicine and Health, The University of Sydney, New South Wales, Australia
[2] Monash Centre for Health Research and Implementation, School of Public Health and Preventative Medicine, Monash University, Melbourne, Victoria, Australia
[3] Global and Women's Health, School of Public Health and Preventative Medicine, Monash University, Victoria, Australia
[4] School of Nursing and Midwifery, Faculty of Health, University of Technology Sydney, Sydney, Australia
[5] School of Primary Care, Population Sciences and Medical Education, Faculty of Medicine, University of Southampton, Southampton, United Kingdom
[6] NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom

Address for correspondence Edwina Dorney, BAppSc, MBBS (Hons), MPH, Faculty of Medicine and Health, The University of Sydney Central Clinical School, Medical Foundation Building K25, Sydney, NSW 2006, Australia (e-mail: edwina.dorney@sydney.edu.au).

Semin Reprod Med 2022;40:157–169

Abstract

Preconception care (PCC) involves a wide-ranging set of interventions to optimize health prior to pregnancy. These interventions seek to enhance conception rates, pregnancy outcomes, childhood health, and the health of future generations. To assist health care providers to exercise high-quality clinical care in this domain, clinical practice guidelines from a range of settings have been published. This systematic review sought to identify existing freely accessible international guidelines, assess these in terms of their quality using the AGREE II tool, and assess the summary recommendations and the evidence level on which they are based. We identified 11 guidelines that focused on PCC. Ten of these were classified as moderate quality (scores ranging from 3.5 to 4.5 out of 7) and only one was classified as very high quality, scoring 6.5. The levels of evidence for recommendations ranged from the lowest possible level of evidence (III) to the highest (I-a): the highest quality evidence available is for folic acid supplementation to reduce risk of neural tube defects and the role of antiviral medication to prevent HIV transmission. This systematic review identified that high-quality guidelines on PCC are lacking and that few domains of PCC recommendations are supported by high-quality evidence.

Keywords
- preconception
- pre-pregnancy
- clinical practice guideline
- policy
- systematic review

What Is Preconception Care and Why Is It Important?

Preconception care (PCC) entails a comprehensive set of interventions that aim to optimize health prior to pregnancy.[1] These include the identification, education, and modification of behavioral, biomedical, and social risk factors that can adversely affect the health of parents and their offspring.[2] While many women seek care when pregnant, interventions delivered during pregnancy alone

Issue Theme Preconception (Part 1); Guest Editors, Kirsten I. Black, MBBS, MMed, FRANZCOG, PhD, FFSRH, DDU and Jacqueline A. Boyle, MBBS, FRANZCOG, MPH&TM, PhD

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

DOI https://doi.org/10.1055/s-0042-1748190.
ISSN 1526-8004.

do not achieve the best health outcomes for women and their babies.[3] Optimizing the health of women and their partners prior to pregnancy improves conception rates, pregnancy outcomes, childhood health, and the health of future generations.[3]

Who Needs Preconception Care?

While the entire population stands to benefit from good preconception health, certain priority groups endure higher risk and therefore require targeted attention. Priority populations are considered to be populations that experience health inequity and disadvantage in accessing health care.[4] This can be due to demographic, social, and cultural factors, and the broader social determinants of health. Priority populations experience increased rates of adverse health outcomes, and their needs must be recognized in the health service delivery and policy implementation to reduce health disparities.[4]

However, several barriers have been identified in the delivery of PCC for those who are able to access it. In the primary care setting, these barriers include time constraints, lack of access to health care providers, and a lack of resources for assisting in the delivery of PCC.[5,6]

Clinical Practice Guidelines and Impact on Clinical Care

In 2008, the clinical workgroup for the select panel on PCC identified over 80 clinical content areas to be addressed in PCC.[7] Given there is such range of care areas to be covered in the provision of PCC, education and resources for health care providers are required to facilitate the provision of PCC. Clinical practice guidelines (CPGs) are evidence-based resources designed to assist health care providers deliver high-quality clinical care.[8] They promote supported, shared decision making for specific clinical scenarios. High-quality, accessible CPGs can enhance the delivery of PCC by providing health care providers with evidence-based recommendations and increase consistency of care.[9] Global resources that facilitate the sharing of knowledge and information have been suggested as a means to improve education and support practitioners in low- and middle-income countries to deliver PCC.[10]

Rationale and Objectives

This systematic review aims to identify and assess the quality of existing CPGs for PCC. It also aims to appraise the level of evidence underpinning these guidelines and assess if they support the delivery of equitable PCC by incorporating the needs of priority populations. The findings can inform strategies to improve delivery of comprehensive PCC.

Methods

This review was registered with the International Prospective Register of Systematic Reviews (PROSPERO, CRD420212 68130) and follows the recommendations in the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA-2020) guidelines.[11]

Inclusion Criteria

CPGs, or documents providing guidance on PCC to health care providers, such as consensus or position statements from a national or international organization, were eligible for inclusion if they were evidence based (reference list available), published since 2008 in English, or an English translation was available, and freely accessible to an international audience. Documents authored by private organizations or that were local or regional in their focus were excluded. Eligible documents were grouped into five categories determined by their practical application for the health care providers providing PCC.

Search Strategy

We conducted a systematic, online search across four academic health databases (OVID Medline, EBM Reviews Complete, EMBASE, and CINAHL), nine international clinical guideline registers (National Institute for Health and Care Excellence [NICE] Guidelines, Scottish Intercollegiate Guideline Network, National Guideline Clearinghouse [Agency for Healthcare and Research Quality], National Health and Medical Research Council Australia Guidelines Portal, International Guidelines Registry, World Health Organization, International Practice Guideline Registry Platform, Geneva Foundation for Medical Education and Research—Obstetrics and Gynecology Guidelines), ten related professional organizations (Centers for Disease Control and Prevention [CDC], National Academy of Medicine [NAM], American College of Obstetricians and Gynaecologists [ACOG], American Academy of Family Physicians [AAFP] Royal College of Obstetricians and Gynaecologists [RCOG] United Kingdom [UK], Faculty of Sexual and Reproductive Health UK, College of Family Physicians of Canada, Royal Australian and New Zealand College of Obstetricians and Gynaecologists [RANZCOG], Royal Australian College of General Practitioners [RACGP], Federation of Obstetric and Gynecologic Societies of India [FOGSI]), and two widely available online platforms (Google and Google Scholar).

Professional organizations searched were in the fields of primary care, reproductive health, public health, or family medicine, from the United States, the United Kingdom, Canada, Australia, and India. These professional organizations were selected as they are organizations from nations with a demonstrated interest in PCC and established PCC programs. The complete list of search terms used for PCC and CPGs for each platform is outlined in **Supplementary Material A** (online only). Search terms were adjusted to align with different database requirements. Searches were conducted in August 2021.

Review Process

Titles and abstracts were screened by two independent reviewers (E.D. and R.W., K.H., or L.M.) and any conflicts resolved by a third reviewer (K.I.B.). Full-text review was conducted by E.D. and R.W., K.H., or L.M., and any conflicts were again resolved by K.I.B. Reference lists and available supplementary files for CPGs were examined to identify any additional documents for inclusion.

Assessment of Guideline Quality

The AGREE-II tool was used to assess the quality of each guideline.[12] The AGREE II tool assesses 23 aspects of guideline quality across six domains, and two overall assessments of guideline quality with a maximum possible score of 7. Three reviewers appraised each guideline (E.D. and R.W., K.H., or K.I.B.). AGREE-II domain scores were calculated individually, and all domains were weighted equally. The threshold for determining a high-quality domain score was set at greater than 80% (equates to domain scores of 5.5–6) as adopted by other studies using the AGREE II tool.[13,14]

Data Extraction

The following data were extracted from each document: guideline authorship and publication information, target population, inclusion of men, inclusion of priority populations, consumer input, and summary of recommendations.

Table 1 Level of evidence and grade of recommendation

Level of evidence	
I-a	Evidence was obtained from at least one properly conducted randomized controlled trial that was done before pregnancy
I-b	Evidence was obtained from at least one properly conducted randomized controlled trial that was done not necessarily before pregnancy
II-1	Evidence was obtained from well-designed controlled trials without randomization
II-2	Evidence was obtained from well-designed cohort or case–control analytic studies, preferably from one center of research
II-3	Evidence was obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments could also be re-graded as this type of evidence
III	Opinions were gathered from respected authorities, based on clinical experience, descriptive studies and case reports, or reports of expert committees
Grade of recommendation	
A	There is good evidence to support the recommendation that the condition be considered specifically in a PCC evaluation
B	There is fair evidence to support the recommendation that the condition be considered specifically in a PCC evaluation
C	There is insufficient evidence to recommend for or against the inclusion of the condition in a PCC evaluation, but recommendation to include or exclude may be made on other grounds
D	There is fair evidence to support the recommendation that the condition be excluded in a PCC evaluation
E	There is good evidence to support the recommendation that the condition be excluded in a PCC evaluation

Assessment of Level of Evidence

We assessed the level of evidence informing each recommendation and determined the grade of each recommendation. For recommendations that were not directly referenced within the text, the reference list for the guideline document was searched and all related citations assessed. For consistency and comparison, we used the criteria shown in ►**Table 1** which was previously employed in a review of the components of PCC to assess the levels of evidence for each recommendation.[15] Each component was extracted by one reviewer (E.D.), and cross-checked by a second reviewer (J.A.B.).

Results

Guideline Identification and Selection

Searches identified 6,340 documents for screening. Of these, five documents were found in searches across international guideline registers and three on professional organizations' Web sites. Of the 188 documents selected for full-text review, 8 could not be retrieved. Some CPGs were not freely available to an international audience including two CPGs focused on PCC, one from China,[16] and the NICE Clinical Knowledge Summary on PCC from the United Kingdom.[17] A further 110 documents were excluded with reasons shown in ►**Fig. 1**. The remaining 70 documents were classified under the following headings determined by their content and how they are relevant to health care providers.

- PCC-focused CPG.
- Relevant but not a focused PCC CPG.
- Condition-specific CPG with a brief section on PCC.
- Condition-specific CPG with a comprehensive section on PCC.
- Health behavior issue that can be incorporated in PCC.

Given the variation in these guideline categories, and the extensive processes required to analyze their content, we limited our analysis for the current review to the 11 documents identified as PCC-focused CPGs.

Characteristics of PCC-Focused CPGs

The characteristics of the 11 PCC CPGs are shown in ►**Table 2**. Five documents were from the United States,[18–22] two each from Canada[23,24] and Australia,[25,26] one from India,[27] and one was an international collaboration from the International Federation of Obstetrics and Gynecology (FIGO).[28] Four guidelines had limited scope with two offering guidance on Zika virus only,[21,22] one guideline related to non-communicable diseases,[28] and one for people living with human immunodeficiency virus (HIV).[23] Three included guidance specifically for priority populations,[23,24,26] three acknowledged additional needs of priority populations,[19,27,28] and the remaining five guidelines did not differentiate care for priority populations.[18,20–22,25]

Assessment of Guideline Quality

The scaled scores for each domain of the AGREE-II tool are shown in ►**Table 3**. There was significant variation in all aspects of guideline quality, with the minimum range of 47

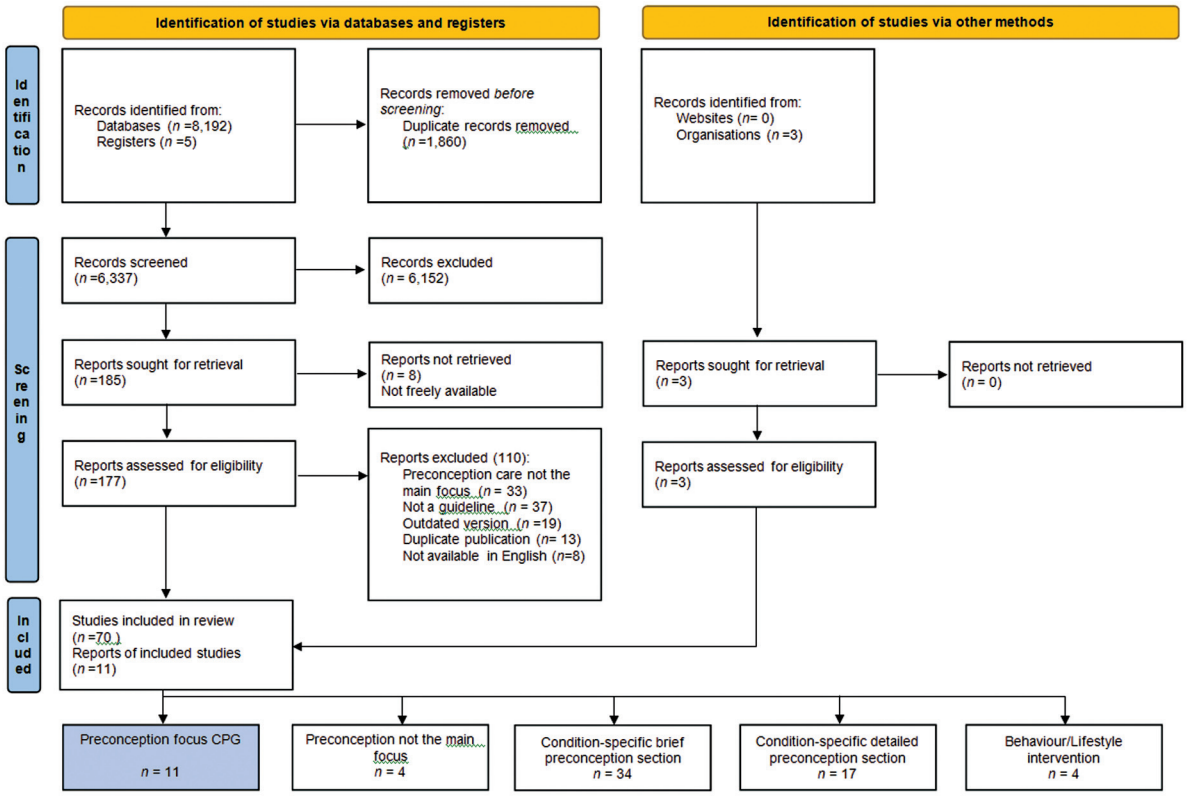

Fig. 1 Search results of international clinical practice guidelines for preconception care.

percentage points across the six domain scores. Domain 6, Editorial Independence, had the widest range of 86 percentage points. Domain 3, Rigor of Development, and domain 5, Applicability, were the lowest scoring domains across the sample.

Ten guidelines were classified of moderate quality (overall assessment: 3.5–4.5) with only one guideline classified as very high-quality scoring (6.5).

Guideline Content

The content and number of recommendations varied significantly across the guidelines. The number of recommendations from the CPGs ranged from 2 to 113 (►**Table 4**), which posed some challenges in drawing comparisons and summarizing the guideline advice. Given this variation, an analysis was made using the previously defined 82 clinical content areas of PCC and is shown in ►**Table 5**.[7] Only one new clinical content area of Zika virus was identified, bringing the total number of content areas to 83 (the guideline with 113 recommendations had several recommendations within a given content area). No CPG addressed all 83 content areas, and the range of content areas addressed ranged from 3 to 58.

Assessment of Level of Evidence

The level of evidence supporting each recommendation within each guideline is shown in ►**Table 4** (the full data extraction template is available in **Supplementary Material B** [online only]). Where a CPG referenced a lower level of evidence to support a recommendation, even when there is known higher-level evidence to support the recommendation (e.g., a level III document was cited, rather than a level I-a), the cited level of evidence was used. Where a CPG referenced the document by Jack et al on the clinical content of PCC,[7] we used the stated level of evidence within this document, as the lead author (B.J.) is an author for this review and we could be certain of the level of evidence. Where a CPG had more than one content area within a recommendation, the range of the level of evidence was provided, with documentation of the content area that had the highest level of evidence. One guideline could not be assessed because it did not reference its recommendations and had a limited reference list.[27]

Given that there was significant variation in the phrasing and categorization of recommendations across the 11 included CPGs, data for the levels of evidence have been reported in the following ways: level of evidence within a given CPG (►**Table 4**), and level of evidence to support each clinical content area of PCC (►**Table 5**). The levels of evidence in ►**Table 5** were compared with the levels of evidence for each clinical content area reported in 2008[7] to assess if there has been advancement in the evidence to support PCC. This occurred across the six clinical content areas of family planning and reproductive life planning, weight status, HIV, diabetes mellitus, vitamin D, and Zika virus.

The levels of evidence ranged from I-a to III with the highest quality evidence available for folic acid supplementation to reduce the risk of neural tube defects and antiviral medication to prevent HIV transmission.

Table 2 Characteristics of the included guidelines

Guideline title	Year of publication	Authorship/Organization	Intended audience	General or specific scope of guidance	Inclusion of men	Inclusion of priority populations	Consumer input
Prevention of non-communicable diseases by interventions in the preconception period: a FIGO position paper for action by healthcare practitioners	2020	Jacob et al[28] International Journal of Gynecology and Obstetrics	All health care providers, health care delivery organizations, public health policy makers	Specific Non-communicable diseases	Yes	Acknowledged (social determinants of health, LMICs)	No
Committee opinion no. 762: Prepregnancy counselling	2019	ACOG	Obstetricians and gynecologists	General	Acknowledged	Acknowledged LGBTQIA+, socioeconomic status	No
Zika virus and sexual transmission: updated preconception guidance	2018	Chen LH and Hamer DH Journal of Travel Medicine	Travel medicine specialists	Specific Zika virus	Yes	No	No
No. 354—Canadian HIV pregnancy planning guidelines	2018	Loutfy M et al Journal of obstetrics and gynecology Canada	All health care providers seeing women and men of reproductive age living with HIV	Specific People living with HIV	Yes	Yes Social determinants of health, sexual diversity, ethnocultural backgrounds and religion	No
Update: Interim guidance for preconception counselling and prevention of sexual transmission of Zika virus for men with possible Zika virus exposure - United States, August 2018	2018	Polen KD et al Morbidity and mortality weekly report; USA	Medical professionals	Specific Zika virus	Yes	No	No
Preconception care in family-centered maternity and newborn care: national guidelines	2018	PHAC	All health care providers, community health centers, allied health	General	Yes	Yes Social determinants of health, indigenous, ethnocultural backgrounds, LGBTQ	No
Pre-pregnancy counselling (C-Obs3a)	2017	RANZCOG	All health care providers providing care to women before pregnancy	General	No	No	Yes
Guidelines for preventive activities in general practice	2017	RACGP	Family physicians	General	No	Yes Indigenous, CALD, rural and remote, socioeconomic status	No
Good clinical practice recommendations on preconception care	2016	FOGSI	All health care providers seeing women and men of reproductive age	General	Yes	Acknowledged Socioeconomic status	No
Preconception care (position paper)	2015	AAFP	Family physicians	General	Yes	No	No
Recommendations for preconception counselling and care	2013	Farahi N and Zolotor A American Family Physician	Family physicians	General	No	No	No

Abbreviations: AAPF, American Academy of Family Physicians; ACOG, American College of Obstetricians and Gynecologists; CALD, culturally and linguistically diverse; FOGSI, Federation of Obstetric Gynecological Societies of India; LGBTQ, lesbian, gay, bisexual, queer; LGBTQIA+, lesbian, gay, bisexual, queer, intersex, asexual, and gender nonconforming; LMICs, low- and middle-income countries; PHAC, Public Health Agency of Canada; RACGP, Royal Australian College of General Practitioners; RANZCOG, Royal Australian and New Zealand College of Obstetrics and Gynecology.

Table 3 Scaled AGREE-II domain scores and overall guideline assessment

Guideline	Domain 1 Scope and purpose	Domain 2 Stakeholder involvement	Domain 3 Rigor of development	Domain 4 Clarity of presentation	Domain 5 Applicability	Domain 6 Editorial independence	Overall assessment score out of 7
Jacob et al: Prevention of noncommunicable diseases by interventions in the preconception period: a FIGO position paper for action by healthcare practitioners	78%	59%	27%	80%	29%	86%	4.0
ACOG: Committee opinion no. 762: prepregnancy counselling	91%	39%	6%	65%	18%	0%	4.5
Chen and Hamer: Zika virus and sexual transmission: updated preconception guidance	76%	17%	25%	83%	21%	50%	4.0
Loutfy et al: No. 354-Canadian HIV pregnancy planning guidelines	100%	89%	72%	98%	64%	83%	6.5
Polen et al: Update: interim guidance for preconception counselling and prevention of sexual transmission of Zika virus for men with possible Zika virus exposure - United States, August 2018	94%	24%	28%	65%	11%	61%	4.0
PHAC: preconception care in family-centered maternity and newborn care: National guidelines	48%	63%	24%	54%	25%	0%	4.0
RANZCOG: pre-pregnancy counselling (C-Obs3a)	58%	54%	24%	51%	9%	81%	3.5
RACGP: guidelines for preventive activities in general practice	72%	53%	17%	61%	6%	54%	4.0
FOGSI: good clinical practice recommendations on preconception care	69%	24%	19%	80%	13%	0%	3.5
AAFP: preconception care (position paper)	43%	30%	15%	69%	15%	0%	3.5
Farahi et al: recommendations for preconception counselling and care	63%	50%	26%	67%	3%	17%	4.5

Table 4 Level of evidence and grade of recommendations

Guideline title	Number of recommendations	Number of references	Level of included evidence	Grade of recommendations
Jacob et al: Prevention of noncommunicable diseases by interventions in the preconception period: a FIGO position paper for action by healthcare practitioners	10	77	I-b–III	A
ACOG: Committee opinion no. 762: prepregnancy counselling	16	75	II-2–III	A–C
Chen and Hamer: Zika virus and sexual transmission: updated preconception guidance	2	11	II-3	A
Loutfy et al: No. 354 - Canadian HIV pregnancy planning guidelines	36	103	I-a–III	A–C
Polen et al: update: interim guidance for preconception counselling and prevention of sexual transmission of Zika virus for men with possible Zika virus exposure - United States, August 2018	5 scenario-based recommendations	42	II-3	A
PHAC: preconception care in family-centered maternity and newborn care: National guidelines	12	228	I-a–III	A–B
RANZCOG: pre-pregnancy counselling (C-Obs3a)	4	13	II-2–III	A–B
RACGP: guidelines for preventive activities in general practice	15	39	I-a–III	A–B Unable to assess all[a]
FOGSI: good clinical practice recommendations on preconception care	113	8	Unable to assess[b]	Unable to assess[b]
AAFP: preconception care (position paper)	17 (women) 10 (men)	74	I-a–III	A–C
Farahi and Zolotor[20]: recommendations for preconception counseling and care	7	57	I-a–III	A–B

[a]Unable to assess with the specified criteria of this systematic review. Level of evidence and grade of recommendation provided within the guideline.
[b]Not all recommendations were referenced and some were unable to be graded.

Table 5 Components of PCC included in CPGs

Component of PCC (number of recommendations)	Documented level of evidence from Jack et al[7]	Highest level of evidence from CPGs	Increase in quality of evidence	Jacob et al[28] Prevention of noncomm-unicable disease	ACOG CO-762 Prepregnancy counseling	Chen and Hamer[22] Zika virus	Loutfy et al Canadian HIV pregnancy planning guidelines	Polen et al[21] Zika virus	PHAC Preconception care	RANZCOG Pre-pregnancy Counseling	RACGP Preventive activities prior to pregnancy	FOGSI Good clinical practice for PCC	AAFP Preconception care Position paper	Farahi and Zolotor[20] Recommendations for PCC
Health promotion[8]														
Family planning and reproductive life plan	III	II-2	Yes	Yes	Yes	Limited For Zika only	Yes	Limited For Zika only	Yes	No	Yes	Yes	Yes	Yes
Physical activity	II-2	II-2	No	Yes	Yes	No	Refers to other guideline	No	Yes	Yes	Yes	Yes	Limited For women of high BMI only	No
Weight status	III	II-2	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Nutrient intake	III	III	No	Yes	Yes	No	Refers to other guideline	No	Yes	Yes	Yes	Limited Overweight/ underweight	No	Limited Post–bariatric surgery only
Folate	I-a	I-a	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Immunizations	III	III	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Substance use	II-2 (tobacco) III (alcohol)	II-2 (smoking) III (alcohol)	No	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
STIs	III	III	No	No	Yes	No	Yes	No	Yes	No	No	Yes	Yes	Yes
Immunization[6]														
HPV	II-2	II-2	No	No	Yes	No	No	No	No	No	No	Yes	No	No
Hepatitis B	III	III	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	No	Yes
Varicella	III	III	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Measles, mumps, and rubella	II-3	III	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Influenza	III	III	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	No	Yes
Diphtheria–tetanus –pertussis	III	III	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Infectious disease[16]														
HIV	I-b	I-a (counseling on strategies to reduce horizontal and perinatal HIV transmission risk)	Yes	No	Yes	No	Yes	No	Yes	No	Yes	Yes	No	Yes
Hepatitis C	III	III	No	No	Yes	No	Yes	No	No	No	No	No	No	No
Tuberculosis	II-2	III	No	No	Yes	No	No	No	No	No	No	Yes	No	Yes
Toxoplasmosis	III	III	No	No	Yes	No	Yes	No	Yes	No	Yes	Yes	No	No
Cytomegalovirus	II-2	III	No	No	No	No	Yes	No	No	No	Yes	No	No	No
Listeriosis	III	III	No	No	Yes	No	No	No	Yes	No	Yes	No	No	No
Parvovirus	III	III	No	No	No	No	No	No	No	No	Yes	No	No	No
Malaria	III	III	No	No	No	No	No	No	No	No	No	No	No	No

(*Continued*)

Table 5 (*Continued*)

Component of PCC (number of recommendations)	Documented level of evidence from Jack et al[7]	Highest level of evidence from CPGs	Increase in quality of evidence	Jacob et al[28] Prevention of noncomm-unicable disease	ACOG CO-762 Prepregnancy counseling	Chen and Hamer[22] Zika virus	Loutfy et al Canadian HIV pregnancy planning guidelines	Polen et al[21] Zika virus	PHAC Preconception care	RANZCOG Pre-pregnancy Counseling	RACGP Preventive activities prior to pregnancy	FOGSI Good clinical practice for PCC	AAFP Preconception care Position paper	Farahi and Zolotor[20] Recommendations for PCC
Gonorrhea	II-2	III	No	No	Yes	No	Yes	No	Yes	No	No	Yes	No	Yes
Chlamydia	I-a	I-a	No	No	Yes	No	Yes	No	Yes	No	No	Yes	No	Yes
Syphilis	II-1	III	No	No	Yes	No	Yes	No	Yes	No	Yes	Yes	No	Yes
Herpes simplex virus	II-1	III	No	No	No	No	Refers to other guideline	No	No	No	Yes	Yes	No	Yes
Asymptomatic bacteruria	II-1	N/A	N/A	No	No	No	No	No	No	No	No	No	No	No
Periodontal disease	I-b	III	No	No	No	No	Refers to other guideline	No	Yes	No	Yes	No	No	No
Bacterial vaginosis	1-b	N/A	N/A	No	No	No	No	No	No	No	No	No	No	No
Group B *Streptococcus*	I-2	N/A	N/A	No	No	No	No	No	No	No	No	No	No	No
Medical conditions[11]														
Diabetes mellitus	I II-2 (overweight and obese adults)	II-1	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes
Thyroid disease	II-1			Yes	Yes	No	No	No	Yes	No	Yes	Yes	No	Yes
Phenylketonuria	II-1	N/A	N/A	No	No	No	No	No	No	No	No	No	No	No
Seizure disorders	II-2			No	No	No	No	No	Yes	No	Yes	Yes	No	Yes
Hypertension	II-2	II-2	No	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes
Rheumatoid arthritis	III	III	No change	No	No	No	No	No	No	No	No	Yes	No	No
Lupus	II-2	III	No	No	No	No	No	No	No	No	No	Yes	No	No
Renal disease	II-2			No	No	No	No	No	No	No	No	No	No	No
Cardiovascular disease	III-3	III	No	No	No	No	No	No	NO	No	No	Yes	No	No
Thrombophilia	III (women not using warfarin) II-3 (women using warfarin)	III	No	No	Yes	No	No	No	No	No	Yes	Yes	No	Yes
Asthma	II-3	III	No	No	No	No	No	No	Yes	No	No	Yes	No	Yes
Psychiatric condition[3]														
Depression/Anxiety	III	III	No	No	Yes	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes
Bipolar disease	III	III	No	No	Yes	No	No	No	Yes	No	No	Yes	No	No
Schizophrenia	III	III	No	No	Yes	No	No	No	No	No	No	Yes	No	No
Parental exposure[3]														
Alcohol	I-a	II-2	No	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Tobacco	I-a	I-a	No	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Illicit substances	III	III	No	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes

Table 5 (*Continued*)

Component of PCC (number of recommendations)	Documented level of evidence from Jack et al[7]	Highest level of evidence from CPGs	Increase in quality of evidence	Jacob et al[28] Prevention of noncomm-unicable disease	ACOG CO-762 Prepregnancy counseling	Chen and Hamer[22] Zika virus	Loutfy et al Canadian HIV pregnancy planning guidelines	Polen et al[21] Zika virus	PHAC Preconception care	RANZCOG Pre-pregnancy Counseling	RACGP Preventive activities prior to pregnancy	FOGSI Good clinical practice for PCC	AAFP Preconception care Position paper	Farahi and Zolotor[20] Recommendations for PCC
Family and genetic history[5]														
All individuals	III	III	No	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Ethnicity based	II-3	III	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	No	No
Family history	II-3	II-3	No	No	Yes	No	No	No	Yes	Yes	Refers to other guideline	Yes	Yes	Yes
Previous pregnancies	III	III	No	No	Yes	No	No	No	Yes	No	Refers to other guideline	Yes	Yes	No
Known genetic conditions	II-3	II-3	No	No	Yes	No	No	No	Yes	No	Refers to other guideline	Yes	Yes NTDs only	Yes
Nutrition[12]														
Dietary supplements	III	N/A	N/A	No	No	No	No	No	No	No	No	No	No	No
Vitamin A	III	III	No	No	Yes	No	No	No	Yes	No	No	No	No	Limited Post–bariatric surgery only
Folic acid	I-a	I-a	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Multivitamins	II-2	III	No		Yes	No	Refers to other guideline	No	Yes	No	No	No	No	Limited Post–bariatric surgery only
Vitamin D	II-3	II-2	Yes	Yes	Yes	No	No	No	Yes	No	Yes	No	No	Limited Post–bariatric surgery only
Calcium	I-b	III	No	No	Yes	No	No	No	Yes	No	Yes	No	No	No
Iron	I-b	II-2	No	Yes	Yes	No	No	No	Yes	No	Yes	Yes	No	Limited Post–bariatric surgery only
Essential fatty acids	I-b	N/A	N/A	No	No	No	No	No	No	No	No	No	No	No
Iodine	II-2	III	No	Yes	No	No	No	No	No	Yes	Yes	Limited Thyroid section	No	No
Overweight	I-b	II-2	No	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Underweight	III	III	No	Yes	Yes	No	No	No	Yes	No	Yes	Yes	No	Yes
Eating disorders	III	III	No	No	Yes	No	No	No	No	No	No	Yes	No	Yes
Environmental exposure[5]														
Mercury	III	III	No	No	Yes	No	No	No	Yes	No	Yes	No	Limited Men only	Yes
Lead	II-2	III	No	No	Yes	No	No	No	Yes	No	No	No	Limited Men only	No
Soil and water hazards	III II (BPA avoidance)	III	No	Yes	No	No	No	No	Yes	No	No	No	No	No
Workplace exposure	III	III	No	No	Yes	No	No	No	Yes	Yes	Yes	No	No Discussed for men	Yes
Household exposure	III	III	No	No	Yes	No	No	No	Yes	Yes	Yes	No	No	Yes

(*Continued*)

Table 5 (*Continued*)

Component of PCC (number of recommendations)	Documented level of evidence from Jack et al[7]	Highest level of evidence from CPGs	Increase in quality of evidence	Jacob et al[28] Prevention of noncomm-unicable disease	ACOG CO-762 Prepregnancy counseling	Chen and Hamer[22] Zika virus	Loutfy et al Canadian HIV pregnancy planning guidelines	Polen et al[21] Zika virus	PHAC Preconception care	RANZCOG Pre-pregnancy Counseling	RACGP Preventive activities prior to pregnancy	FOGSI Good clinical practice for PCC	AAFP Preconception care Position paper	Farahi and Zolotor[20] Recommendations for PCC
Psychosocial risk[3]														
Inadequate financial resources	III	III	No	No	No	No	Yes	No	Yes	No	Yes	Yes	No	No
Access to care	III	III	No	No	Limited Screening for genetic conditions	No	Yes	No	Yes	No	Yes	Yes	No	No
Physical/sexual abuse	III	III	No	No	Yes	No	No	No	Yes	No	No	Yes	Yes	Yes
Medication[3]														
Prescription	II-2	II-2	No	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Over-the-counter medication	III	III	No	No	Yes	No	Yes	No	No	Yes	Yes	Checklist only	Yes	No
Dietary supplements	II-3	III	No	No	Yes	No	No	No	No	No	Yes	No	No	No
Reproductive history[5]														
Prior preterm birth infant	I-a	III	No	No	No	No	No	No	Yes	No	Yes	Checklist only	No	No
Prior cesarean delivery	II-2	III	No	No	No	No	No	No	Yes	No	No	Checklist only	No	No
Prior miscarriage	I-a	III	No	No	No	No	No	No	Yes	No	Yes	Yes	No	No
Prior stillbirth	II-2	III	No	No	No	No	No	No	No	No	Yes	Checklist only	No	No
Uterine anomalies	II-3	III	No	No	No	No	No	No	Limited	No	No	No	No	No
Special populations[4]														
Women with disabilities	III	N/A	N/A	No	No	No	No	No	No	No	No	No	No	No
Immigrant and refu-gee populations	III	III	No	Yes	No	No	No	No	Yes	No	Yes	No	No	No
Cancer	III	III	No	No	No	No	No	No	No	No	No	Yes	No	No
Men	III	I-b	Yes	Yes	Limited	Yes	Yes	Yes	Yes	No	No	Yes	Yes Detailed separate section	Limited Reproductive life plan
Additional component														
Zika	N/A	II-3	Yes	No	Yes	Yes	No	Yes	No	Yes	No	No	No	No
Number of content areas covered (85)				**17**	**57**	**3**	**27**	**3**	**58**	**25**	**53**	**58**	**26**	**45**

Abbreviations: ACOG, American College of Obstetricians and Gynaecologists; BMI, body mass index; BPA, bisphenol A; CPGs, clinical practice guidelines; HIV, human immunodeficiency virus; HPV, human papilloma virus; NTDs, Neural Tubes Defects; PCC, preconception care; PHAC, Public Health Agency of Canada; RACGP, Royal Australian College of General Practitioners; RANZCOG, Royal Australian and New Zealand College of Obstetrics and Gynecology; STIs, sexually transmitted infections.

Discussion

This systematic review aimed to assess the availability and quality of guidelines for PCC. While a plethora of guidelines that refer to preconception were identified, only 11 focused primarily on PCC. Most were of moderate quality with inconsistent adherence to AGREE-II criteria. Four of the 11 CPGs focused on particular areas of health such as Zika virus, non-communicable diseases, and people living with HIV. The number of recommendations varied significantly between the CPGs and no one document covered all the recognized clinical content areas of PCC. Several CPGs acknowledged content areas that were not covered and offered links to other guidelines for this information.

Guideline Quality

Ten guidelines were assessed as moderate quality with only one assessed as high quality. This was the Canadian HIV Pregnancy Planning guideline, which scored highly across five domains, receiving its lowest score in domain 5, Applicability. The authors note the additional development and publication of a best practice document in 2020 to address the application of the CPG.[29] This document repackaged the 36 guideline recommendations in five standards of care for ease of use. This best practice document was designed to further support health care providers in the application of this guideline and highlights the potential value of guideline implementation tools to increase use and consistent application of recommendations within CPGs. The AGREE-II provides a methodological framework for the development of high-quality CPGs. Future CPGs in PCC must adhere to this framework, across all six domains, to produce robust CPGs to enhance the delivery of PCC.

Level of Supporting Evidence

The level of evidence on which the recommendations were based was variable with high-quality evidence available for only a few recommendations, namely, folic acid supplementation and HIV transmission prevention. Six clinical content areas have seen an increase in the level of supporting evidence since the previous comprehensive assessment in 2008.[7] This aspect of the analyses highlighted areas where additional research is required. Recommendations for 54 of the 83 content areas were based on the consensus of clinical experience, descriptive studies and case reports, or reports of expert committees. It may not be feasible, ethical, or necessary to conduct RCTs in all these areas to attain the highest levels of evidence possible. Researchers and funding bodies should consider identifying and targeting aspects of PCC where the most significant gains can be made, particularly for priority populations. CPGs need to be updated with the most recent evidence to encourage uptake and translation to care. Monitoring the uptake of CPGs and improvements in population-level preconception health indicators is needed to track progress, and evaluate translation to care, health improvements, and reduced inequalities.[30]

Populations Addressed within PCC CPGs

The WHO acknowledges that PCC stands to benefit women and men, regardless of pregnancy intention.[1] Only 6 of the 11 included documents provided PCC guidance for men, with a further two documents acknowledging men's PCC health. The CPG from the AAFP contained a dedicated section for men, including a table outlining recommendations for preconception interventions for men. The CPGs pertaining to Zika virus and the HIV pregnancy planning guideline contained specific recommendations for men embedded within other recommendations. Evidence suggests that men of reproductive age are not receiving PCC.[31–33] A recent survey of over 500 men in the United Kingdom found that they wanted to engage in positive preconception health behaviors. Almost one in five of the men surveyed had visited a primary health provider for preconception health advice and those who had received advice were more likely to adopt positive health behaviors prior to pregnancy.[33] Therefore, not including men in strategies to improve provision of PCC is a missed opportunity to improve preconception health globally. Consistently including men's preconception health in PCC CPGs may support and empower health care providers to ask men about their reproductive intentions and provide them with PCC, along with their partner.

The degree to which guidelines included content relating to disadvantaged populations was assessed through data extraction and items within domains 1, 3, and 5 of the AGREE-II tool. Only three CPGs included priority populations in their recommendations, with a further three CPGs acknowledging additional needs in care. The RANZCOG CPG detailed a section on health inequity, outlining strategies to assist family physicians to deliver equitable PCC. The CPG from Public Health Canada contained multiple segments addressing the needs of priority populations including a segment on the determinants of health, with other sections for indigenous women and women with specific needs. The HIV Pregnancy Planning guideline embedded recommendations for people from priority populations within other recommendations. Women and men from priority populations experience increased rates of adverse health outcomes.[4,34] They also face barriers to accessing health care. PCC guidelines must incorporate guidance on the specific needs of priority populations to allow health care providers to deliver equitable health care.

Women from priority populations are keen to engage in opportunities to receive PCC, yet challenges exist in its delivery.[35,36] Education and training for health care providers have been suggested to enhance the delivery of equitable PCC. Therefore, further work in education and training for health care providers and implementation guideline tools that promote culturally appropriate provision of PCC are required to address the needs of priority populations.

CPGs in Practice

The presentation of a CPG, from its title to its display of recommendations, is key to its accessibility, implementation, and use.[9] A study on guideline development in Australia demonstrated the importance of end-user input to develop focused clinical questions that respond to clinical need.[37]

Such input can help focus evidence-based recommendations thereby increasing their relevance, acceptability, and feasible implementation in clinical practice. Given that the target population for PCC is all people of reproductive age, and that PCC is often delivered opportunistically across different levels of care and even social care, it is necessary to have comprehensive CPGs that answer clinical questions and promote collaboration and provision of high-quality and consistent care. The scope of clinical content to be covered by PCC should be clear and where a CPG does not address all PCC content areas, acknowledgment of and reference to other guidelines that cover missing content should be included. As PCC needs of individuals vary widely, the care delivered using comprehensive CPGs can subsequently be tailored to an individual's physical and mental health conditions, health behaviors, and social context.[38]

Strengths and Limitations

Only guidelines that were freely accessible to an international audience were included in this systematic review. This was to mimic the clinical scenario of when a clinician may search for information to augment care within a consultation. However, these inclusion criteria limited the number of CPGs included in the study.

Strengths included the involvement of an international panel of PCC experts during protocol development, title and abstracts screening, study selection and assessment of quality, and level of evidence. Comprehensive data extraction and analyses aligned with the previously identified 82 clinical content areas of PCC[7] and built on existing understanding of PCC globally.

Conclusion

Preconception care is a key component of preventive health care that should be provided to all people of reproductive age, with care taken to ensure the inclusion of men and priority populations. This systematic review identified that current guidelines on PCC can be improved with inclusion of a more comprehensive set of clinical content areas, more rigorous development processes, and strategies to improve feasible and acceptable guideline application.

Authors' Contribution

The authors certify that:

All information is truthful and as complete as possible.

All authors have participated in planning of the project.

All authors have been responsible for the writing of the manuscript.

Research was conducted in accordance with the ethical and research arrangements of the organizational institutions involved.

Conflict of Interest

We declare that we received no financial or other support or any financial or professional relationships which may pose a competing interest.

References

1 World Health Organization. Preconception care: maximizing the gains for maternal and child health. A Policy Brief. Geneva2013
2 Dorney E, Black KI. Preconception care. Aust J Gen Pract 2018;47 (07):424–429
3 Stephenson J, Heslehurst N, Hall J, et al. Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. Lancet 2018;391(10132):1830–1841
4 Agency for Healthcare Research and Quality. About Priority Populations. Rockville, MD. 2019 [updated June 2021]. Accessed March 22, 2022 at: https://www.ahrq.gov/priority-populations/about/index.html
5 Mazza D, Chapman A, Michie S. Barriers to the implementation of preconception care guidelines as perceived by general practitioners: a qualitative study. BMC Health Serv Res 2013;13 (01):36
6 Heyes T, Long S, Mathers N. Preconception care: practice and beliefs of primary care workers. Fam Pract 2004;21(01):22–27
7 Jack BW, Atrash H, Coonrod DV, Moos MK, O'Donnell J, Johnson K. The clinical content of preconception care: an overview and preparation of this supplement. Am J Obstet Gynecol 2008;199 (06, Suppl 2):S266–S279
8 Clinical Practice Guidelines We Can Trust. In: Graham R, Mancher M, Wolman DM, eds. Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines. Washington, DC:: National Academies Press (US);; 2011
9 Biezen R, Roberts C, Buising K, et al. How do general practitioners access guidelines and utilise electronic medical records to make clinical decisions on antibiotic use? Results from an Australian qualitative study. BMJ Open 2019;9(08):e028329
10 Mason E, Chandra-Mouli V, Baltag V, Christiansen C, Lassi ZS, Bhutta ZA. Preconception care: advancing from 'important to do and can be done' to 'is being done and is making a difference'. Reprod Health 2014;11(03, Suppl 3):S8
11 Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372(71):n71
12 Brouwers MC, Kho ME, Browman GP, et al; AGREE Next Steps Consortium. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ 2010;182(18):E839–E842
13 Chiappini E, Bortone B, Galli L, de Martino M. Guidelines for the symptomatic management of fever in children: systematic review of the literature and quality appraisal with AGREE II. BMJ Open 2017;7(07):e015404
14 Quintyne KI, Kavanagh P. Appraisal of international guidelines on smoking cessation using the AGREE II assessment tool. Ir Med J 2019;112(02):867
15 Atrash H, Jack B. Preconception care to improve pregnancy outcomes: the science. J Hum Growth Dev 2020;30(03):355–362
16 Obstetrics Subgroup, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association. Guideline of preconception and prenatal care (2018). . [in Chinese]Zhonghua Fu Chan Ke Za Zhi 2018;53(01):7–13
17 National Institute for Health Care and Excellence. Pre-conception - advice and management. 2019. Accessed March 22, 2022 at: https://cks.nice.org.uk/pre-conception-advice-and-management#!topicsummary
18 American Academy of Family Physicians. Preconception Care (Position Paper) 2015. Accessed March 22, 2022 at: https://www.aafp.org/about/policies/all/preconception-care.html
19 ACOG Committee Opinion No. 762: Prepregnancy counseling. Obstet Gynecol 2019;133(01):e78–e89
20 Farahi N, Zolotor A. Recommendations for preconception counseling and care. Am Fam Physician 2013;88(08):499–506
21 Polen KD, Gilboa SM, Hills S, Oduyebo T, Kohl KS, Brooks JT, et al. Update: interim guidance for preconception counseling and prevention of sexual transmission of Zika virus for men with

possible Zika virus exposure - United States, August 2018. Morbidity and mortality weekly report. 2018;67(31):868–871
22 Chen LH, Hamer DH. Zika virus and sexual transmission: updated preconception guidance. J Travel Med 2018;25(01):1
23 Loutfy M, Kennedy VL, Poliquin V, et al. No. 354 - Canadian HIV pregnancy planning guidelines. J Obstet Gynaecol Can 2018;40 (01):94–114
24 Shaw E, Barney L, DiMeglio G, et al. Preconception Care in Family-Centred Maternity and Newborn Care: National Guidelines. Ottawa, Ontario:: Public Health Agency of Canada; 2018
25 Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG). Pre-pregnancy Counselling (C-Obs3a). Melbourne;2017
26 Royal Australian College of General Practitioners. Guidelines for Preventive Activities in General Practice Melbourne: RACGP; 2017
27 Federation of Obstetric Gynecological Societies of India (FOGSI). Good Clinical Practice Recommendations on Preconception Care. Mumbai;2016
28 Jacob CM, Killeen SL, McAuliffe FM, et al. Prevention of non-communicable diseases by interventions in the preconception period: a FIGO position paper for action by healthcare practitioners. Int J Gynaecol Obstet 2020;151(Suppl 1):6–15
29 Loutfy M, Kennedy VL, Boucoiran I, et al. A clinical practice guide: What HIV care providers need to know about HIV pregnancy planning to optimize preconception care for their patients. Jammi 2020;5(01):8–20
30 Schoenaker DAJM, Stephenson J, Connolly A, et al;UK Preconception Partnership. Characterising and monitoring preconception health in England: a review of national population-level indicators and core data sources. 2022;13(02):137–150
31 Frey KA, Engle R, Noble B. Preconception healthcare: what do men know and believe? J Men's Health 2012;9(01):25–35
32 Hogg K, Rizio T, Manocha R, McLachlan RI, Hammarberg K. Men's preconception health care in Australian general practice: GPs' knowledge, attitudes and behaviours. Aust J Prim Health 2019;25 (04):353–358
33 Shawe J, Patel D, Joy M, Howden B, Barrett G, Stephenson J. Preparation for fatherhood: a survey of men's preconception health knowledge and behaviour in England. PLoS One 2019;14 (03):e0213897
34 Jardine J, Walker K, Gurol-Urganci I, et al; National Maternity and Perinatal Audit Project Team. Adverse pregnancy outcomes attributable to socioeconomic and ethnic inequalities in England: a national cohort study. Lancet 2021;398(10314): 1905–1912
35 Tuomainen H, Cross-Bardell L, Bhoday M, Qureshi N, Kai J. Opportunities and challenges for enhancing preconception health in primary care: qualitative study with women from ethnically diverse communities. BMJ Open 2013;3(07):e002977
36 Hawkey AJ, Ussher JM, Perz J. What do women want? Migrant and refugee women's preferences for the delivery of sexual and reproductive healthcare and information. Ethn Health 2021; •••:1–19. Doi: 10.1080/13557858.2021.1980772
37 Chakraborty S, Brijnath B, Dermentzis J, Mazza D. Defining key questions for clinical practice guidelines: a novel approach for developing clinically relevant questions. Health Res Policy Syst 2020;18(01):113
38 Stephenson J, Schoenaker DA, Hinton W, et al; UK Preconception Partnership. A wake-up call for preconception health: a clinical review. Br J Gen Pract 2021;71(706):233–236