

PROTOCOL

Open Access



Early pregnancy loss incidence in high-income settings: a protocol for a systematic review and meta-analysis

L. Schummers^{1*} , N. Oveisi^{1,2}, M. S. Ohtsuka^{1,2}, J. A. Hutcheon³, K. A. Ahrens⁴, J. Liauw³ and W. V. Norman^{1,5}

Abstract

Background: Early pregnancy loss (unintended pregnancy loss before 20 completed weeks of gestation) is a common adverse pregnancy outcome, with previous evidence reporting incidence ranging from 10 to 30% of detected pregnancies. The objective of this systematic review and meta-analysis is to determine the incidence and range of early pregnancy loss in contemporary pregnant populations based on studies with good internal and external validity. Findings may be useful for clinical counseling in pre-conception and family planning settings and for people who experience early pregnancy loss.

Methods: We will search MEDLINE, EMBASE, and CINAHL databases using combinations of medical subject headings and keywords. Peer-reviewed, full-text original research articles that meet the following criteria will be included: (1) human study; (2) study designs: controlled clinical trials or observational studies with at least 100 pregnancies in the denominator, or systematic reviews of studies using these designs; (3) conducted in high-income countries; (4) reporting early pregnancy loss incidence, defined as unintended early pregnancy loss occurring prior to 20 weeks' gestation expressed as the number of losses among all pregnancies in the study period; (5) among a contemporary (1990 or later) general population of pregnancies; and (6) published between January 1, 1990, and August 31, 2021. We will assess the quality of included studies according to the United States Preventive Services Task Force Criteria for Assessing Internal and External Validity of Individual Studies. If appropriate, based on methodological comparability across included studies, we will conduct meta-analyses using random effects models to estimate the pooled incidence of early pregnancy loss among all studies with both good internal and external validity, with meta-analyses stratified by study design type (survey-based or self-reported and medical record-based), by induced abortion restrictions (restricted vs. unrestricted), and by gestational age (first trimester only vs. all gestational ages before 20 weeks).

Discussion: This systematic review will synthesize existing evidence to calculate a current estimate of early pregnancy loss incidence and variability in reported incidence estimates in high-income settings. The findings of this review may inform updates to clinical counseling in pre-conception and family planning settings, as well as for patients experiencing early pregnancy loss.

Systematic review registration: We have registered this review with the International Prospective Register of Systematic Reviews (PROSPERO #226267).

Background

Early pregnancy loss (unintended pregnancy loss before 20 completed weeks of gestation) is a common adverse pregnancy outcome, with reported incidence ranging from 10 to 30% of detected pregnancies [1–3]. Early

*Correspondence: laura.schummers@ubc.ca

¹ Department of Family Practice, University of British Columbia, E303 -

4500 Oak Street, Vancouver, BC V6H 3N1, Canada

Full list of author information is available at the end of the article



© The Author(s) 2021. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

pregnancy loss spans a range of subtypes, including spontaneous abortion, missed abortion, incomplete abortion, molar pregnancy, and others. Current clinical practice guidelines on early pregnancy loss diagnosis and management published by the American College of Obstetricians and Gynecologists (ACOG) and the UK's National Institute for Health and Care Excellence (NICE) cite incidence estimates of 10% [4] and 20% [5], respectively [2, 6, 7]. The estimates are drawn from small ($n < 600$), highly selected clinical cohort studies conducted in the 1980s–1990s [1–3]. These estimates may not be applicable to general pregnant populations due to the selection of predominantly white and college-educated pregnant people with a planned pregnancy. With many changes in the characteristics of pregnant populations in the past 30 years (particularly increased frequency of delayed child-bearing [8], assisted reproductive technology utilization [9], and pregnancies to persons with comorbidities such as obesity, diabetes mellitus, or hypertension [10–12]), the incidence of early pregnancy loss reported in studies before 1990 may not be generalizable to contemporary populations.

Furthermore, these commonly cited estimates of early pregnancy loss incidence may not be applicable to clinical counseling in most settings. This is because these estimates are based on the detection of pregnancy and early pregnancy loss within studies with specific research protocols [1, 3] that are unlikely to be replicated in standard pregnancy experience and care outside of research settings. These studies collected prospective, serial beta-human chorionic gonadotropin measurements to identify pregnancies and losses. Outside of research settings, pregnancy identification is based on pregnancy symptoms or pregnancy tests conducted at home or at a health care visit at approximately 5–6 weeks of gestation, with 23–28% of pregnancies being identified ≥ 7 weeks' gestation. For clinical counseling purposes, determining the incidence of early pregnancy loss among pregnancies identified in non-research settings is more relevant because this reflects the risk for standard patients [13, 14].

Estimates of early pregnancy loss among pregnancies identified in non-research settings can be obtained from several sources, including population-based administrative databases (e.g., pregnancy registries created by abstracting from medical records and/or billing claims data based on clinical pregnancy care) and reproductive health surveys (e.g., routinely administered nationally representative reproductive health surveys such as the National Survey of Family Growth [15], from the USA, or the National Survey of Sexual Attitudes and Lifestyles [16] from the UK). Population-based administrative database studies have yielded early pregnancy loss incidence

estimates ranging from 12% [17] to 17% [18], while surveys have yielded estimates from 18% [19] to 24% [10]. These population-based estimates may better approximate clinically relevant measures of early pregnancy loss incidence than those drawn from highly selected clinical cohorts.

The objective of this systematic review is to determine the incidence and range of early pregnancy loss in contemporary pregnant populations based on studies with good internal and external validity. Findings may be useful for clinical counseling in pre-conception and family planning settings and for people experiencing early pregnancy loss [20–22].

Methods

The design and implementation of this systematic review will adhere to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement [23]. We have registered this review with the International Prospective Register of Systematic Reviews (PROSPERO) (systematic review identification number 226267). This study was deemed exempt from ethics review from the University of British Columbia and Children's and Women's Health Centre of British Columbia Research Ethics Board.

The key question underlying this systematic review is: "What is the incidence of early pregnancy loss in contemporary general pregnant populations in high-income settings?" We will approach this question using the modified PICOT framework [24] outlined in Table 1.

Data sources and search strategy

We will search MEDLINE, EMBASE, and CINAHL databases, using a search strategy developed in consultation with a research librarian (see Additional file 1: Search Strategy) using relevant medical subject headings and keywords. We piloted the search strategy for each database using a list of 17 papers that we identified a priori as meeting our intended inclusion criteria; we revised our search strategy to minimize the number of abstracts that would need to be reviewed while capturing these key papers in our search (Table 2). We will augment this search strategy by hand-searching the bibliographies of eligible studies meeting inclusion criteria for additional relevant articles not identified in our database search and a preliminary gray literature key-word search using Google (for relevant newspaper articles, retracted publications, and other publications from relevant stakeholders) and gray literature databases (OpenGrey, TRIP Pro, New York Academy of Medicine's Grey Literature Report, and Canadian Institute for Health Information). We will review and evaluate gray literature using the same criteria as the peer-reviewed literature.

Table 1 Modified PICOT chart outlining the framework underlying this systematic review of the literature reporting early pregnancy loss incidence

	Included	Excluded
Population	All recognized pregnancies, defined by either self-report or report to a health care provider or indicated by a pregnancy-related clinical encounter, in OECD-classified high-income settings, representing general pregnant populations.	Pregnancies not recognized by the pregnant person or pregnancies occurring in a setting not classified as high-income by OECD; study populations restricted to assisted reproductive technology settings
Outcome	Early pregnancy loss, defined as unintended pregnancy loss occurring prior to 20 weeks' gestation expressed as the number of losses among all pregnancies in the study period, including all types of unintended pregnancy loss occurring before 20 weeks of gestation or only common types of early pregnancy loss (spontaneous, missed, incomplete abortions only)	Induced abortion, stillbirth (intrauterine fetal demise after 20 completed weeks of gestation), and less common subtypes of early pregnancy loss examined separately (hydatidiform mole/molar pregnancy, anembryonic pregnancy, ectopic pregnancy)
Time	Jan 1, 1990–August 31, 2021	Before Jan 1, 1990, or after August 31, 2021

Because this systematic review is not evaluating a specific intervention or exposure, our PICOT framework does not include an intervention or comparator components

OECD Organization for Economic Cooperation and Development

Table 2 Search strategy summary for a systematic review of early pregnancy loss in high-income settings

Keywords	Early pregnancy loss*, spontaneous abortion*, miscarriage*, fetal loss*, pregnancy loss*, anembryonic pregnanc*, embryonic loss*, spontaneous miscarriage*, early pregnancy failure*, pregnancy failure*, hydatidiform mole, septic abortion*, missed abortion*, incomplete abortion*, ectopic pregnanc*, risk*, rate*, prevalen*, inciden*, report*, trend*, impact*Keywords terms for high-income countries (as defined by World Bank; "High-Income OECD Countries" ²⁵) (see Additional file 1: Search Strategy).
Database-specific subject headings	
MEDLINE	<i>Subject heading (MeSH):</i> Spontaneous abortion, septic abortion, missed abortion, incomplete abortion, ectopic pregnancy, , hydatidiform mole, risk, morbidity, incidence, prevalence. MeSH terms for high-income countries (as defined by World Bank; "High Income OECD Countries" ²⁵) (see Additional file 1: Search Strategy).
CINAHL	<i>Subject heading:</i> Spontaneous abortion, incomplete abortion, hydatidiform mole, ectopic pregnancy, incidence, prevalence, morbidity.
EMBASE	<i>Subject heading (Emtree):</i> Spontaneous abortion, septic abortion, incomplete abortion, missed abortion, blighted ovum, hydatidiform mole, risk, morbidity, incidence, prevalence. Emtree terms for high-income countries (as defined by World Bank; "High-Income OECD Countries" ²⁵) (see Additional file 1: Search Strategy).

Eligibility criteria

Peer-reviewed, full-text original research articles that meet all of the following inclusion criteria will be included in this review: (1) human study; (2) study designs: controlled clinical trials or observational studies (prospective cohort, retrospective cohort, cross-sectional, chart review, survey) with at least 100 pregnancies in the denominator, or systematic reviews of studies using these designs; (3) conducted in high-income countries (as defined by the World Bank; "High-Income OECD Countries" [25]); (4) reporting early pregnancy loss incidence, defined as unintended early pregnancy loss occurring prior to 20 weeks' gestation expressed as the number of losses identified in typical practice settings (i.e., not specific research settings) among all pregnancies in the study period; (5) among a contemporary (1990 or later) general population of pregnancies; (6) published between January 1, 1990, and August 31, 2021. Studies meeting at least one of the following exclusion criteria will be excluded: (1) non-human study; (2) controlled clinical trials or

observational studies with fewer than 100 pregnancies in the denominator; studies using any other designs (case-control, case reports or series, editorials, opinions, commentaries, or other designs not specified in inclusion criteria); (3) conducted outside OECD high-income setting; (4) not reporting early pregnancy loss incidence; (5) study population not contemporary (including pregnancies exclusively before January 1, 1990); (6) study population restricted to assisted reproductive technology setting; (7) study population sampled using any sampling method (e.g., restriction, oversampling, case-control) based on a clinical condition or characteristic, defined as any condition, disease, or characteristic with a diagnosis code, treatment with a specific medication or procedure, or recruitment from a specialty clinic serving those with a specific disease or condition. Studies that selected the study population based on age, body mass index, or other social, demographic, or environmental characteristics will not be excluded under this criterion; (8) studies reporting only uncommon types of early pregnancy loss

Table 4 Incidence of early pregnancy loss and quality assessment for studies included in the systemic review

Author and year	Early pregnancy loss incidence (n/N=%; or weighted estimated for survey studies) with 95% CI	Internal validity rating	External validity rating

national populations. Our assessment of external validity will consider the similarity of the regional or national population being represented to the general obstetric population of high-income settings (the target population for this review). For example, a maximum external validity rating of “good” would require the study population to be the full population or employ representative sampling from the full population of pregnancies in an OECD high-income country or large region (e.g., state or province, multiple counties or cities); restriction to one city or county would result in a maximum external validity rating of “fair”; restriction to one hospital/clinic, region, or sample characteristic (e.g., occupation, racial/ethnic group) would result in a maximum external validity rating of “poor”. Likewise, a maximum external validity rating of “good” requires that the age range use the full reproductive age range (or at least ages 18–44), while restriction to an age range of more than 10 years would result in an external validity rating of “fair,” and restriction to an age range <10 years would result in a rating of “poor.” External validity ratings will also consider pregnancy detection methods that do not apply in standard clinical or at-home pregnancy detection settings. If a study population is restricted by marital status (e.g., only married people), pregnancy intention (e.g., only planned pregnancies), or pregnancy history (e.g., parity or loss), the maximum external validity rating will be “fair.” For survey studies, we will report response rates, which are an important component of external validity for this study design. See Table 4 for a drafted table showing reported incidence and quality assessments. See Additional file 4: Quality Assessment Rationale for criteria that will be used in rating study internal and external validity.

Meta-analysis

If deemed appropriate, based on methodological comparability across included studies, we will conduct a quantitative meta-analysis of early pregnancy loss incidence

to combine estimates from all studies with good internal and external validity. We will present incidence estimates from individual studies included in the meta-analysis along with the pooled incidence from the meta-analysis (Table 5). We will conduct the meta-analysis using random effects models with inverse-variance weighting using the Hartung-Knapp-Sidik-Jonkman method to estimate an average incidence value for early pregnancy loss across studies; this method is robust to biases that can arise due to a small number of included studies or variability in sample size across studies [33]. We will assess heterogeneity among included studies according to (i) overlap of confidence intervals around estimated incidence values, (ii) the I^2 statistic (a quantification of inconsistency among studies, indicating the proportion of variability across studies that is due to heterogeneity), (iii) and the Tau² statistic (τ^2 , a measure of between-study variance). We will consider an I^2 value < 25% to indicate non-important heterogeneity, 25–<50% to indicate modest heterogeneity, 50–<75% to indicate substantial heterogeneity, and $\geq 75\%$ to indicate considerable heterogeneity [34]. In addition, we will calculate a 90% prediction interval around our overall early pregnancy loss incidence estimate, which provides a measure of dispersion or variability in incidence values from the underlying populations from which study cohorts were drawn [35].

We will conduct meta-analyses stratified by gestational age (first trimester only vs. all gestational ages before 20 weeks) and study design type (administrative data derived from medical records vs. survey or patient-reported data) and by induced abortion restrictions (restricted vs. unrestricted). We will examine heterogeneity within strata of the stratified analysis to determine if accounting for the clinical and methodological sources of heterogeneity that we identified a priori are sufficient to account for any important observed heterogeneity. We will conduct all meta-analyses using Stata 14.0.

Table 5 Incidence of early pregnancy loss in high-income settings, meta-analysis findings

Study	Incidence n/N	Sample size used to estimate early pregnancy loss	Incidence with 95% CI, plotted and numeric	Weight assigned to study (%)

Discussion

This systematic review will examine the incidence of early pregnancy loss among contemporary populations in high-income settings. This review will provide the best available evidence regarding early pregnancy loss incidence and the range of incidence values. We will determine variability in reported incidence by study design, induced abortion legal status, and gestational age for early pregnancy losses and summarize these findings using meta-analysis.

Findings of this systematic review and meta-analysis will need to be interpreted in light of potential limitations. Early pregnancy loss includes a range of subtypes, which may be etiologically heterogeneous. By combining these subtypes, this review will not determine the incidence of each type of early loss separately and will specifically exclude studies focused only on rare subtypes. The expected data sources include data extracted from medical records (e.g., using health administrative data) and self-reported data (e.g., from survey studies), which can generate estimates subject to early pregnancy loss misclassification. Although our bias analysis will specifically account for induced abortions being misclassified as pregnancy losses, there may be further misclassification (e.g., stillbirths occurring after 20 weeks of gestation misclassified as an early pregnancy loss), which we will not account for analytically.

Pre-conception and family planning clinical counseling, as well as clinical care for patients experiencing early pregnancy loss, should include current information on the best available estimates of early pregnancy loss risk. Given that current obstetrics clinical practice guidelines related to early pregnancy loss care report incidence based on highly selected populations published 20–30 years ago, clinical counseling may not reflect the best available evidence on this incidence of this common adverse pregnancy outcome.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13643-021-01815-1>.

Additional file 1. Search Strategy.

Additional file 2. Induced abortion regulation classification table.

Additional file 3. Data extraction form.

Additional file 4. Quality Assessment Rationale.

Acknowledgements

The authors gratefully acknowledge Saeyong Kim, Medical Librarian at the University of British Columbia, for their valuable contribution to our search strategy.

Authors' contributions

All authors contributed to the study design, conceptualized the systematic literature search, revised multiple versions of the manuscript, and approved the

final draft for submission. LS and NO conceptualized this systematic review and meta-analysis and drafted all sections of the manuscript. NO developed the comprehensive search strategy in consultation with a research librarian.

Funding

This study is supported by project funding: Operating Grant from the Canadian Institutes of Health Research (#DA5-170277) and a Clinical and Translational Seed Grant from the BC Children's Hospital Research Institute and Women's Health Research Institute funded by the British Columbia Women's Health Foundation. Our study team is also supported by various salary awards. LS is supported by a Canadian Institutes of Health Research Fellowship: Patient-Oriented Research Award – Transition to Leadership Stream (#TLS-170676) and a Michael Smith Foundation for Health Research Trainee award (#17934). JAH is supported by a Canada Research Chair in Perinatal Population Health. KAA is supported by a Faculty Development Award from the Maine Economic Improvement Fund. WVN is supported by a Michael Smith Foundation for Health Research Scholar Award (#2012-5139 HSR) and by a Canadian Institutes for Health Research-Public Health Agency of Canada Applied Public Health Chair in Family Planning Research (#CPP-329455-107837).

Availability of data and materials

All data included in this systematic review and meta-analysis will be drawn from published original research and will be available through those papers directly. We will make our meta-analysis dataset publicly available along with the completed meta-analysis final paper.

Declarations

Ethics approval and consent to participate

We have submitted an application for research ethics to the University of British Columbia and Children's and Women's Health Centre of British Columbia Research Ethics Board (#H20-02183).

Consent for publication

The authors have all consented for this material to be submitted for publication.

Competing interests

The authors declare that they have no competing interests.

Author details

¹Department of Family Practice, University of British Columbia, E303 - 4500 Oak Street, Vancouver, BC V6H 3N1, Canada. ²School of Population and Public Health, University of British Columbia, 2206 E Mall, Vancouver, BC V6T 1Z3, Canada. ³Department of Obstetrics and Gynaecology, University of British Columbia, Suite 930, 1125 Howe Street, Vancouver, BC V6Z 2K8, Canada. ⁴Muskie School of Public Service, University of Southern Maine, 32 Bedford St, Portland, ME 04101, USA. ⁵Faculty of Public Health & Policy, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT, UK.

Received: 18 December 2020 Accepted: 15 September 2021

Published online: 25 October 2021

References

1. Wilcox AJ, Weinberg CR, O'Connor JF, et al. Incidence of early loss of pregnancy. *N Engl J Med*. 1988;319(4):189–94. <https://doi.org/10.1056/nejm198807283190401>.
2. Zinaman MJ, Clegg ED, Brown CC, O'Connor J, Selevan SG. Estimates of human fertility and pregnancy loss. *Fertil Steril*. 1996;65(3):503–9.
3. Wang X, Chen C, Wang L, Chen D, Guang W, French J. Conception, early pregnancy loss, and time to clinical pregnancy: a population-based prospective study. *Fertil Steril*. 2003;79(3):577–84. [https://doi.org/10.1016/s0015-0282\(02\)04694-0](https://doi.org/10.1016/s0015-0282(02)04694-0).
4. American College of Obstetricians & Gynecologists. ACOG Practice Bulletin No. 200: early pregnancy loss. *Obstet Gynecol*. 2018;132(5):197–207.
5. Ectopic pregnancy and miscarriage: diagnosis and initial management. NICE guideline [NG126] 17 April 2019.

6. Knudsen UB, Hansen V, Juul S, Secher NJ. Prognosis of a new pregnancy following previous spontaneous abortions. *Eur J Obstet Gynecol Reprod Biol.* 1991;39(1):31–6.
7. Edmonds DK, Lindsay KS, Miller JF, Williamson E, Wood PJ. Early embryonic mortality in women**Supported by Action Research for the Crippled Child. *Fertil Steril.* 1982;38(4):447–53. [https://doi.org/10.1016/s0015-0282\(16\)46579-9](https://doi.org/10.1016/s0015-0282(16)46579-9).
8. Matthews TJ, Hamilton BE. Delayed childbearing: more women are having their first child later in life. *NCHS Data Brief.* 2009;21:1–8.
9. Sunderam S, Kissin DM, Crawford SB, et al. Assisted reproductive technology surveillance - United States, 2015. *MMWR Surveill Summ (Washington, DC : 2002).* 2018;67(3):1–28. <https://doi.org/10.15585/mmwr.ss6703a1>.
10. Dissanayake MV, Darney BG, Caughey AB, Horner-Johnson W. Miscarriage occurrence and prevention efforts by disability status and type in the United States. *J Womens Health.* 2020;29(3):345–52. <https://doi.org/10.1089/jwh.2019.7880>.
11. The Practice Committee of the American Society for Reproductive Medicine. Evaluation and treatment of recurrent pregnancy loss: a committee opinion. *Fertil Steril.* 2012;98(5):1103–11. <https://doi.org/10.1016/j.fertnstert.2012.06.048>.
12. Schummers L, Hutcheon JA, Hacker MR, et al. Absolute risks of obstetric outcomes by maternal age at first birth: a population-based cohort. *Epidemiology.* 2018;29(3):379–87. <https://doi.org/10.1097/ede.00000000000000818>.
13. Branum AM, Ahrens KA. Trends in timing of pregnancy awareness among US women. *Matern Child Health J.* 2017;21(4):715–26. <https://doi.org/10.1007/s10995-016-2155-1>.
14. Lang K, Nuevo-Chiquero A. Trends in self-reported spontaneous abortions: 1970–2000. *Demography.* 2012;49(3):989–1009. <https://doi.org/10.1007/s13524-012-0113-0>.
15. Lepkowski JM, Mosher WD, Davis KE, Groves RM, van Hoewyk J, Willem J. National Survey of Family Growth, cycle 6: sample design, weighting, imputation, and variance estimation. *Vital Health Stat 2.* 2006;142:1–82.
16. Polland A, Davis M, Zeymo A, Venkatesan K. Comparison of correlated comorbidities in male and female sexual dysfunction: findings from the Third National Survey of Sexual Attitudes and Lifestyles (Natsal-3). *J Sex Med.* 2018;15(5):678–86. <https://doi.org/10.1016/j.jsxm.2018.02.023>.
17. Buss L, Tolstrup J, Munk C, et al. Spontaneous abortion: a prospective cohort study of younger women from the general population in Denmark. Validation, occurrence and risk determinants. *Acta Obstet Gynecol Scand.* 2006;85(4):467–75. <https://doi.org/10.1080/00016340500494887>.
18. Adolfsson A, Larsson P-G, Genus och M, Linköpings U, Institutionen för klinisk och experimentell m, Hälsouniversitetet. Cumulative incidence of previous spontaneous abortion in Sweden in 1983–2003: a register study. *Acta Obstetricia et Gynecologica Scandinavica.* Oxford: Informa UK Ltd; 2006. p. 741–7.
19. Curtin SC, Abma JC, Ventura SJ, Henshaw SK. Pregnancy rates for U.S. women continue to drop. *NCHS Data Brief.* 2013;136:1–8.
20. Coomarasamy A, Dhillon-Smith RK, Papadopoulou A, et al. Recurrent miscarriage: evidence to accelerate action. *Lancet.* 2021;397(10285):1675–82. [https://doi.org/10.1016/s0140-6736\(21\)00681-4](https://doi.org/10.1016/s0140-6736(21)00681-4).
21. Coomarasamy A, Gallos ID, Papadopoulou A, et al. Sporadic miscarriage: evidence to provide effective care. *Lancet.* 2021;397(10285):1668–74. [https://doi.org/10.1016/s0140-6736\(21\)00683-8](https://doi.org/10.1016/s0140-6736(21)00683-8).
22. The L. Miscarriage: worldwide reform of care is needed. *Lancet.* 2021;397(10285). [https://doi.org/10.1016/s0140-6736\(21\)00954-5](https://doi.org/10.1016/s0140-6736(21)00954-5).
23. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev.* 2015;4:1. <https://doi.org/10.1186/2046-4053-4-1>.
24. Echevarria IM, Walker S. To make your case, start with a PICOT question. *Nursing.* 2014;44(2):18–9. <https://doi.org/10.1097/01.NURSE.0000442594.00242.f9>.
25. World Bank Country and Lending Groups – World Bank Data Help Desk. <Datahelpdesk.worldbank.org>. <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups>. Accessed 26 July 2020.
26. Parekh-Bhurke S, Kwok CS, Pang C, et al. Uptake of methods to deal with publication bias in systematic reviews has increased over time, but there is still much scope for improvement. *J Clin Epidemiol.* 2011;64(4):349–57. <https://doi.org/10.1016/j.jclinepi.2010.04.022>.
27. Jones RK, Kost K. Underreporting of induced and spontaneous abortion in the United States: an analysis of the 2002 National Survey of Family Growth. *Stud Fam Plann.* 2007;38(3):187–97. <https://doi.org/10.1111/j.1728-4465.2007.00130.x>.
28. Center for Reproductive Rights. The World's Abortion Laws. Center for Reproductive Rights. <https://maps.reproductiverights.org/worldabortionlaws>. Accessed 10 Sept 2021.
29. Lash TL, Fox MP, MacLehose RF, Maldonado G, McCandless LC, Greenland S. Good practices for quantitative bias analysis. *Int J Epidemiol.* 2014;43(6):1969–85.
30. Covidence Systematic Review Software. Melbourne: Veritas Health Innovation; 2020.
31. The Global Abortion Policies Database. World Health Organization. <https://abortion-policies.srhr.org>. Published 2020. Accessed 19 Oct 2020.
32. Procedure Manual Section 4. Evidence review development. [Uspreventiveservicestaskforce.org](https://www.uspreventiveservicestaskforce.org/uspstf/procedure-manual-section-4-evidence-review-development). <https://www.uspreventiveservicestaskforce.org/uspstf/procedure-manual-section-4-evidence-review-development>. Accessed 26 July 2020.
33. Inthout J, Ioannidis JP, Borm GF. The Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method. *BMC Med Res Methodol.* 2014;14(1):25. <https://doi.org/10.1186/1471-2288-14-25>.
34. Deeks JJ, Higgins JP, Altman DG, Group obotCSM. Chapter 10: Analysing data and undertaking meta-analyses. In: JPT H, Thomas J, Chandler J, et al., editors. *Cochrane Handbook for Systematic Reviews of Interventions*. Cochrane Training; 2021. chap 10.
35. Borenstein M, Higgins JPT, Hedges LV, Rothstein HR. Basics of meta-analysis: I^2 is not an absolute measure of heterogeneity. *Res Synth Methods.* 2017;8(1):5–18. <https://doi.org/10.1002/jrsm.1230>.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

