75 HEALTH FOR ALL

World Health Organization

human reproduction programme hrp research for impact

UNDP-UNFPA-UNICEF-WHO-WORLD BANK

Infertility prevalence estimates

1990–2021

75 HEALTH FOR ALL

World Health Organization

human reproduction programme hrp

research for impact

UNDP · UNFPA · UNICEF · WHO · WORLD BANK

Infertility prevalence estimates

1990–2021

Infertility prevalence estimates, 1990–2021

ISBN 978-92-4-006831-5 (electronic version)
ISBN 978-92-4-006832-2 (print version)

Contents

List of tables

List of figures

List of annexes

Foreword

This report, the first of its kind in a decade, reveals an important truth: infertility does not discriminate. For millions around the world, the path to parenthood can be difficult to access, if not impossible. Globally, an estimated 1 out of every 6 people are affected by the inability to have a child at some point in their life. This is regardless of where they live and what resources they have.

Infertility affects millions. Even still, it remains understudied, and solutions underfunded, and inaccessible to many, as the result of high costs, social stigma and limited availability.

The causes of infertility are varied and often complex, and is something that both men and women experience. Indeed, a wide variety of people, in all regions, may require fertility care.

As with any health issue, it is imperative that we know more. This report emphasizes the importance of quantifying infertility, as well as knowing who needs fertility care, and how risks can be reduced. Using a universal definition and consistent methods to measure infertility will improve our understanding of this common challenge that can negatively impact mental health and cause economic hardship.

Access to sexual and reproductive health services is the primary way for people to have the best chance of having the number of children they desire. Addressing infertility is also important for achieving the health and gender equality targets of the 2030 Sustainable Development Goals. The data in this report emphasize the need to provide access to prevention, diagnosis and treatment of infertility. However, in most countries, these services are inadequate.

This report will help policy-makers, civil society organizations, health service providers, researchers and others stakeholders to understand the magnitude of infertility, which is critical for monitoring, assessing, and improving equitable access to quality fertility care services, as well as addressing risk factors and consequences of infertility. It is my hope that governments use this report to develop evidence-based policies and adopt proven solutions, as part of their efforts to strengthen health systems to help people fulfil their fertility intentions and live healthier lives.

Dr Tedros Adhanom Ghebreyesus
Director-General, World Health Organization

Acknowledgements

The World Health Organization (WHO) Department of Sexual and Reproductive Health and Research thanks all individuals who contributed to developing these infertility prevalence estimates.

WHO appreciates the work of the research team that supported the generation of these estimates: **Marta Bornstein** (Division of Epidemiology, Ohio State University, Columbus, United States of America (USA)), **Carie Jean Cox** (Independent Consultant, Luxembourg City, Luxembourg), **Courtney Johnson** (Department of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis, USA), **Nedelina Tchangalova** (University of Maryland Libraries, College Park, Maryland, USA) and **Marie Elizabeth Thoma** (Department of Family Science, University of Maryland, Maryland, USA).

The estimates presented in this report are also published as a peer reviewed article: Cox C.M., Thoma M.E., Tchangalova N., Mburu G., Bornstein M.J., Johnson C.L., and Kiarie J., Infertility prevalence and the methods of estimation from 1990 to 2021: a systematic review and meta-analysis, Human Reproduction Open. Nov 12;2022(4):hoac051. doi: 10.1093/hropen/hoac051.

The following advisory committee members provided inputs and feedback on the methodology and protocol used to develop these estimates: **Rudolph Kantum Adageba** (Ruma Fertility and Specialist Hospital, Kumasi, Ghana), **Patricia F. Anderson** (Taubman Health Sciences Library, University of Michigan, Ann Arbor, USA), **Rachid Bezad** (Faculty of Medicine and Hospital Les Orangers, Mohammed V University, Rabat, Morocco), **Sarah Bradley** (SHOPs Plus Project, Abt Associates, Maryland, USA), **Silke Dyer** (Department of Obstetrics and Gynaecology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa), **Jasmine Fledderjohann** (Department of Sociology, Lancaster University, Bailrigg, United Kingdom of Great Britain and Northern Ireland), **Marcos Horton** (Pregna Medicina Reproductiva, Buenos Aires, Argentina), **LaTeesa James** (Taubman Health Sciences Library, University of Michigan, Ann Arbor, USA), **Tianjing Li** (School of Medicine, University of Colorado, Colorado, USA), **Ginny Ryan** (Department of Obstetrics and Gynecology, University of Iowa, USA), and **Lauren Wise** (Department of Epidemiology, Boston University School of Public Health, Boston, USA).

Additional feedback on the estimates was received from the following participants in the WHO Technical Consultation on Estimates of Infertility Prevalence held on 6–8 July 2021: **Rachid Bezad** (Faculty of Medicine and Hospital Les Orangers, Mohammed V University, Rabat, Morocco), **Jacky Boivin** (School of Psychology, Cardiff University, Cardiff, United Kingdom), **Anjani Chandra** (National Center for Health Statistics, US Centers for Disease Control and Prevention, USA), **Barbara Collura** (Resolve, McLean, Virginia, USA), **Mae Dirac** (Departments of Health Metrics and Family Medicine, University of Washington, Seattle, USA), **Silke Dyer** (Department of Obstetrics and Gynaecology, University of Cape Town, Cape Town, South Africa), **Farid Foroutan** (Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Canada), **Natalia Gogliormella** (National Medically Assisted Reproduction Programme, Ministry of Health, Buenos Aires, Argentina), **Apoorva Jadhav** (Policy Evaluation and Communication Division, Office of Population and Reproductive Health, Bureau for Global Health, Washington, DC, USA), **Neils Keiding** (Department of Public Health, University of Copenhagen, Copenhagen, Denmark), **Germaine M. Buck Louis** (College of Health and Human Services, George Mason University, Fairfax, USA), **Manala Makua** (National Department of Health, Johannesburg, South Africa), **Victoria Mansur** (National Programme for Assisted Reproduction, Ministry of Health, Buenos Aires, Argentina), **Alexander McLain** (Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, USA), **Ashraf Nabhan** (Department of Obstetrics and Gynaecology, Ain Shams University, Cairo, Egypt), **Zozo Nene** (Faculty of Health Sciences, University of Pretoria, South Africa), **Steven Ory** (Herbert Wertheim College of Medicine, Florida International University, Florida, USA), **Antoinette Righarts** (Dunedin School of Medicine, Dunedin, New Zealand), **Iqbal Shah** (Department of Global Health and Population, Harvard T.H. Chan School of Public Health, Boston, USA), **Rémy Slama** (Environmental Epidemiology Unit, INSERM, La Tronche, Grenoble, France), **Gretchen Stevens** (Independent Consultant, Los Angeles, USA), **Lauren Wise** (Department of Epidemiology, Boston University School of Public Health, Boston, USA), **Hafida Yartaoui** (Family Planning Division, Ministry of Health, Rabat, Morocco).

The following WHO staff participated in the technical consultation or otherwise reviewed these estimates: **Mohamed Mahmoud Ali, Ian Askew, Jenny Cresswell, Lale Say** and **Nandita Thatte** (Department of Sexual and Reproductive Health and Research); **Christine Sonja Autenrieth, Zoe Brillantes, Bochen Cao**, and **Diana Estevez Fernandez** (Division of Data, Analytics and Delivery for Impact); **Karima Gholbzouri**, (WHO Regional Office for the Eastern Mediterranean); **Rodolfo Gomez Ponce de Leon** (WHO Regional Office for the Americas / Pan American Health Organization [PAHO]); and **Chandani Anoma Jayathilaka** (WHO Regional Office for South-East Asia).

The overall process of generating these estimates was led by **Gitau Mburu** under the guidance of **James Kiarie**, and with the support of **Ian Askew** and **Pascale Allotey**, (Department of Sexual and Reproductive Health and Research). **Therese Curtin** provided administrative support.

The work to generate these estimates was financially supported by the UNDP-UNFPA-UNICEF-WHO-World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), World Health Organization.

Design and layout: Lushomo

Copy-editing: Kelly Safreed-Harmon

Photo credits :
Cover page photo © photobomb
Page ix top photo © Jan Antonin Kolar on Unsplash
Page ix bottom photo © Harsha KR
Page x photo © ccbarr
Page 1 photo © WHO/Ahmad Yusni
Page 25 photo © WHO/Yoshi Shimizu
Page 33 photo © Gifts for moms
Page 37 photo © WHO/Anna Usova
Page 77 photo ©WHO/Khadija Farah

Abbreviations

CI	confidence interval
HIC	high-income countries
LMIC	low- and middle-income countries
OR	odds ratio
SDG	Sustainable Development Goal
SE	standard error
SRHR	sexual and reproductive health and rights
TTP	time-to-pregnancy
WHO	World Health Organization

Executive summary

Introduction

Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse. Infertility impacts millions of people worldwide, often with devastating consequences. Addressing infertility is an important component of sexual and reproductive health and rights, but in most countries, infertility policies and services are inadequate. Addressing infertility is central to achieving Sustainable Development Goal (SDG) 3 – *Ensure healthy lives and promote well-being for all at all ages* – and SDG 5 – *Achieve gender equality and empower all women and girls*. Addressing infertility is also central to achieving the human rights to the enjoyment of the highest attainable standard of physical and mental health and to decide the number, timing and spacing of one's children.

Understanding the magnitude of infertility is critical for developing appropriate interventions, for monitoring access to quality fertility care, and for mitigating risk factors for and consequences of infertility. Yet there is considerable variation in estimates of infertility. Differences in how infertility is defined and measured partly contribute to this variation.

This report provides insight into global and regional infertility prevalence by analyzing all relevant studies from 1990 to 2021, taking into account different study approaches.

Addressing infertility is an important component of sexual and reproductive health and rights, and is central to achieving SDG 3 and SGD 5

It is central to achieving:

The highest attainable standard of physical and mental health

The ability to decide the number, timing and spacing of one's children

In turn meeting:

Sustainable Development Goal 3: Ensure healthy lives and promote well-being for all at all ages.

Sustainable Development Goal 5: Achieve gender equality and empower all women and girls.

Methods

These global and regional infertility prevalence estimates were generated and reported in accordance with the Guidelines for Accurate and Transparent Health Estimates Reporting, (GATHER), which is widely used for reporting health estimates of this nature. The process included the following steps :

A **search strategy** was developed to identify studies reporting on infertility prevalence between 1990 and 2021. Several major electronic databases were searched, as were websites and conference proceedings.

Relevant **data were extracted** from the selected studies. The extracted data included the infertility prevalence rates that were reported in the studies, as well as information about the study design, study population characteristics and other factors.

Data analyses were performed to obtain information about approaches used in estimating infertility, and to generate infertility prevalence estimates. These estimates reflected the pooled findings of the selected studies. The overall lifetime and period prevalence of infertility were estimated, and additional analyses provided comparisons of infertility prevalence in terms of factors such as geographic regions and country income levels.

Methodological process:

Results

Included studies
The search identified 12,241 records of potentially relevant studies. Screening of these records led to the selection of 133 studies that met the criteria for inclusion in the systematic review. From these, 91 data points were used to generate pooled 12-month infertility estimates.

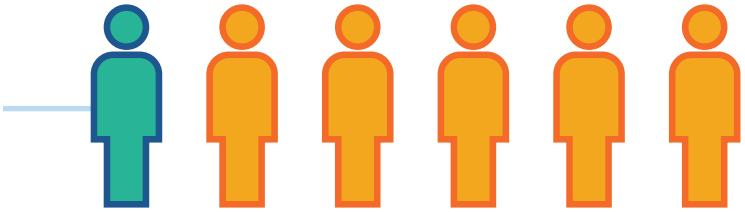
Global infertility prevalence estimates[1]
Based on data from 1990 to 2021, the 2022 global infertility prevalence estimates are:

- Approximately one in six people have experienced infertility at some stage in their lives, globally.
- **Lifetime prevalence** of infertility is estimated to be 17.5% (95% confidence interval [CI]: 15.0, 20.3).
- **Period prevalence** of infertility is estimated to be 12.6% (95% [CI]: 10.7, 14.6).

Global infertility prevalence estimates

2022 global infertility prevalence estimates are:

Approximately **one in six** people have experienced infertility at some stage in their lives, globally.



17.5%
Estimated lifetime prevalence of infertility (95% confidence interval: 15.0, 20.3).

Lifetime prevalence is defined as the proportion of a population who have ever experienced infertility in their life.

12.6%
Estimated period prevalence of infertility (95% confidence interval: 10.7, 14.6).

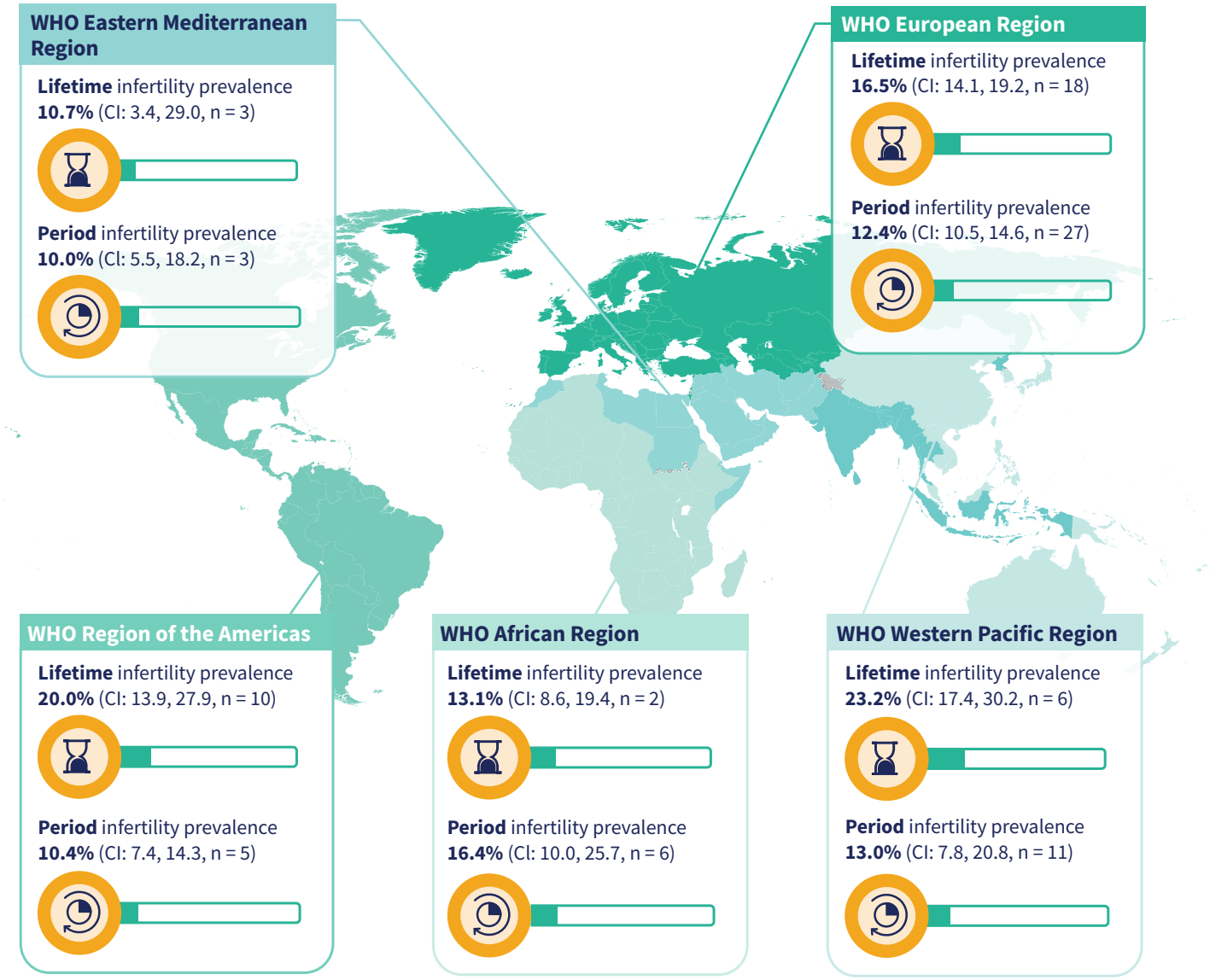
Period prevalence is defined as the proportion of a population with infertility at a given point or interval in time, which may be current or in the past.

Regional infertility prevalence estimates
There is **some variation** in infertility prevalence across regions, but data gaps and overlapping confidence intervals mean that **regional differences** identified in this analysis **may not be substantial or conclusive**. Some regions had very few studies with relevant prevalence estimates, and no studies were identified for the World Health Organization (WHO) South-East Asia Region.

The available data indicate that estimated **lifetime prevalence** of infertility is **highest** in the WHO Western Pacific Region (23.2%) and **lowest** in the WHO Eastern Mediterranean Region (10.7%). Estimated **period prevalence** of infertility is **highest** in the WHO African Region (16.4%) and **lowest** in the Eastern Mediterranean Region (10.0%). All confidence intervals for these estimates overlap based based on 3 or fewer studies, suggesting that the observed differences may not be substantial or conclusive.

[1] Unless otherwise specified, these estimates refer to 12-month period or lifetime prevalence in keeping with the following definition of infertility adopted by the World Health Organization (WHO): *Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse*

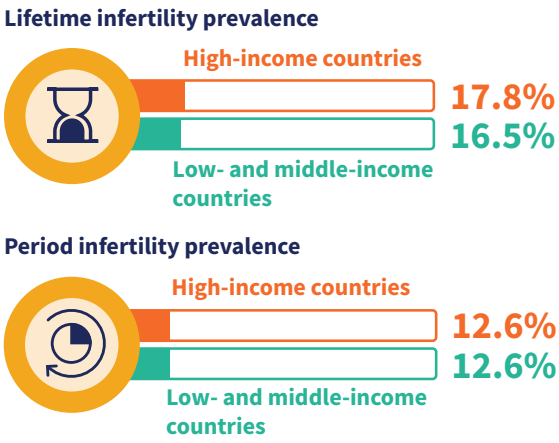
Regional infertility prevalence estimates



CI = Confidence interval
n = number of studies

WHO = World Health Organization
No studies were available for the WHO South-East Asia Region

Estimates of infertility prevalence are similar across countries with different income levels. Lifetime infertility prevalence was 17.8% for high-income countries and 16.5% for low- and middle-income countries. Period infertility prevalence was 12.6% for high-income countries and 12.6% for low- and middle-income countries.



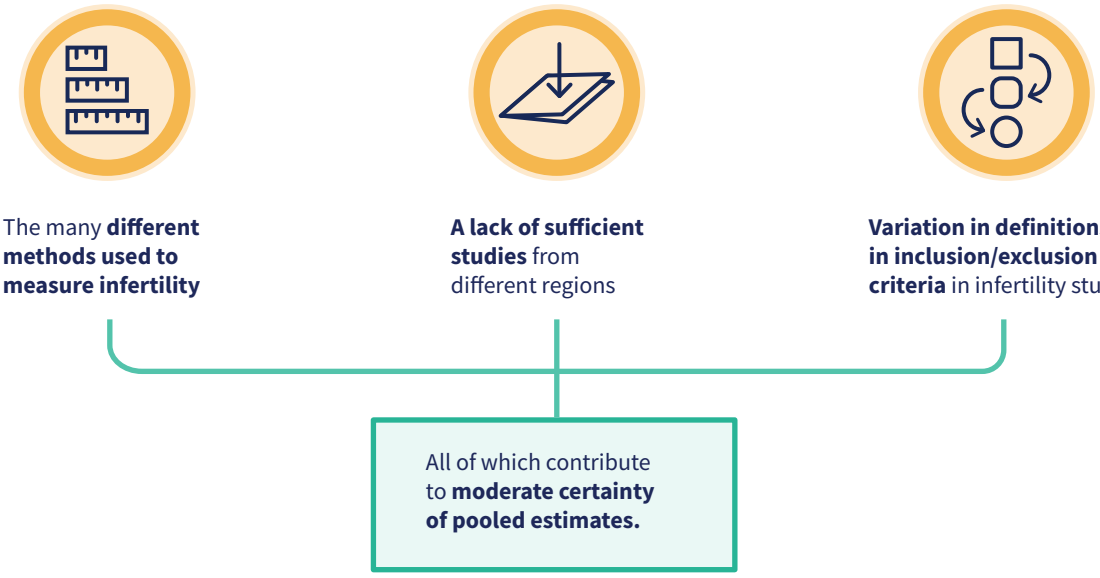
Research gaps, measurement challenges, and implications for future research

Across the individual studies that contributed data to these estimates, reported infertility prevalence varied greatly. This may partly reflect the many **different methods** used to measure infertility. In addition, there is a **lack of sufficient studies from some regions**, as well as variation in definitions and in inclusion and exclusion criteria in studies estimating infertility, which all contribute to **moderate certainty of pooled estimates**.

Moving forward, researchers must **use more consistent, systematic and comprehensive processes** to improve the evidence base relating to infertility prevalence at the global, regional and national levels.

Research challenges

Across the individual studies that contributed data to these estimates, reported infertility prevalence varied greatly. This may be due to:



Recommendations for future infertility prevalence research

1. Estimating prevalence of infertility
The field needs a standard set of questions for ascertaining infertility prevalence that could be adopted by Demographic and Health Surveys and other standard population-based surveys. Questions should be flexible enough to allow for different definitions and approaches in order to facilitate comparison. At a minimum, 12-month period infertility that is consistent with the WHO definition should be measured.

2. Selecting a methodological approach
When selecting an approach to estimate infertility prevalence, researchers should consider the objectives, data sources, resources, and validity and reliability of data.

3. Reporting estimates
Detailed methodological and analytical information should be provided when reporting estimates of infertility prevalence. When feasible, estimates for total, primary, and secondary infertility prevalence, with stratification by age and sex, should be reported.

4. Making comparisons across studies
Estimates should only be compared where they are as similar as possible in relation to various study characteristics such as definitions, methodological approaches, and exclusion criteria.

Policy and programmatic implications

Valid and reliable estimates of infertility are needed to understand its burden and to facilitate appropriate policy formulation, as well as advocacy, provision, and monitoring of prevention efforts and fertility care services. These estimates clearly show that a large number of people may require infertility management and fertility care services in different regions of the world. Currently, challenges can be observed in relation to the availability, accessibility, and quality of interventions to prevent, diagnose and treat infertility in most countries. It is anticipated that these estimates will improve our understanding of the prevalence and burden of disease related to infertility globally and regionally, and will provide a basis for policy and practice to achieve universal access to fertility care.

Conclusion

Human health and gender equality are central elements of the Sustainable Development Goals, which call on governments to ensure universal access to sexual and reproductive health and rights. Fertility care is a core part of sexual and reproductive health, and responding to infertility can mitigate gender inequality. The drive to achieve the Sustainable Development Goals therefore must encompass actions to respond more effectively to the needs of people with infertility, leaving no one behind. These estimates show high prevalence of infertility globally and regionally, a finding that should be used to support the development of policies and practices that will help individuals and couples achieve their desired family size. Findings also provide insight into how the estimation of infertility prevalence can be improved in order to obtain more actionable data, including data that allow for more meaningful comparisons across settings and time.

1. Introduction

This section provides background information on how infertility prevalence has been measured in the past, why there are limitations to earlier assessments of infertility prevalence, and how this report advances knowledge and strategic information about infertility prevalence.

Addressing infertility is an important component of sexual and reproductive health and rights (SRHR) but has been neglected in the global SRHR agenda. Infertility has devastating societal and health consequences, including social stigma, economic hardship, and gender-based violence, as well as poor mental health *(1, 2)*. Addressing infertility is central to achieving Sustainable Development Goal (SDG) 3 – *Ensure healthy lives and promote well-being for all at all ages* – and SDG 5 – *Achieve gender equality and empower all women and girls*.

Furthermore, every human being has a right to the enjoyment of the highest attainable standard of physical and mental health *(3)*. Individuals and couples have the right to decide the number, timing and spacing of their children *(4)*. Men and women of full age, without any limitation due to race, nationality or religion, have the right to marry and to found a family *(5)*. If infertility is not addressed, it can negate the realization of these essential human rights. Failure to address infertility will hamper global efforts to ensure universal access to sexual and reproductive health and rights. Consequently, urgent efforts are required to improve the prevention, management, and treatment of infertility worldwide *(6)*.

Understanding the magnitude of infertility is critical for monitoring, assessing, and improving equitable access to quality fertility care services, as well as addressing risk factors for and consequences of infertility. Yet there has been considerable variability in its previous estimation (**Figure 1.1**). As many researchers have noted, this variability hinders accurate comparisons across regions, populations, and time *(7-13)*.

Unlike other types of conditions, infertility is defined by the absence of an event (i.e., not getting pregnant), usually after a defined period of time. The World Health Organization (WHO) specifies a 12-month duration, defining infertility as "a disease of the male or female reproductive system characterized by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse". *(14)*. However, many studies have utilized other definitions of infertility that incorporate longer durations, such as 24 or 60 months *(11)*, or involve non-duration-based definitions to include health conditions that warrant infertility services or relationship factors, such as single persons or same-sex couples as suggested by Zegers-Hochschild et al.*(15)*. In addition, while some researchers propose that time-to-pregnancy (TTP) be used to ascertain infertility *(16, 17)*, many studies use self-reported or constructed binary measures of infertility *(12)*. In addition, studies vary in their definition and application of numerators and denominators, study designs, survey instruments, and analytic methods, all of which can affect conclusions regarding the true magnitude of infertility *(13, 18)*.

Figure 1.1. Wide-ranging findings from previous estimates of infertility

Previous estimates of infertility prevalence suggested that the number of individuals or couples affected by infertility ranged from 48.5 million couples globally *(19)* to 186 million ever-married women in developing countries alone *(20)*. In addition, a 2012 study that used data from 277 demographic health surveys and Bayesian hierarchical modeling to generate estimates for 190 countries and territories using a duration of five years or more to define infertility *(19)* concluded that 1.9% of women exposed to the risk of pregnancy experienced primary infertility, (defined by the authors as the inability to have any live birth), and 10.5% experienced secondary infertility, (defined by the authors as the inability to have an additional live birth). A 2007 literature review of 25 population surveys found that the prevalence of infertility when defined by a duration of 12 months or more ranged from 3.5% to 16.7% in more developed nations and from 6.9% to 9.3% in less developed nations *(21)*. In 2016, another review and meta-analysis of 52 studies reported a mean infertility prevalence of 10% worldwide, with pooled prevalence lowest and highest in Australia and Africa, respectively *(22)*.

Consequently, it is important to assess how differences in definitions and study designs may affect infertility estimates. Understanding the impacts of these variations can provide important insights for developing a standardized methodological approach. In addition, pooling of prevalence data through a meta-analytical approach is necessary for generating global and regional estimates. The estimates presented in this report therefore aimed to generate global and regional estimates while taking into account variation in measurement approaches. The work was guided by two research questions shown in **Figure 1.2**.

Figure 1.2. Key questions addressed in these estimates

1. What approaches have been used to estimate prevalence of infertility among representative populations?
2. What is the contemporary prevalence of infertility globally, and how do prevalence estimates differ by methodological approach and study design?

> **Understanding the magnitude of infertility is critical for monitoring, assessing, and improving equitable access to quality fertility care services, as well as addressing risk factors for and consequences of infertility.**

2. Methods

This section describes how studies reporting infertility prevalence data were identified. It also describes which items of data were extracted from each study and explains how data were analyzed.

These estimates were reported according to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) *(23)*. A systematic review and meta-analysis was conducted in accordance with the updated Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) *(24)* and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) *(25)*, based on a pre-registered protocol *(26)*.

2.1 Data sources and identification of relevant studies

To identify peer-reviewed publications, the following electronic databases were searched: PubMed (US National Library of Medicine), Web of Science (Clarivate Analytics), CINAHL (EBSCO), Family & Society Studies Worldwide (EBSCO), Public Health (ProQuest), and Google Scholar. Relevant articles and reviews were hand-searched. To identify grey literature, a search was conducted of electronic databases (Public Health [ProQuest] and ProceedingsFirst [OCLC]), relevant websites, and conference proceedings. Additionally, experts in the field were consulted.

The search strategy included terms related to infertility (e.g., infertility, subfertility, infecundity, childlessness) and estimation (e.g., estimate, prevalence). Searches were limited to between 1990 and 2021 with no language restrictions. The year 1990 was selected as the lower bound cut-off for four reasons. First, this ensured that the estimates were contemporary. Second, an analysis of trends in infertility prevalence in 190 countries and territories had found that levels of infertility in 2010 were similar to those in 1990 in most regions of the world *(19)*. Third, it was necessary for the range of time to be long enough to capture all relevant methodological approaches. Finally, Schmidt and Münster *(8)* conducted a review of the prevalence of infertility and its measurement in "industrialized countries" spanning 1970 to 1992, and the estimates presented here were intended to extend and expand on this previous work. Records retrieved from all searches underwent title, abstract and full-text screening, with the aid of reference management software. Two members of the research team independently assessed whether studies were eligible for inclusion, based on predetermined criteria (**Figure 2.1**), with disagreements resolved through discussion to reach consensus.

Figure 2.1. Inclusion criteria

General population and clinic-based studies were included if they met all of the following criteria:

- designed to be a representative sample of a general population of women and/or men;
- reported estimates of the prevalence or cumulative incidence of infertility;
- collected data during or after 1990;
- specified, in their definition of infertility, a duration of at least six months in which pregnancy is not reached or defined infertility as a subjective evaluation of one's difficulty conceiving or maintaining a pregnancy;
- presented original research using primary or secondary data; and
- used one of the following study designs: cross-sectional, cohort, case-control (if the control group was a representative sample of the general population and the disease of interest [i.e., cases] was not infertility), or randomized trial (if the study reported an overall estimate for a representative sample of the general population at baseline, before any interventions were administered).

Studies were considered representative if they recruited, based on their study design, all eligible members of a population (i.e., census) or applied probability-based sampling. Clinic-based studies that applied consecutive sampling for 12 or more months were defined as a census of the clinic population and thus were considered eligible for inclusion. Furthermore, for clinic-based studies to meet the requirement of representing a general population, their samples had to have been drawn from a clinic that serves the general population (i.e., a primary health care clinic or an obstetrics and/or gynecology clinic) and were representative of the clinic population as a whole.

Studies were excluded based on criteria shown in **Figure 2.2**. Duplicate publications that generated multiple estimates of prevalence of infertility using the same data source, definition of infertility, and approach to estimation were eliminated.

Figure 2.2. Exclusion criteria

Studies were excluded if they met any of the following criteria:

- reported cause-specific prevalence of infertility only, such as tubal factor infertility, or male-factor or female-factor infertility;
- estimated only the proportion seeking fertility treatment or receiving a diagnosis of infertility;
- did not use individuals as the unit of analysis (e.g., studies in which the prevalence was calculated based on total pregnancies, rather than individuals);
- measured childlessness without an intention to estimate infertility (e.g., a combined measure of voluntary and involuntary childlessness or a measure that did not distinguish reasons for involuntary childlessness);
- included menopausal and/or surgically sterile individuals in their numerator, which would inflate the numerator with individuals who have completed their reproductive life span either naturally or surgically;
- did not define their measure of infertility; or
- reported results only as an abstract or unpublished data.

2.2 Data extraction

Data that were extracted from each study are shown in **Figure 2.3**.

Figure 2.3. Data extracted from studies

Study characteristics

- **study design**
- **data collection details**
- **methodological approach or approaches** (prospective time to pregnancy [TTP] design, retrospective TTP design, current duration design, self-reported infertility measure [direct], constructed infertility measure [indirect], and undetermined)
- **infertility estimates** (reported proportion of study sample with infertility)

Study population characteristics

- **sample type** (population-based sample, clinic-based sample)
- **sex of respondent** (female respondent, male respondent, combined)
- **income level of the country where the study was conducted**, according to World Bank classification at time of analysis (2021) *(27)* (high-income country [HIC], low- and middle-income country [LMIC])
- **Geographic region** (based on World Health Organization regions: African Region, Region of the Americas, South-East Asia Region, European Region, Eastern Mediterranean Region, Western Pacific Region)

Definitional characteristics

- **type of prevalence** (period, lifetime)
- **numerator** (duration-only, duration and treatment, self-perceived infertility, intention to conceive) (also categorized based on whether intentions were considered or not, i.e., trying to conceive)
- **denominator** (individuals regardless of risk of pregnancy, individuals at risk of pregnancy regardless of intentions, individuals attempting to conceive)

For studies that included data collected both before and after 1990, only estimates calculated from data collected during or after 1990 were extracted. For studies that presented estimates for multiple time periods after 1990, the most recent estimate was extracted. In instances where necessary information was not reported in a manuscript, an effort was made to obtain the information by e-mailing the corresponding author.

2.3 Data analysis

2.3.1 Risk of bias assessment

The risk of bias for each study was assessed using a risk of bias tool proposed by Hoy *et al.* *(28)* which was slightly modified to better fit with infertility definitions assessed for these estimates (**Annex 1**). The tool includes eight items assessing external and internal validity. For each item, studies were rated as either low or high risk. Studies that provided insufficient information to permit a judgement for a given item were classified as high risk. An overall summary score was generated from the sum of the eight individual items (one point awarded for each item labeled as low risk). The overall summary score was divided into the following tertiles: 1) low risk of bias: 6–8 points, 2) moderate risk of bias: 3–5 points, and 3) high risk of bias: 0–2 points. The potential for publication bias was assessed through funnel plots.

2.3.2 Descriptive analysis

First, the methodological approaches used to estimate the prevalence of infertility were identified and described. Next, the overall number of studies was reported, and the numbers of studies by study descriptor variables. In analyzing the estimates of infertility prevalence, the focus was on the definition adopted by WHO *(14)*, i.e., "a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse," hereafter referred to as "12-month infertility." The number of studies and range of estimates of 12-month infertility overall and by study descriptor variables were examined and reported.

2.3.3 Meta-analysis and meta-regression

Meta-analysis was applied to estimate period and lifetime prevalence of 12-month infertility overall and stratified by income level, region, respondent type, and methodological approach. The standard error (SE) of each study's infertility prevalence estimate were calculated either: 1) by extracting the SE directly or calculating from the 95% confidence interval (CI) ((upper interval–lower interval)/3.92), or when this information was not available, 2) a SE was calculated based on the formula for obtaining a standard error from a proportion (p) ([SQRT(p*(1-p))/N]). Sensitivity analyses were further conducted to examine the influence of studies that used an approximated SE compared to studies in which the SE could be estimated directly.

Estimates of 12-month infertility were transformed using the logit function ([ln(p/(1-p)]). Corresponding SEs were logit transformed using the delta method [SQRT((1/(p*(1-p))^2)*(SE^2)). To ensure independence across studies for the meta-analyses and assess the sensitivity of analytic choices on selection of estimates, the maximum or the minimum lifetime and period infertility prevalence estimates were selected for studies in which multiple estimates were presented (either in the same record or a duplicate record, which for the purposes of the meta-analysis was defined as an estimate that was generated from the same data source).

Pooled estimates for studies were generated using the maximum value of the prevalence estimate for studies presenting multiple estimates, then the same was done using the minimum value in sensitivity analyses. Random-effects meta-analysis models were used to generate pooled estimates, 95% confidence intervals, I^2 statistics (i.e., proportion of total variability in point estimates that can be attributed to heterogeneity), and forest plots. A decision to present pooled estimates was not solely based on I^2 values, but was informed by consideration that higher I^2 values are inevitable where sample sizes are large, and standard errors are precise *(29)*, which was consistent with the included studies. Pooled estimates were stratified by period or lifetime infertility, income classification (i.e., HIC or LMIC), geographic region, methodological approach, and respondent's sex. Using a random-effects meta-analysis model, funnel plots were derived of the logit transformed prevalence estimates against their standard errors.

Meta-regression using restricted maximum likelihood was applied to generate adjusted period and lifetime prevalence estimates of 12-month infertility after accounting for region, methodological approach, whether or not numerator included intentions, denominator categories, and risk of bias score. The covariates in the model were chosen based on variables of interest in estimation (i.e., region, methodological approach) or having a sufficient number of studies across each variable categorization and region. The exponentiated regression coefficient obtained from the meta-regression of the logit transformed infertility prevalence estimates provides odds ratios for a given unit change in the covariate. Stata 16.1 was used to conduct meta-analyses and meta-regression *(30)*.

2.3.4 Sensitivity analyses

In meta-analysis, sensitivity analysis was conducted by estimating pooled lifetime and period prevalence of 12-month infertility stratified by 1) maximum versus minimum values for linked studies or SE calculation assumptions, 2) all studies versus highest-quality studies (risk of bias > 6), and 3) studies from the general population only versus all studies (i.e., population- and clinic-based studies).

2.3.5 Rating certainty of evidence

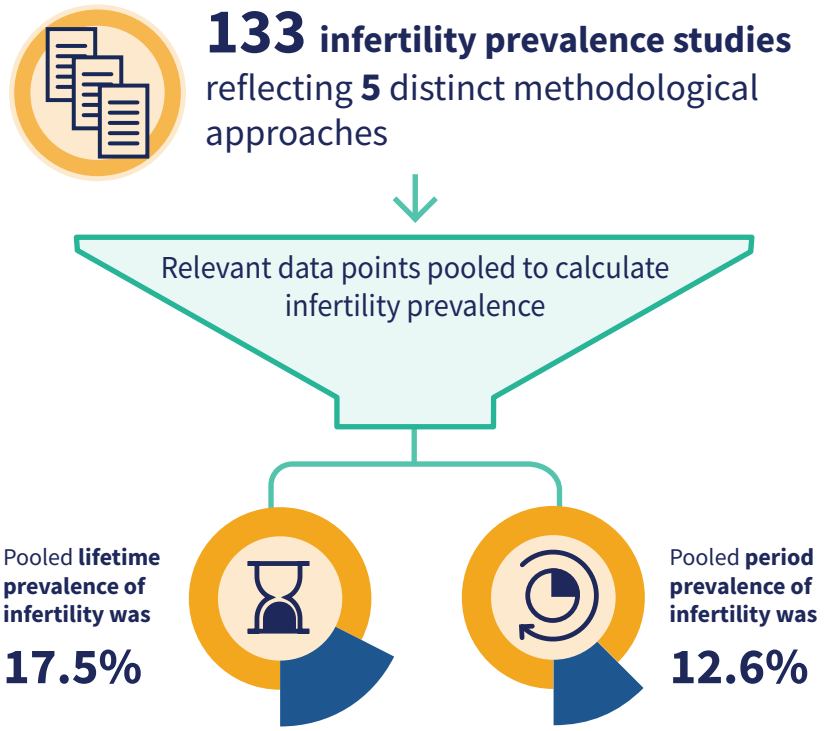
The GRADE framework *(31)* was used for rating the certainty in inferences drawn from the estimates. Specifically, the GRADE guidance relating to overall prognosis was adopted *(32)* as it is the most applicable to questions on prevalence of a condition. The GRADE framework rates certainty in inferences as high, moderate, low, or very low. Certainty may decrease due to concerns about risk of bias, inconsistency, indirectness, imprecision, and publication bias. For concerns about risk of bias, the sensitivity analyses conducted by the research team (exclusion of high risk of bias studies to determine if conclusions from pooled estimates differ) were used. For concerns about inconsistency, reliance was not placed on the I^2 statistics, as these tend to overestimate heterogeneity amongst studies with large sample sizes and number of events *(29)*; instead, inconsistency (heterogeneity) was also informed by visual inspection of forest plots. Specifically, overlap of point estimates and 95% confidence intervals across the individual studies was examined. Indirectness was assessed by comparing the research questions posed by the authors of individual studies to those posed in the investigation that yielded these estimates. For imprecision, the width of the 95% CI of the pooled estimates was assessed. Given that the evidence in these estimates will be used in various contexts and settings, a formal threshold for rating imprecision was not determined; rather, consideration was given to whether the upper and lower bounds of the 95% CI are sufficiently close to the reported pooled estimate. Finally, publication bias was assessed through visual inspection of funnel plots.

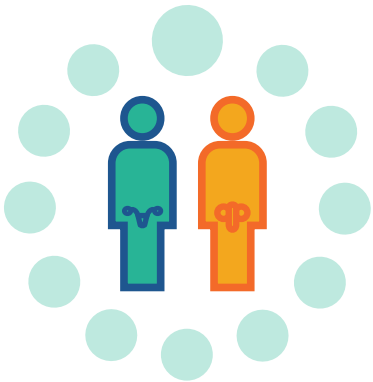
3. Results

This section presents findings from the literature search and the analysis of data extracted from relevant studies.

A total of 133 studies met inclusion criteria, and these studies reflected five distinct methodological approaches to estimating infertility. The findings from all studies that reported 12-month infertility prevalence (n = 84) were pooled to calculate pooled lifetime and period prevalence of infertility at the global and regional levels. Relevant data points from studies were used to pool estimates. Overall pooled lifetime prevalence of infertility was 17.5%, and overall pooled period prevalence of infertility was 12.6%.[2] There was some variation in infertility prevalence across different geographic regions. Unless otherwise specified, prevalence refers to 12-month infertility, consistent with the WHO definition.

Research process



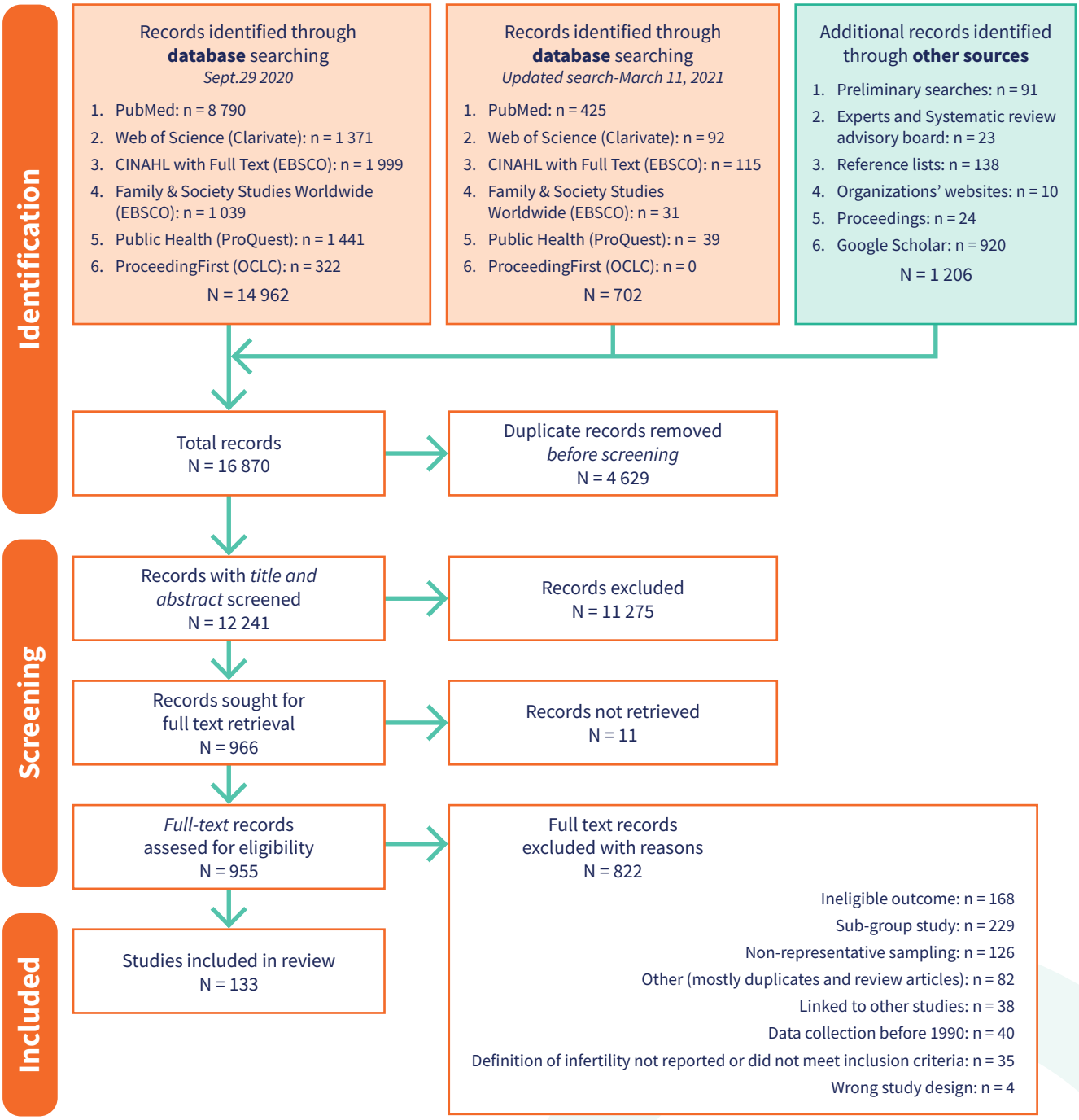


Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after **12 months or more** of regular unprotected sexual intercourse

[2] Unless otherwise specified, these estimates refer to 12-month period or lifetime prevalence in keeping with the following definition of infertility adopted by the World Health Organization (WHO): *Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse.*

A PRISMA flow diagram illustrating the literature search, article selection and final included studies is shown in **Figure 3.1.**

Figure 3.1. Identification of studies via databases and other methods



3.1 Description of studies

The literature search yielded 16 870 records. Following the removal of duplicates, 12 241 unique records were screened. The screening resulted in the selection of 133 studies for inclusion in this study (**Annex 2**). An overview of the study characteristics and infertility estimates for each study can be found in **Annex 3**.

The vast majority of studies were cross-sectional in design (n = 115). Thirteen studies used a cohort study design and five used a case-control study design for which only data for the control groups were extracted, which were representative samples of a general population.

Total number of studies analysed: 133

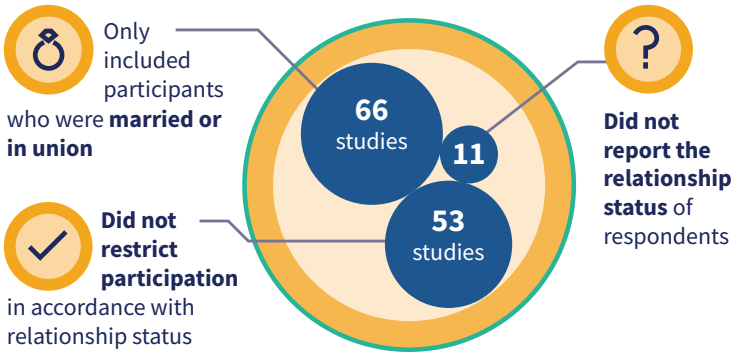
Most common study design: **cross-sectional (86%)**

Most common infertility definition: **12-month definition**

Age of study populations: heterogeneous

- Many studies included participants of "reproductive age", defined in different ways
- Some studies had an age limit beyond reproductive age
- Some studies had no age limit
- Some studies did not report age

Relationship status of study populations:



The sample in 85 studies included individuals of reproductive age, which was defined differently across studies but often confined to individuals aged 15–49 or 20–44 years.

Eighteen studies provided a lower age limit without an upper age limit and/or an age limit that extended beyond reproductive age. Fifteen studies limited the sample to a single age or a smaller age range that captures women in different stages of their reproductive life (e.g., 20–34 years, 30–49 years). For seven studies, all measuring lifetime prevalence of infertility, the sample included individuals beyond reproductive age. Ten studies did not report the age range of respondents in their analytic sample. Three studies reported estimates for two different age groupings and are thus represented in multiple tallies.

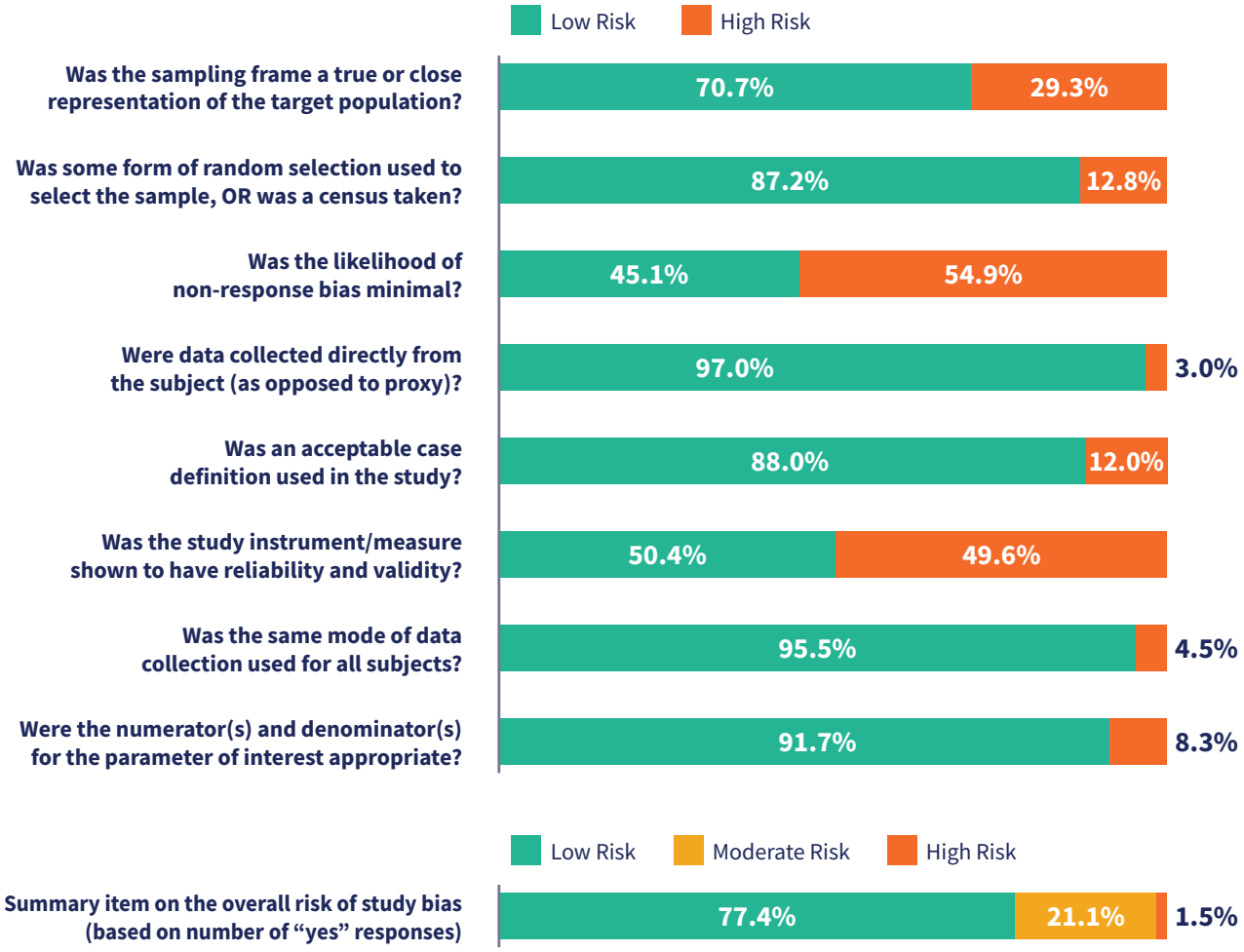
Sixty-six studies restricted their sample to individuals who were married or in union, 53 studies did not restrict their sample by relationship status, and a few studies reported both estimates separately. Eleven studies did not report the relationship status of respondents. Some studies explicitly or implicitly excluded individuals not engaged in heterosexual intercourse. One study reported the percent of respondents self-identifying as gay, lesbian, or bisexual.

The most common definition applied to estimates of infertility prevalence was a 12-month definition of infertility in 101 studies. Thirty studies applied a 24-month definition of infertility while 14 studies applied a demographic 60-month definition of infertility. Twenty-nine studies applied definitions

with durations other than 12, 24, or 60 months (e.g., 6 months, 36 months) or with no duration (self-perceived infertility). Among the studies that defined infertility by duration, all studies measured infertility in months with no studies measuring infertility in menstrual cycles. Many studies reported estimates for multiple definitions of infertility. Sixty studies reported total infertility estimates (i.e., primary and secondary infertility combined in a single estimate), and 34 studies reported total, primary, and secondary infertility estimates. The remaining 39 studies reported some other combination of total, primary, and/or secondary infertility estimates.

The overall risk of bias was low for 77.4% of studies, moderate for 21.1% of studies, and high for 1.5% (**Figure 3.2**). For five out of eight individual items assessed, at least 87.2% of studies were rated as low risk. Only one item, the item measuring the likelihood of non-response, had more than half (54.9%) of studies rated as high risk. The funnel plots, which were used to examine publication bias, were symmetrical for studies reporting estimates of lifetime and period prevalence of infertility. See more details here: https://doi.org/10.1093/hropen/hoac051.

Figure 3.2. Risk of bias of included studies



3.2 Methodological approaches for estimating infertility prevalence

The review comprised studies that fell into six methodological categories: 1) prospective TTP design, 2) retrospective TTP design, 3) current duration design, 4) self-reported infertility measure (direct), 5) constructed infertility measure (indirect), and 6) undetermined. For 13 studies, the approach could not be determined based on the information provided in the manuscript. **Table 3.1** provides a description of each approach and common applications based on the studies included in the review. **Table 3.2** reports the number of studies and range of estimates by methodological approach.

Methodological approaches used in infertility prevalence studies

The review comprised studies that fell into **6** methodological categories:

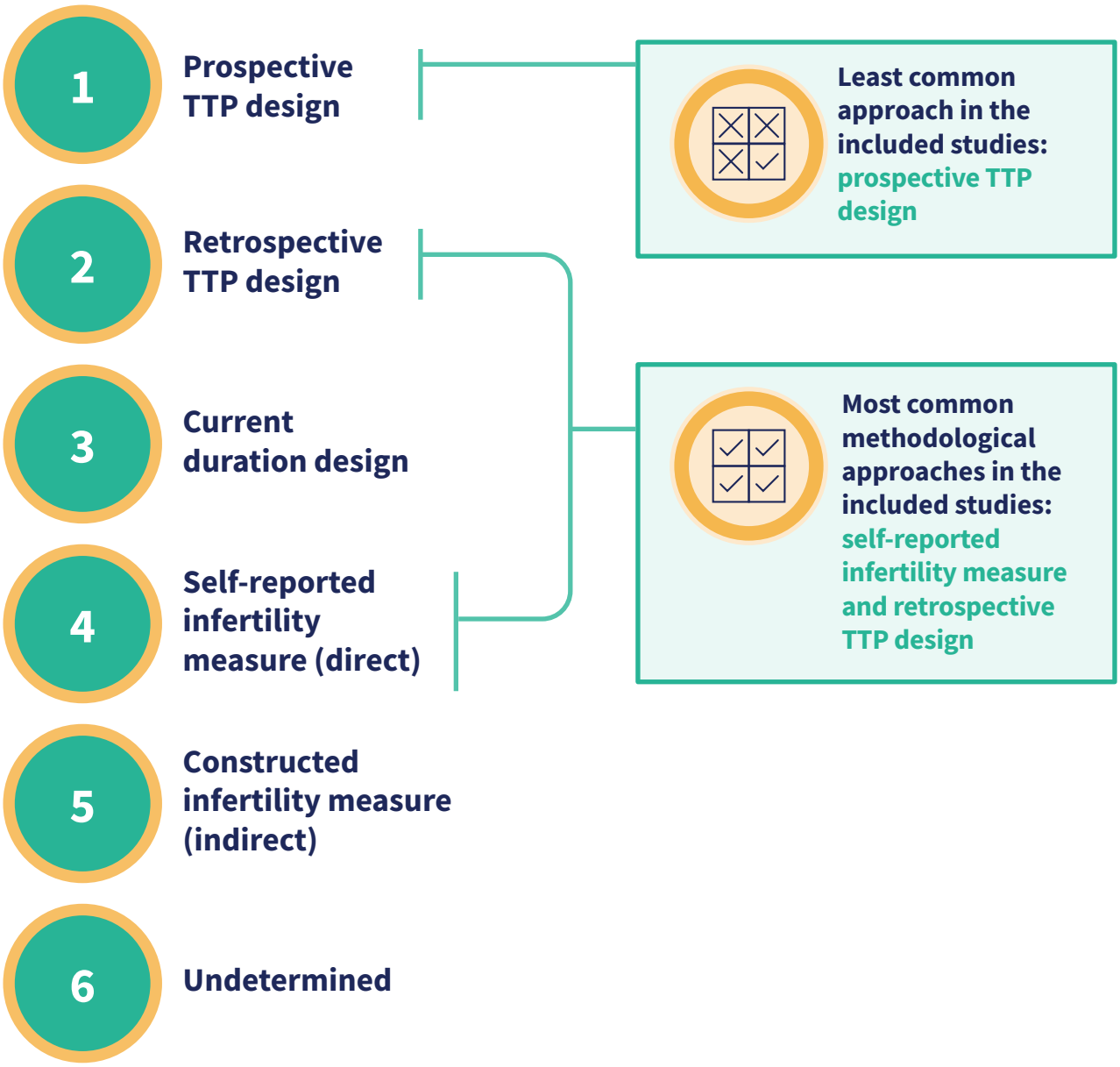


Table 3.1. Five approaches to measuring infertility prevalence identified from the systematic review

	Prospective time-to-pregnancy design[a]	Retrospective time-to-pregnancy design	Current duration design	Self-reported infertility measure (direct)	Constructed infertility measure (indirect)
Description	• Participants are enrolled prior to period of unprotected intercourse (PUI) (incident cohort) or during a period of unprotected intercourse (prevalent cohort). • Participants are followed until pregnancy, infertility treatment, or study conclusion (administrative censoring).	• Participants are asked to recall the PUI or pregnancy attempt time prior to becoming pregnant (pregnancy-based approach). • Alternatively, participants may be asked about a PUI and/or time-to-pregnancy (TTP) in a specified time regardless of outcome (historical prospective approach).	• Participants are enrolled during a current PUI or pregnancy attempt. • Current duration (CD) is calculated as the interval between when the PUI or pregnancy attempt began and date of interview. • CD values are used to estimate a summary TTP distribution for the population using survival methods and under certain analytic assumptions.	Participants are queried directly about their ability to conceive either within a specified duration of time (e.g. 12 months) or based on their subjective evaluation.	• Infertility status is determined based on the presence or absence of a pregnancy or live birth among couples exposed to conception for a defined period. • Exposure to conception is inferred from survey questions and/or a reproductive calendar.
Sample questions for querying respondents	• [For those planning to conceive] Are you pregnant (asked at specified intervals during follow-up)? • [For those planning to conceive] pregnancy is ascertained by pregnancy testing over follow-up period	• How long had/have you been trying to become pregnant? • How many months did you have regular intercourse without contraception before you became pregnant?	• [For those at risk of pregnancy at interview]: Series of questions on dates of last use of contraception, pregnancy, or birth. Current duration is calculated from start of at-risk interval to date of interview. • [Among those at risk of pregnancy at interview] How long have you been trying to become pregnant? (number of months or years)	• Have you ever experienced a period of at least 12-months where you were having unprotected intercourse (or attempting to become pregnant) but did not become pregnant? • Have you and a partner ever had difficulty conceiving?	Constructed based on a series of questions or reproductive calendar on relationship status, birth history, contraceptive use, and, in some instances, sexual activity and desire to have another child.
Common research objectives	• Assess the biologic capacity for reproduction (i.e., fecundity) • Examine the relationship between risk factors on fecundity	• Estimate fecundity or measure infertility prevalence • Identify and/or examine risk factors, which need to be anchored around the start of the PUI or pregnancy attempt	• Generate population-based estimates of infertility prevalence • Identify and/or examine risk factors, which need to be anchored around the start of the PUI or pregnancy attempt	• Estimate infertility prevalence • Assess association between infertility and risk factors, outcomes, and/or treatment seeking behavior	Generate population-based estimates of infertility prevalence with nationally representative demographic and reproductive health survey data

	Prospective time-to-pregnancy design[a]	Retrospective time-to-pregnancy design	Current duration design	Self-reported infertility measure (direct)	Constructed infertility measure (indirect)
Common applications for[b]:					
Type of prevalence[c]	Period prevalence	Period or lifetime prevalence	Period prevalence	Period or lifetime prevalence	Period prevalence
Duration cut-off for infertility	• 12-months • 24-months	• 12-months • 24-months	• 12-months • 24-months	• 12-months • No duration (subjective measure)	• 12-months • 60-months
Pregnancy intentions considered in numerator	Always considered	Sometimes considered	Sometimes considered	Sometimes considered	Commonly not considered
Denominator considered	Those attempting to conceive	Those ever at risk of pregnancy or attempting to conceive	Those at risk of pregnancy or attempting to conceive at time of interview	Ever and not at risk of pregnancy (e.g. all women of reproductive age)	Ever and not at risk of pregnancy (e.g. all women of reproductive age)

[a] The prospective time-to-pregnancy design approach is considered the gold standard.
[b] Common applications are summarized based on the studies included in the systematic review.
[c] Period prevalence is defined as the proportion of individuals/couples with infertility at a given point or interval in time, which may be current or past depending on the study aims. Lifetime prevalence is defined as the proportion of individuals/couples who have ever experienced infertility in their life.

Table 3.2. Range of 12-month period and lifetime infertility prevalence estimates by methodological approach and other study descriptors

Study Characteristics	Number of studies[a]	Number and range of 12-month total infertility prevalence estimates (%)[b]			
	All studies (studies with 12-month estimates)	Number of period estimates[c]	Period Prevalence	Number of lifetime estimates[c]	Lifetime prevalence
Total	**133 (84)**	**69**	**1.6-34.0**	**65**	**3.3-39.7**
Methodological approaches					
Prospective TTP design	3 (3)	3	13.6-28.0	-	-
Retrospective TTP design	34 (24)	25	5.0-32.0	15	3.3-35.3
Current duration design	6 (5)	10	9.4-34.0	-	-
Self-reported infertility measure	61 (39)	16	4.0-18.0	45	4.2-39.7
Constructed infertility measure	23 (8)	12	6.0-17.0	-	-
Undetermined	13 (6)	3	1.6-13.3	5	10.1-20.9
Definitional characteristics					
Numerator (Duration only)					
Intentions included[d]	65 (46)	22	7.0-32.0	42	4.2-39.7
Intentions not considered	61 (37)	44	1.6-34.0	14	3.3-35.3
Numerator (Duration and/or receipt of care included)					
Intentions included[4]	8 (7)	2	12.0-12.3	8	11.0-26.0
Intentions not considered	2 (2)	1	18.0	1	35.0

Study Characteristics	Number of studies[a]	Number and range of 12-month total infertility prevalence estimates (%)[b]			
	All studies (studies with 12-month estimates)	Number of period estimates[c]	Period Prevalence	Number of lifetime estimates[c]	Lifetime prevalence
Numerator (Subjective evaluation with or without duration)					
Intentions included[d]	10 (1)	-	-	3	11.4-16.4
Intentions not considered or unknown	10 (1)	1	7.74	-	-
Denominator					
All regardless of risk of pregnancy	74 (41)	19	1.6-17.0	35	3.3-35.0
Ever at risk of pregnancy[e]	37 (26)	30	4.2-34.0	13	8.2-35.3
Attempting to conceive[d]	40 (30)	20	9.4-32.0	17	5.8-39.7
Study population characteristics					
Sample type					
General population-based	118 (71)	47	1.6-34.0	65	3.3-39.7
Clinic-based	15 (13)	22	5.0-28.0	-	-
Sex of respondent					
Female	109 (72)	54	1.6-34.0	56	3.3-39.7
Male	10 (10)	5	7.0-15.3	9	8.2-21.8
Combined[f]	18 (9)	10	4.2-28.0	-	-
Not reported	1 (-)	-	-	-	-
Income Level[g]					
High-income countries	70 (55)	43	5.0-34.0	52	4.2-35.3
Low- and Middle-income countries	65 (29)	26	1.6-32.0	13	3.3-39.7
Region[h]					
African Region	24 (8)	6	9.5-32.0	4	9.3-15.8
Eastern Mediterranean Region	15 (6)	3	5.2-15.2	4	3.3-21.2
European Region	47 (37)	32	5.0-34.0	25	9.0-31.8
South-East Asia Region	12 (-)	-	-	-	-
Region of the Americas	24 (15)	16	4.0-15.7	15	4.2-35.3
Western Pacific Region	29 (19)	12	1.6-28.0	17	8.2-39.7

[a] Some studies reported multiple prevalence estimates by applying different definitional or study population characteristics. In these instances, studies were included in more than one tally.
[b] 12-month estimates of resolved and unresolved infertility. Outlier 12-month infertility estimate is not reported in Table 3.2. Outliers were determined based on their magnitude and justification in the respective studies regarding their ability to capture infertility.
[c] Some studies reported multiple prevalence estimates by applying different definitional or study population characteristics. In these instances, multiple estimates from a single study may be included in the same tally.
[d] Includes individuals wanting a child and/or trying to conceive.
[e] Includes any individual ever at risk of a pregnancy. May include studies that used marital status as a proxy for being at risk of pregnancy.
[f] Includes studies that reported estimates for male and female respondents or couple respondents.
[g] Defined based on World Bank classifications at the time of the systematic review (The World Bank. Countries and economies. 2021; Available from: https://data.worldbank.org/country).
[h] Defined based on World Health Organization regional groupings (World Health Organization. 2022; Available from: https://www.who.int/about/who-we-are/regional-offices).

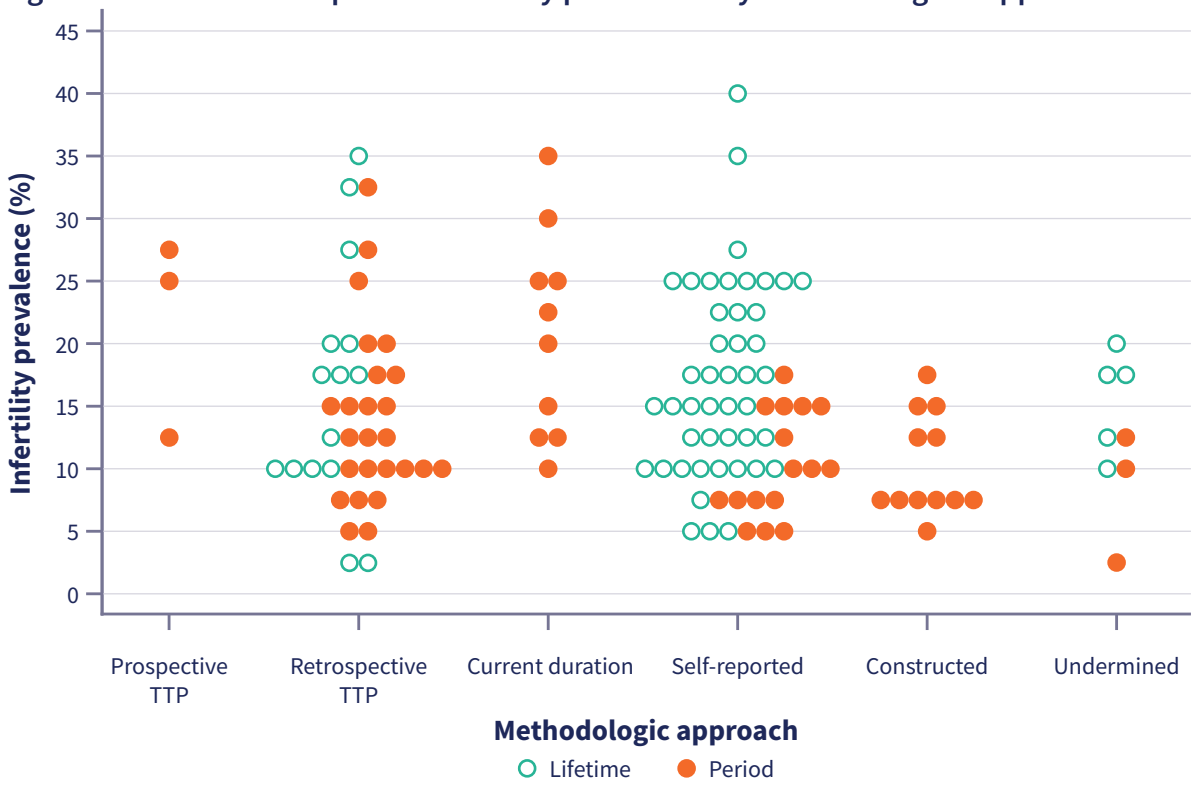
Of the studies included in these estimates, the self-reported infertility measure was applied most often followed by the retrospective TTP design. The prospective TTP design was the least used approach. Six studies reported multiple estimates generated by different approaches and are thus included in the count for multiple approaches. Three studies combined two approaches to generate a single estimate. In these instances, these studies were categorized based on the primary approach used for generating the prevalence estimate.

Across studies, period prevalence was measured using all approaches, whereas lifetime prevalence was mainly measured using the self-reported infertility measure approach. The 12-month definition was the most common definition applied across all approaches except for the constructed infertility measure for which a 5-year definition was more commonly applied.

Use of a retrospective TTP design was more common in high-income countries, particularly Europe, whereas use of the constructed infertility measure approach was more common in low- and middle-income countries. The self-reported infertility measure approach was widely applied in studies conducted in both HIC and LMIC. China was the only country in which we were able to identify a study that used a prospective TTP design approach, where participants were recruited from premarital and preconception clinics. The self-reported infertility measure approach was the most common approach applied in studies conducted in the WHO African Region, WHO Region of the Americas, and WHO Western Pacific Region. The self-reported infertility measure approach was also commonly applied in the WHO European Region; however, in this region, the retrospective TTP design approach was the most widely applied approach. The constructed infertility measure was the most common approach used in studies conducted in the WHO South-East Asia Region and the WHO Eastern Mediterranean Region, and was also commonly applied in studies in the African Region and the Region of the Americas.

The majority of 12-month infertility estimates were based on self-reported infertility measures and retrospective TTP designs (**Table 3.2** and **Figure 3.3**). Across approaches, duration-based methods (prospective TTP, retrospective TTP, and current duration designs) showed larger period estimates and ranges of 12-month infertility (5.0–34.0%) compared with self-reported and constructed measures (4.0–18.0%). Lifetime estimates of 12-month infertility were available only for retrospective TTP (3.3–35.3%) and self-reported measures (4.2–39.7%) and were comparable.

Figure 3.3. Lifetime and period infertility prevalence by methodological approach



TTP = time to pregnancy

3.3 Definitional characteristics

3.3.1 Type of prevalence

Eighty-four studies reported a period prevalence and 58 reported a lifetime prevalence with some reporting both. One hundred thirty-four estimates of 12-month infertility were extracted from 84 studies of which 69 were period prevalence and 65 were lifetime prevalence (**Table 3.2**). Period and lifetime estimate ranges of 12-month infertility were both wide and comparable to one another.

3.3.2 Numerator

The majority of studies overall and those reporting 12-month infertility estimates used a numerator defined by duration only (**Table 3.2**). Among duration-only estimates, about half included intentions (mainly defined as those trying to conceive) in the numerator and the other half did not. Some studies reported both. A few studies incorporated duration and receipt of care in the numerator. Twenty studies used a numerator defined by subjective evaluation (i.e., perceived infertility) with or without a specified duration. The range of period and lifetime estimates of infertility among studies that defined the numerator by duration only did not vary considerably by whether the numerator considered intentions (7.0–32.0%, 4.2–39.7%, respectively) or did not consider intentions (1.6–34.0% with one outlier removed, 3.3–35.3%, respectively).

3.3.3 Denominator

Over half of the studies included individuals regardless of their risk of pregnancy in the denominator. The remaining studies were split in how they defined their denominator between those ever at risk of pregnancy and those attempting to conceive (**Table 3.2**). Some studies provided multiple estimates in their publication using different denominators. Among studies reporting 12-month estimates, the distribution among the three categories was more evenly divided than for all studies. Period infertility estimate ranges were lower when the denominator included individuals regardless of risk (1.6–17.0%) compared to individuals ever at risk (4.2–34.0%) or individuals attempting to conceive (9.4–32.0%). Lifetime infertility estimates were relatively similar across denominator categorizations.

3.4 Study population characteristics

3.4.1 Sample type

Most studies drew their sample from the general population (n = 118) whereas only 15 studies drew their sample from a clinic population. Period infertility estimate ranges were similar for general population studies compared to clinic-based studies. There were no lifetime estimates of 12-month infertility available for clinic-based studies.

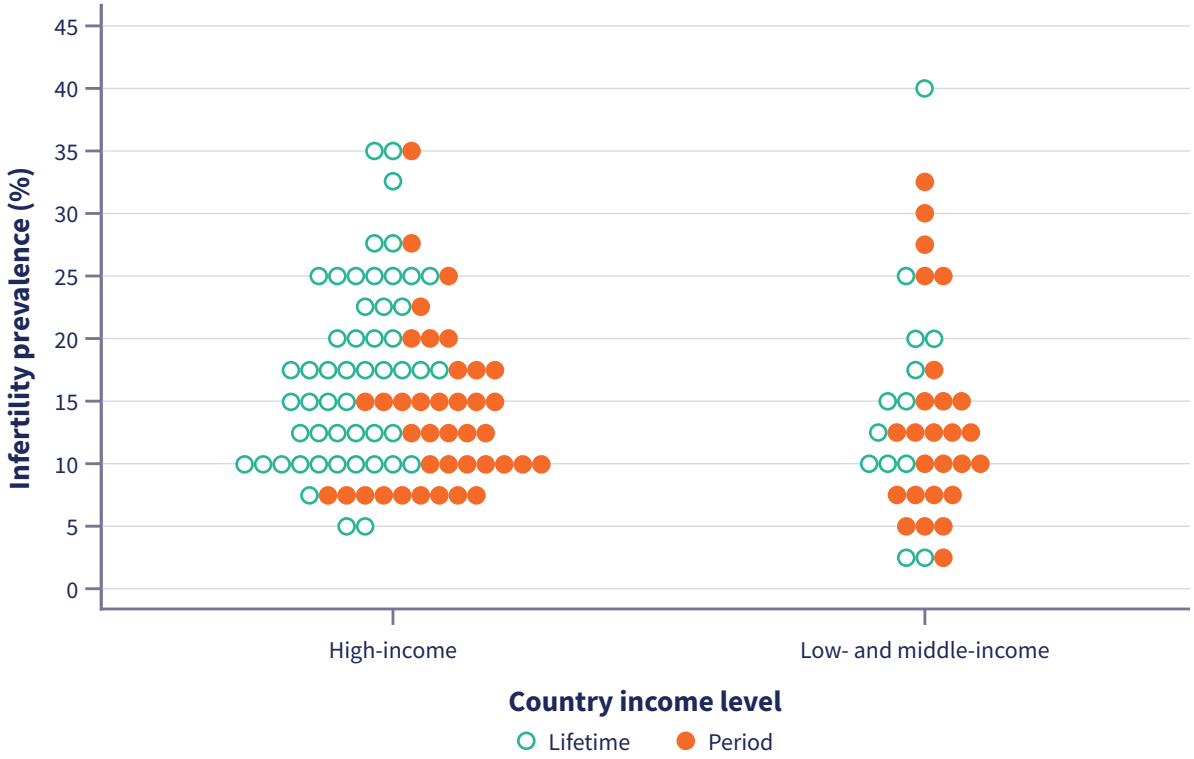
3.4.2 Sex of respondents

A majority of studies included estimates based on female respondents (n = 109) while only 10 studies included estimates based on male respondents (five studies that included separate estimates for female and male respondents were counted in both tallies). Eighteen studies included estimates that combined responses from both male and female respondents or from couples. One study did not report the sex of respondents. The range for period and lifetime estimates of 12-month infertility was smaller and lower for male respondents compared to female respondents.

3.4.3 Income level

The proportion of study populations from HIC and LMIC was similar at 51.9% and 48.1% respectively, whereas 65.5% of the 12-month infertility estimates were from HIC (**Table 3.2**). Two studies presented estimates from both HIC and LMIC. Overall, the range of period and lifetime estimates of 12-month infertility were similar within and across HIC and LMIC (**Figure 3.4**)

Figure 3.4. Lifetime and period infertility prevalence by country income level



3.4.4 Regional availability of studies

The European Region was the region represented in the greatest proportion of studies (35.3% of the total number of studies). The Eastern Mediterranean Region and South-East Asia Region were the least represented regions with 11.3% and 9.0% of the total number of studies, respectively (**Table 3.2**). The regions reporting the greatest number of 12-month infertility estimates were the European Region, the Region of the Americas, and the Western Pacific Region. Very few 12-month estimates were available for the African and Eastern Mediterranean regions, and no 12-month estimates were available for the South-East Asia Region.

3.4.5 Ranges of reported estimates

Overall, period infertility prevalence estimate ranges were largest for the African (9.5-32.0%), European (5.0-34.0%), and Western Pacific regions (1.6-28.0%) compared to the Region of the Americas (4.0-15.7%) and Eastern Mediterranean Region (5.2-15.2%). Lifetime infertility prevalence estimate ranges were largest for the Region of the Americas (4.2-35.3%), the European Region (9.0-31.8%), and the Western Pacific Region of the (8.2-39.7%), and smallest for the African Region (9.3-15.8%) (**Table 3.2**).

Regional availability of data and wide ranges of 12-month infertility estimates

Region most represented in analyzed studies:

WHO European Region

35.3% of the total number of studies, of which 37 studies provided data for 12 month infertility estimates

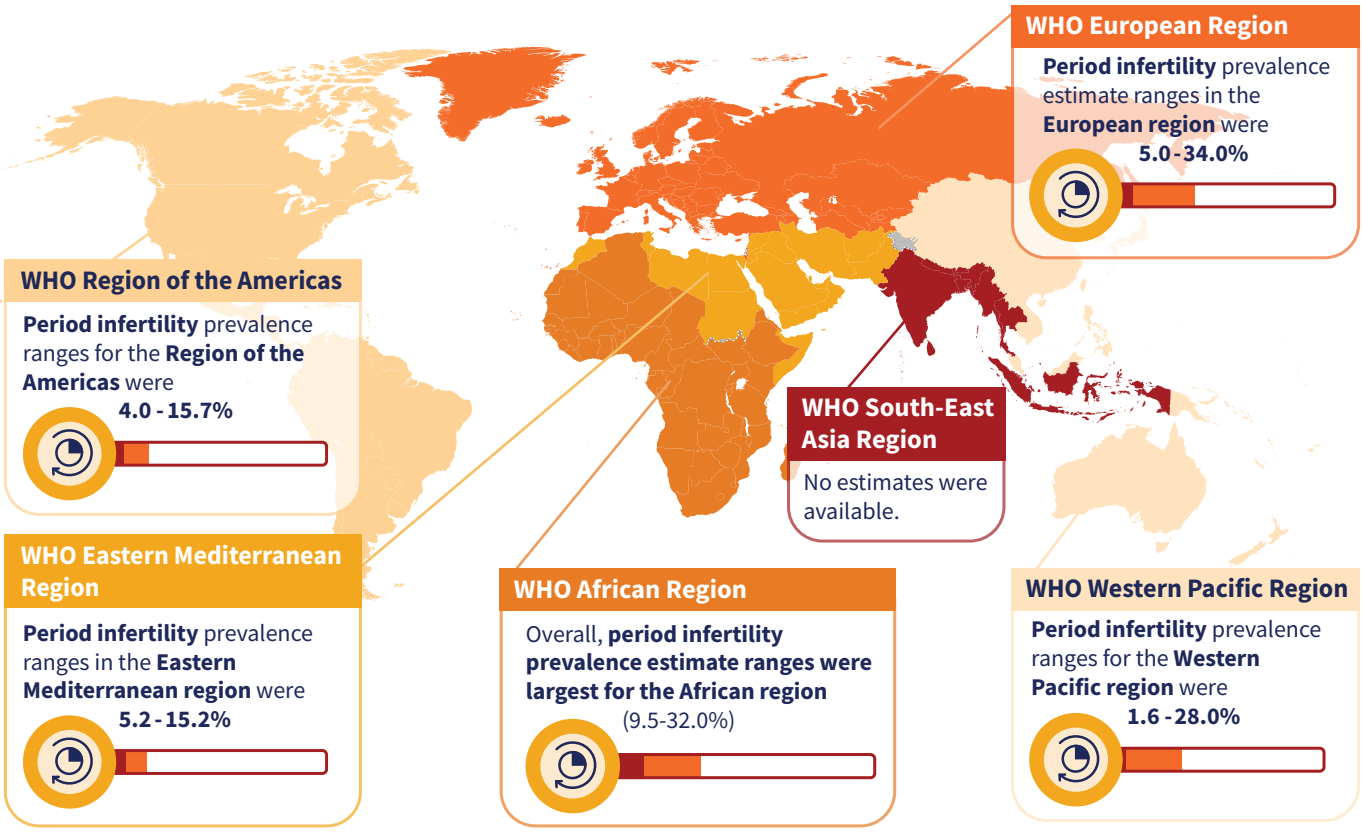
Regions least represented in analyzed studies:

WHO Eastern Mediterranean Region

11.3% of the total number of studies, of which 6 studies provided data for 12-month infertility estimates

WHO South-East Asia Region

9% of the total number of studies, none of which provided data for 12 month infertility estimates



Lifetime infertility prevalence estimate ranges were **largest** for the Region of the Americas (4.2-35.3%) European Region (9.0-31.8%) and Western Pacific Region (8.2-39.7%) and **smallest** for the African Region (9.3-15.8%)

3.5 Pooled 12-month infertility estimates

We pooled all 12-month infertility prevalence estimates using meta-analysis and stratified by whether the measure was estimating lifetime prevalence (n = 39 independent estimates from 37 studies) or period prevalence (n = 52 independent estimates from 43 studies). Overall pooled lifetime and period prevalence estimates were 17.5% (95% CI: 15.0, 20.3) and 12.6% (95% CI: 10.7, 14.6), respectively (**Figure 3.5** and **Figure 3.6**, respectively).

Figure 3.5. Pooled lifetime infertility prevalence estimates

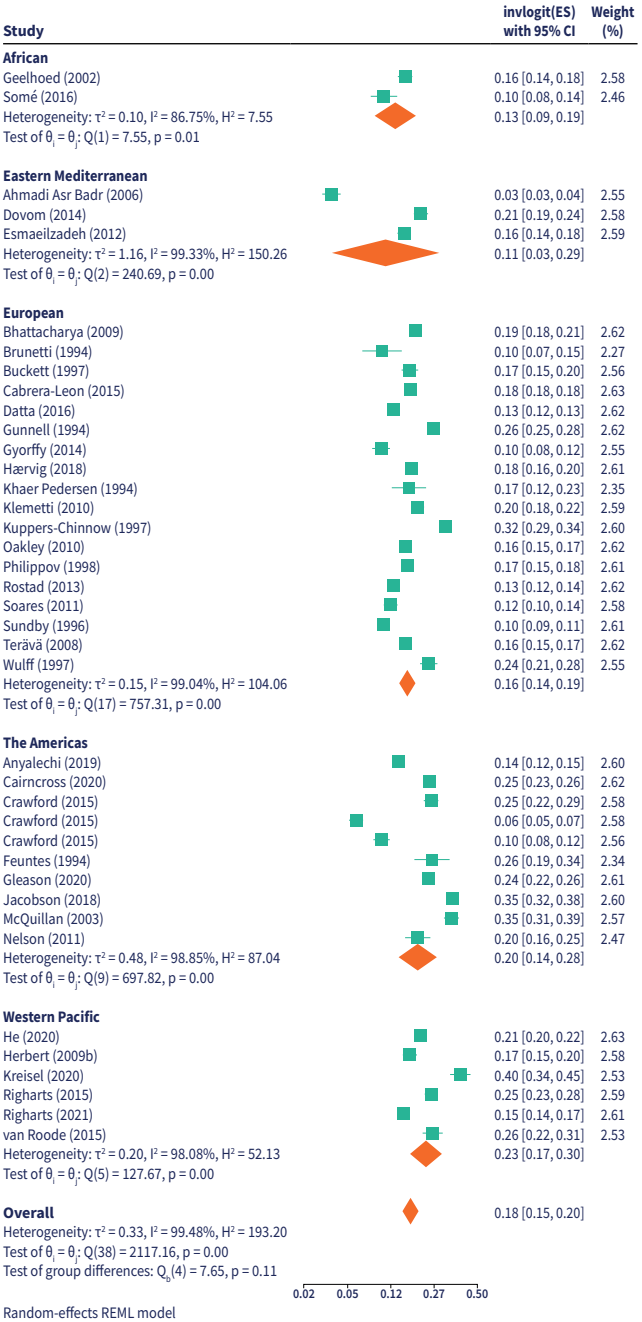
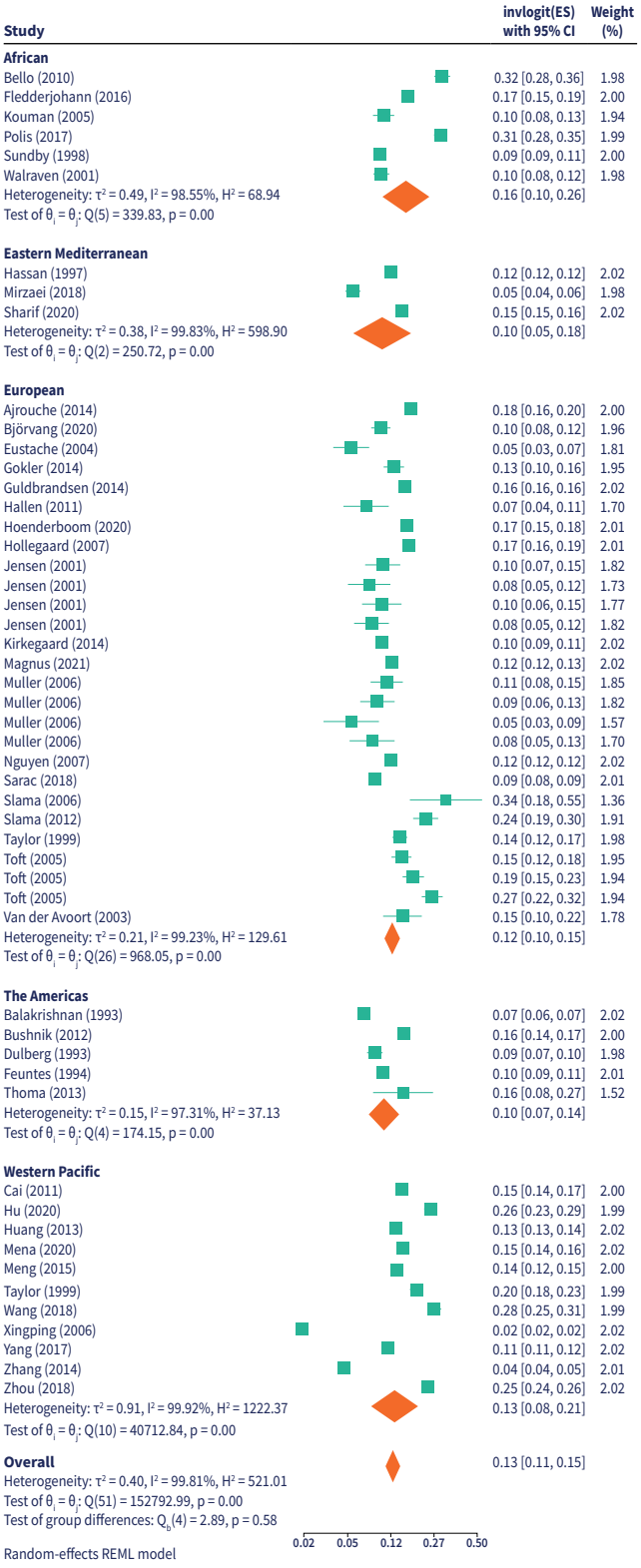


Figure 3.6. Pooled period infertility prevalence estimates



3.5.1 Pooled primary and secondary infertility

For primary 12-month infertility, pooled lifetime and period prevalence was 9.6% (95% CI: 6.3, 14.3, n = 12) and 9.0% (95% CI: 6.6, 12.2, n = 33), respectively (Figure 3.7). For secondary 12-month infertility, pooled lifetime and period prevalence was 6.5% (95% CI: 3.9, 10.7, n = 10) and 4.9% (95%: 2.7, 8.8, n = 17), respectively (Figure 3.8).

Figure 3.7. Pooled lifetime and period infertility prevalence estimates for primary infertility

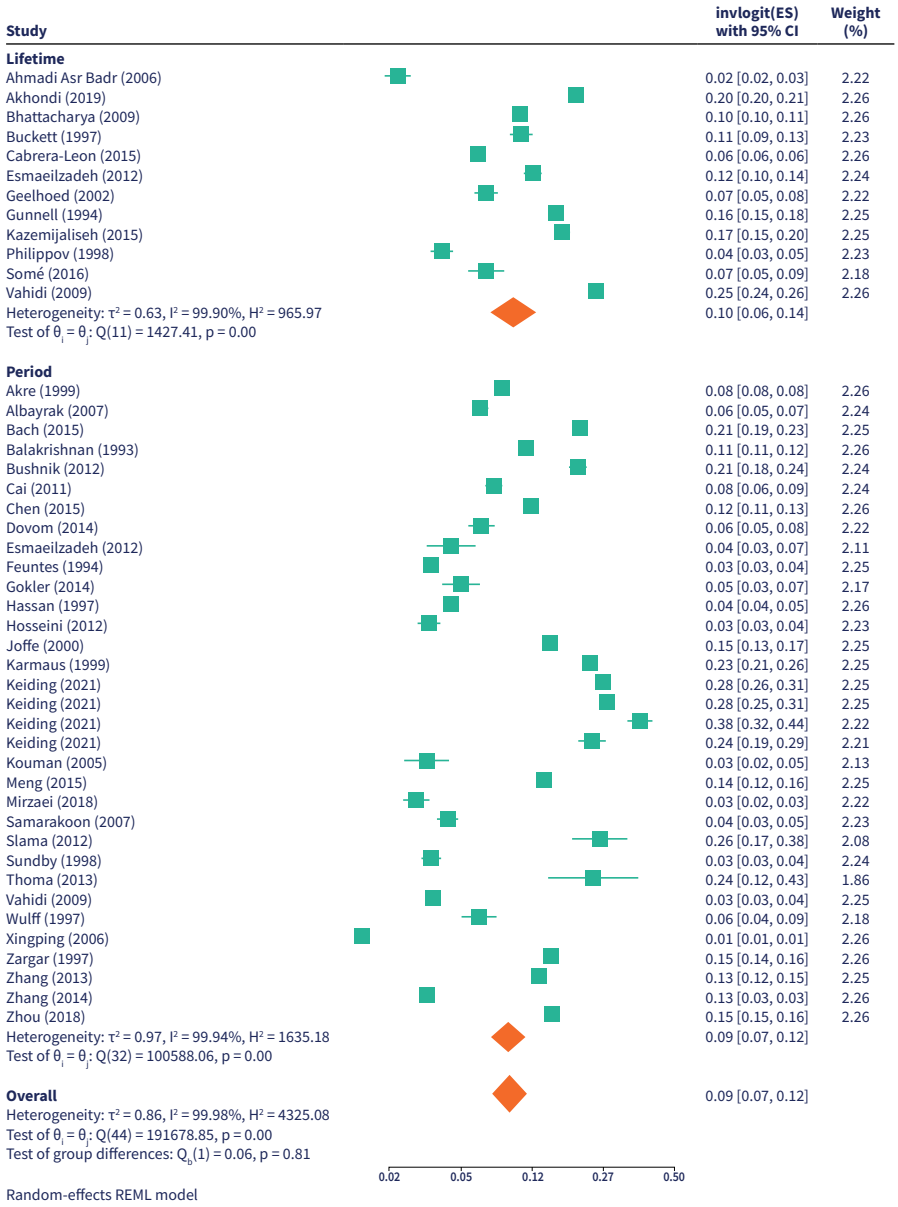
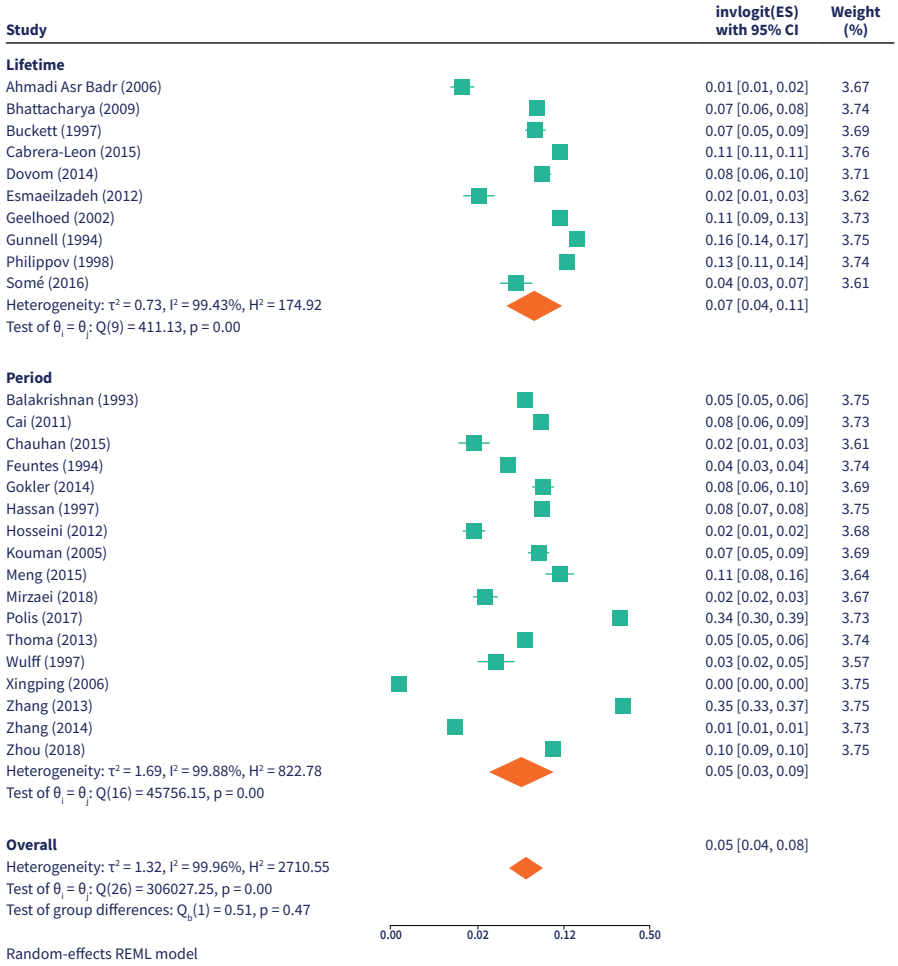


Figure 3.8. Pooled lifetime and period infertility prevalence estimates for secondary infertility



3.5.2 Sensitivity Analyses

For studies that presented more than one 12-month infertility estimate, sensitivity analyses showed minimal variation in lifetime and period estimates when selecting the minimum value over the maximum value for infertility prevalence (**Table 3.3**). Similarly, restricting analyses to only higher-quality studies with a bias score of 7 or 8 (n = 28 for lifetime, n = 16 for period), general population studies (n = 39 for lifetime, n = 30 for period), or studies in which the standard errors could be directly ascertained from the publication (n = 28 for lifetime, n = 39 for period), rather than approximated, also showed little difference in overall infertility prevalence compared with the main findings (**Table 3.3**).

17.5%

Estimated lifetime prevalence of infertility (95% confidence interval [CI]: 15.0, 20.3).

12.6%

Estimated period prevalence of infertility (95% CI: 10.7, 14.6).

Table 3.3. Results from sensitivity analyses

Criterion	Pooled lifetime infertility, % (95% CI)	Pooled period infertility, % (95% CI)
Overall estimates	17.5 (15.0, 20.3)	12.6 (10.7, 14.6)
Sensitivity analysis criterion applied		
Linked studies replaced with minimum value	14.5 (12.3, 17.1)	11.7 (10.0, 13.7)
Limited to high quality studies (bias score >7)	18.1 (15.7, 20.8)	13.9 (10.5, 18.2)
General population studies only	17.5 (15.0, 20.3)	12.4 (9.9, 15.5)
Limited to studies in which standard errors could be obtained directly	19.0 (16.4, 21.9)	12.2 (10.2, 14.6)

CI = confidence interval

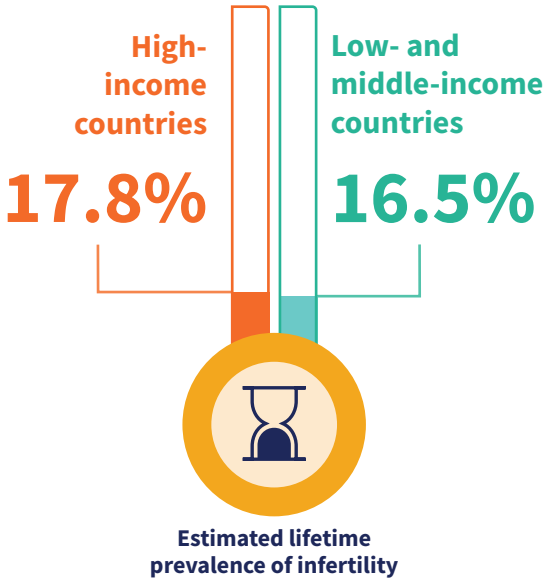
3.5.3 Pooled infertility estimates stratified by region

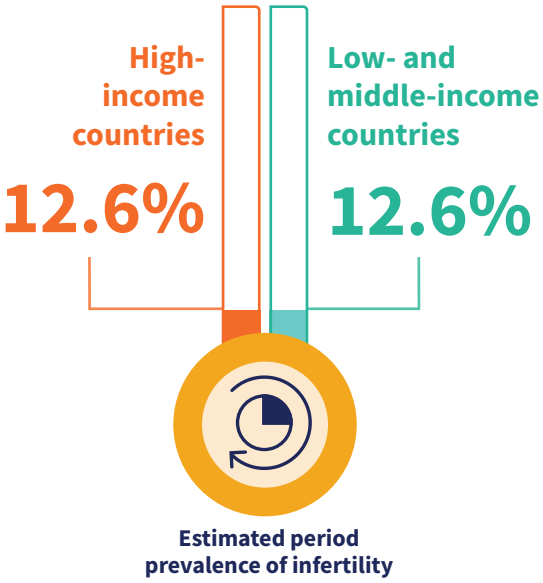
Regional differences in pooled lifetime infertility prevalence showed some variation in magnitude, yet all confidence intervals overlapped (Figure 3.5). The Western Pacific Region had the highest prevalence of lifetime infertility (23.2%, 95% CI: 17.4, 30.2, n = 6), followed by the Region of the Americas (20.0%, 95% CI: 13.9, 27.9, n = 10), the European Region (16.5%, 95% CI: 14.1, 19.2, n = 18), and the African Region (13.1%, 95% CI: 8.6, 19.4, n = 2). The lowest magnitude was found in the Eastern Mediterranean Region (10.7%, 95% CI: 3.4, 29.0, n = 3). Similarly, the magnitude of period infertility estimates varied by region, but all confidence intervals overlapped (Figure 3.6). The highest pooled estimate of period infertility prevalence was in the African Region (16.4%, 95% CI: 10.0, 25.7, n = 6) followed by the Western Pacific Region (13.0%, 95% CI: 7.8, 20.8, n = 11), the European Region (12.4%, 95% CI: 10.5, 14.6, n = 27), the Region of the Americas (10.4%, 95% CI: 7.4, 14.3, n = 5), and the Eastern Mediterranean Region (10.0%, 95% CI: 5.2, 18.2, n = 3). The number of studies for lifetime and period estimates varied across regions, contributing to variation in estimates. Notably, no studies conducted in the South-East Asian Region provided overall 12-month infertility prevalence estimates.

3.5.4 Pooled infertility estimates stratified by income, population, and sex of respondents

When stratified by country income classifications, pooled lifetime infertility prevalence was 17.8% (95% CI: 15.3, 20.7, n = 30) for HIC and 16.5% (95% CI: 10.4, 25.0, n = 9) for LMIC.

Pooled period infertility prevalence was 12.6% (95% CI: 10.8, 14.7, n = 31) for HIC and 12.6% (95% CI: 9.2, 16.9, n = 21) for LMIC.





In terms of respondent population (female, male, combined), the majority of lifetime and period prevalence estimates were based on female respondents (n = 37, n = 41, respectively) compared to male respondents (n = 12, n = 2, respectively) or combined sex (n = 0, n = 9, respectively). Pooled lifetime infertility prevalence estimates were higher when study respondents were female (17.5%, 95% CI: 14.9, 20.5, n = 37) compared with male (12.4%, 95% CI: 10.5, 14.6, n = 12). This pattern was also observed for pooled period estimates, but based on only two studies that used male respondents. Pooled period infertility estimates were 12.6% (95% CI: 10.6, 15.0, n = 41) based on female respondents, 8.7% (95% CI: 0.51, 14.4, n = 2) based on male respondents, and 12.6% (95% CI: 8.2, 18.8, n = 9) based on combined respondents (female, male, couple) (data not shown).

3.5.5 Pooled infertility estimates stratified by methodological approach

The methodological approach varied based on reporting of lifetime or period prevalence estimates. Minimal differences were found in pooled lifetime infertility estimates across the three methodological approaches that were used, with estimates of 16.7% (95% CI: 10.3, 26.0, n = 9), 17.6% (95% CI: 15.0, 20.7, n = 27), and 18.5% (95% CI: 15.6, 21.8, n = 3) for retrospective TTP, self-reported infertility, and undetermined approaches, respectively (**Annex 4**). Corresponding I^2 percentages were 99.6, 98.6, and 87.1, respectively. In contrast, period estimates were highest when using prospective TTP (21.8%, 95% CI: 13.7, 32.9, n = 3) and current duration approaches (26.2%, 95% CI: 19.9, 33.6, n = 4) followed by a retrospective TTP approach (12.9%, 95% CI: 10.7, 15.6, n = 24) (**Annex 4**). Self-reported and constructed approaches were similar with pooled period infertility prevalence of 10.6% (95% CI: 8.1, 13.8, n = 12) and 10.9% (95% CI: 8.0, 14.6, n = 6), respectively. The lowest infertility prevalence was found for the three studies in which the approach could not be determined (6.2%, 95% CI: 1.6, 20.8, n = 3). Corresponding I^2 percentages were 97.5, 68.9, 99.5, 99.0, 98.8, and 99.9, respectively.

3.5.6 Meta-regression results by period and lifetime

Meta-regression results yielded patterns similar to unadjusted pooled lifetime infertility prevalence (**Table 3.4**). Although confidence intervals overlapped, the magnitude of the odds ratios showed generally higher lifetime infertility prevalence in the Americas (odds ratio [OR]: 1.33, 95% CI: 0.81, 2.18) and Western Pacific regions (OR: 1.34, 95% CI: 0.72, 2.49) and lower magnitude in the African (OR: 0.60, 95% CI: 0.24, 1.26) and Eastern Mediterranean (OR: 0.64, 95% CI: 0.31, 1.30) regions relative to the European Region after adjustment for definitional characteristics and bias scores. This corresponded to pooled adjusted lifetime infertility prevalence estimates of 20.5%, 23.4%, 13.0%, and 10.8% for each respective region compared to the European Region (16.8%). In the same model, differences by methodological approach were minimal with adjusted lifetime infertility prevalence estimates of 17.8% for retrospective TTP, 18.5% for undetermined, and 18.2% for the self-reported direct measures. This corresponded to odds ratio associations of 0.85 (95% CI: 0.49, 1.47) for retrospective TTP and 1.02 (95% CI: 0.49, 2.12) for undetermined relative to self-reported direct measures.

Similarly, meta-regression results for period infertility prevalence were consistent with unadjusted results (**Table 3.4**). Relative to studies from the European Region, infertility estimates from the African Region were associated with the largest magnitude of association (OR: 1.95, 95% CI: 1.02, 3.72) followed by the Western Pacific Region (OR: 1.32, 95% CI: 0.77, 2.27) and Eastern Mediterranean regions (OR: 1.11, 95% CI: 0.51, 2.42). Region of the Americas (OR: 0.88, 95% CI: 0.41, 1.87) had a lower magnitude of association relative to estimates from the European Region, although confidence intervals overlapped for all regions with the exception of the African Region. These odds ratio associations were consistent with adjusted period prevalence estimates, which showed the highest prevalence in the African Region (18.1%) followed by the Western Pacific Region (14.2%), European Region (12.6%), Region of the Americas (11.2%), and Eastern Mediterranean Region (10.1%).

3.6 Certainty of the evidence

The certainty in the overall estimates of 12-month lifetime and period prevalence, as well as primary and secondary 12-month prevalence (lifetime and period) is moderate. The certainty was rated down from high to moderate due to serious inconsistency (Annex 5, Tables A–F), based on overlap of point-estimates and 95% confidence intervals reported by individual studies as shown in the forest plots. Estimates from individual studies were non-overlapping. None of the subgroup hypotheses proposed by the review explained the observed heterogeneity, implying that unknown factors, or factors not reported or measured by the individual studies, may be the true underlying explanation for the observed heterogeneity.

Table 3.4. Pooled lifetime and period infertility prevalence estimates and multivariable odds ratios associations by region and methodological approach, adjusting for definitional factors and risk of bias

Study covariates	Infertility prevalence, % (95% CI)	Multivariable model[a] odds ratio (95% CI)
Lifetime prevalence (n = 39 estimates)[b]		
WHO region[c]		
African Region	13.0 (4.6, 21.3)	0.60 (0.24, 1.26)
Eastern Mediterranean Region	10.8 (5.0, 16.6)	0.64 (0.31, 1.30)
European Region	16.8 (13.4, 20.2)	Ref
Region of the Americas	20.5 (15.2, 25.8)	1.33 (0.81, 2.18)
Western Pacific Region	23.4 (15.9, 31.0)	1.34 (0.72, 2.49)
Methodological approach		
Prospective TTP	-	-
Retrospective TTP	17.8 (12.8, 22.9)	0.85 (0.49, 1.47)
Current duration	-	-
Self-reported direct measure	18.2 (15.2, 21.1)	Ref
Constructed measure	-	-
Undetermined	18.5 (9.3, 27.5)	1.02 (0.49, 2.12)
Period prevalence (n = 52 estimates)[b]		
WHO region[c]		
African Region	18.1 (11.7, 24.5)	1.95 (1.02, 3.72)
Eastern Mediterranean Region	10.1 (4.4, 15.7)	1.11 (0.51, 2.42)
European Region	12.6 (10.2, 15.0)	Ref
Region of the Americas	11.2 (6.2, 16.2)	0.88 (0.41, 1.87)
Western Pacific Region	14.2 (10.1, 18.2)	1.32 (0.77, 2.27)
Methodological approach		
Prospective TTP	21.8 (11.1, 32.6)	1.42 (0.53, 3.84)
Retrospective TTP	13.1 (10.5, 15.7)	1.10 (0.65, 1.85)
Current duration	26.0 (14.6, 37.3)	2.43 (1.17, 5.05)
Self-reported direct measure	10.9 (7.8, 14.1)	Ref
Constructed measure	11.1 (6.7, 15.5)	1.31 (0.69, 2.47)
Undetermined	6.2 (2.5, 9.9)	0.48 (0.22, 1.07)

CI = confidence interval
TTP = time-to-pregnancy
(-) indicates that 12-month estimates were not found for respective categories.

[a] Models were adjusted for region, methodological approach (prospective TTP, retrospective TTP, current duration, self-reported binary measure, constructed binary measure, undetermined), numerator included intentions, denominator categories (all regardless of risk, ever at risk, attempting to become pregnant), and risk of bias score (0-8).

[b] Lifetime prevalence (I2 = 98.6%), period prevalence (I2 = 99.2%)

[c] Overall lifetime and period 12-month estimates were not found for studies conducted in the South-East Asia Region.

4. Discussion

This section summarizes key findings about infertility prevalence and reflects on implications for stakeholders in the sexual and reproductive health field. It highlights how findings in this report should guide improvements in how research on infertility prevalence is conducted. In addition, findings in this report provide a basis for raising awareness about the widespread nature of infertility and about the importance of ensuring that fertility services are a key element of sexual and reproductive health and rights in all countries.

Global estimates of infertility are needed to guide planning and coordination of infertility prevention, diagnosis, and treatment efforts. This report is an important milestone in understanding the contemporary prevalence of infertility. It uses evidence from all eligible studies conducted between 1990 and 2021 identified through a comprehensive and systematic analysis of publicly available data.

Key findings:[3]

1. **Infertility affects a large proportion of the global population, with approximately one in six people experiencing infertility in their lifetimes. Lifetime prevalence** of infertility is estimated to be **17.5%** (95% CI: 15.0, 20.3). **Period prevalence** of infertility is estimated to be **12.6%** (95% CI: 10.7, 14.6).

2. For **primary infertility**, estimated pooled lifetime and period prevalence were 9.6% and 9.0% respectively. For **secondary infertility**, estimated pooled lifetime and period prevalence were 6.5% and 4.9% respectively.

3. **Methodological approaches to measuring infertility vary greatly.** Five methodological approaches for measuring infertility were identified in this report: prospective time-to-pregnancy design, current duration design, retrospective time-to-pregnancy design, self-reported infertility measure, and constructed infertility measure.

4. **There is some variation in infertility prevalence across regions, but data gaps and overlapping confidence intervals mean that regional differences identified in this analysis may not be substantial or conclusive.** The Western Pacific Region had the highest prevalence of lifetime infertility (23.2%), followed by the Region of the Americas (20.0%) and the European Region (16.5%). Period infertility was highest in the African Region (16.4%), followed by the Western Pacific Region (13.0%) and the European Region (12.4%). The Eastern Mediterranean Region had the lowest lifetime and period infertility, at 10.7% and 10.0%, respectively. The number of studies for lifetime and period estimates varied across regions, contributing to uncertainty about findings. Notably, no studies from the South-East Asia Region provided 12-month infertility prevalence data that could be used in these analyses.

5. **Estimates of infertility prevalence are similar across countries regardless of country income level.** Lifetime infertility prevalence was 17.8% for high-income countries and 16.5% for low- and middle-income countries. Period infertility prevalence was 12.6% for high-income countries and 12.6% for low- and middle-income countries.

[3] Unless otherwise specified, these estimates refer to 12-month period or lifetime prevalence in keeping with the following definition of infertility adopted by the World Health Organization (WHO): *Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse.*

Lifetime and period prevalence of infertility: why both matter

Overall pooled lifetime and period prevalence estimates of infertility in this report were 17.5% and 12.6%, respectively. Period and lifetime measures of infertility prevalence provide different types of information, both of which are important. Contemporary estimates of period infertility prevalence help countries identify service needs and target resources, whereas estimates of lifetime infertility prevalence provide an understanding of the burden of infertility over people's lifetime.

Surprisingly, this study found that the range of 12-month infertility prevalence estimates was broad and did not vary substantially by lifetime or period prevalence. This may be due to the majority of studies capturing lifetime prevalence from reproductive-aged individuals who may not have completed childbearing. The wide range of estimates persisted even after accounting for definitional or study population characteristics. A prior systematic review *(11)* also found considerable heterogeneity in infertility estimates.

Disaggregating primary and secondary infertility

Infertility can be primary or secondary. Primary infertility is when a pregnancy has never been achieved by a person, and secondary infertility is when at least one prior pregnancy has been achieved.

These estimates report that for primary infertility, pooled lifetime and period prevalence were 9.6% and 9.0% respectively. For secondary infertility, pooled lifetime and period prevalence were 6.5% and 4.9% respectively.

Distinguishing between primary and secondary infertility is important for considering the role of potential etiological factors. While primary infertility data may be useful for making comparisons across time and settings *(33, 34)*, high rates of secondary infertility are associated with infection-related pathology resulting from postpartum infections, unsafe abortions *(35, 36)*, and some sexually transmitted infections *(37)*. Thus, excluding secondary infertility from infertility prevalence estimates would result in an underestimation or misrepresentation of the total burden of infertility in settings with high prevalence of such factors.

The use of meta-analysis in these estimates facilitated the pooling of prevalence data, and found a higher magnitude of overall lifetime prevalence of 12-month infertility compared to period prevalence, as was expected, and a high level of heterogeneity across studies, which was anticipated. The regional prevalence estimates and data availability reported here differ from those reported in a previous study by Mascarenhas et al. *(19)*, which could be due the latter's exclusive use of a demographic infertility measure (5-year exposure period) and different regional groupings than those applied in the estimates presented in this report. (These estimates use the country groupings for the six WHO regions.) The range of infertility estimates for HIC and LMIC were similar in this review, which is consistent with another (non-systematic) review by Boivin et al. *(21)* that examined 12- and 24-month infertility estimates.

4.1 Research gaps and measurement challenges

These estimates of infertility prevalence should be interpreted in the context of key research gaps and measurement challenges.

4.1.1 Lack of sufficient studies from some regions or studies with male participants

The estimates presented in this report reflect major gaps in the availability of studies for certain regions of the world. A larger proportion of eligible studies were from the European Region (35.3% of included studies), whereas the Eastern Mediterranean Region and South-East Asia Region were the least represented (11.3% and 9.0% of included studies, respectively). The lack of a sufficient number of studies across regions precluded the generation and comparison of regional differences in primary and secondary 12-month infertility prevalence. Strikingly, the pooled lifetime estimate of infertility for the African Region includes only two studies *(38, 39)*, which may explain the unexpected and illogical finding of lifetime prevalence being lower than period prevalence in the African Region. Furthermore, no studies from the South-East Asia Region provided overall 12-month infertility prevalence estimates. These gaps are particularly notable in light of the clear need to generate country-level estimates of infertility prevalence to inform national policies and services. Also, there were few studies with male participants, and pooled lifetime and period infertility estimates reported by male respondents were lower than for female respondents. Further work will be needed to provide estimates based on whether infertility is due to male, female or unexplained factors.

4.1.2 Variation in definitions and in inclusion and exclusion criteria in studies estimating infertility

Different approaches, definitions and types of study populations have been used in estimates of infertility prevalence, resulting in a high level of heterogeneity. Although most studies reported either an overall infertility prevalence estimate or overall, primary, and secondary infertility prevalence estimates, this was not consistent across all studies. Very few studies applied a consistent definition and methodological approach across different regions. Numerous studies used definitions of infertility that do not align with the 12-month definition of infertility used by WHO.

Decisions about which populations to include in studies also varied among studies. Some studies exclude people based on relationship status, use of infertility treatment, or pregnancy intentions and reproductive years. These differences may amplify or mask true magnitude and differences in the reported estimates. At the same time, such inclusion and exclusion criteria may also serve practical program purposes. For instance, including receipt of fertility care in the numerator may provide important information related to access to care. Restricting the numerator to those intending to conceive (slightly more than 50% of studies in this study) may generate a more useful estimate for predicting service needs *(40, 41)*, whereas not restricting the numerator to those with intentions may be more useful for examining risk factors associated with infertility *(42)*. Similarly, including individuals outside of reproductive age may have a bearing on how a program identifies services for who is at risk of infertility (e.g., non-contracepting, non-sexually active), yet such definitional issues can affect estimates.

4.1.3 Numerous study designs and methods of estimating infertility

Differences in the type of methodological approach used and the way in which an approach is operationalized make it difficult to ascertain true regional differences in infertility prevalence, and to conduct analyses of trends over time *(8, 11)*. The use of different numerators or denominators within the same study population has been shown to result in different infertility prevalence estimates *(43-45)*. In addition, there was significant variation in the level of detail provided in publications included in these estimates, making it difficult in some cases to discern definitional characteristics.

4.1.4 Certainty of estimates and other limitations

The certainty in the estimates of 12-month period and lifetime prevalence, as well as primary and secondary 12-month prevalence (lifetime and period) was rated moderate due to inconsistency. None of the subgroup hypotheses explained the observed heterogeneity. In addition, more than 50% of studies in these estimates either reported a response rate below 75% or failed to report a response rate. However, most studies were rated as low or moderate risk of bias, with only 1.5% of studies rated as high risk, and excluding high-risk studies had minimal impact on the overall estimates. Funnel plots were also found to be symmetrical, suggesting low potential for publication bias, although caution should generally be exercised in interpreting funnel plots for this purpose *(46)*.

4.2 Implications for research

The findings in these estimates have implications for researching prevalence of infertility, including selecting methodological approaches, reporting estimates and making comparisons across studies. There is a clear need to use consistent, systematic and comprehensive processes to collect and report infertility prevalence data at the global, regional, and country levels. The moderate certainty of these estimates indicates a need to improve how research on infertility is conducted so that inferences drawn from estimates can be presented with greater confidence.

The majority of studies that met criteria for inclusion in the analyses reported here provided estimates of the prevalence of 12-month infertility, suggesting that population-level estimates can be generated globally using the WHO definition of infertility. Flexibility may be required to accommodate different needs relating to population-level estimates; however, at a minimum, studies should collect data that measure infertility prevalence based on the WHO definition.

Recommendations for future infertility prevalence research

1. Estimating prevalence of infertility

The field needs a standard set of questions for ascertaining infertility prevalence that could be adopted by Demographic and Health Surveys and other standard population-based surveys. These questions should be qualitatively examined to ensure comparability in interpretation and relevance across different contexts. Questions should be flexible enough to allow for different definitions and approaches in order to facilitate comparison. At a minimum, 12-month period infertility should be measured in accordance with the WHO definition. Other dimensions such as intentions and receipt of fertility care should be captured. Multiple approaches could also be incorporated to allow for comparisons across methodologies. Measures should allow for disaggregation by lifetime and period infertility, primary and secondary infertility, and male and female respondents.

2. Selecting methodological approach

Researchers should consider research objectives, data sources, resources, and validity and reliability when selecting an approach to estimate infertility prevalence (i.e., prospective time-to-pregnancy design, retrospective time-to-pregnancy design, current duration design, self-reported infertility measure, and constructed infertility measure).

3. Reporting estimates

Researchers should provide detailed methodological and analytical information when reporting estimates of infertility prevalence. It is especially important to specify the survey question or questions used to generate the estimates as well as clearly defining the numerator and denominator. Assumptions regarding whether participants were at risk of pregnancy (e.g., married couples considered a proxy for risk status), should be outlined. Both an estimate of infertility prevalence and corresponding standard error (or confidence interval) should be provided. This is particularly important for studies using complex survey designs or survival analysis in which the standard error cannot be calculated from the sample size and prevalence estimate. Also, when feasible, estimates for total, primary, and secondary infertility prevalence should be reported, with stratification by age and sex.

4. Making comparisons across studies

Estimates should only be compared when they are as similar as possible in relation to various study characteristics such as definitions, methodological approaches, and exclusion criteria. Thus, estimates should be compared when stratified and matched according to key parameters, such as methodological approach, definition, primary or secondary infertility, intention or risk, sex, and age. When differences exist, the reasons for the differences should be examined. For studies in which a standard approach can be applied to make comparisons across different geographic settings, the interpretation of estimates would be aided by the reporting of additional information on contraceptive use and method mix (including fertility awareness-based methods), contraceptive failures, fertility intentions, sexual behavior (frequency, timing, abstinence), parity and gravidity, timing of pregnancy awareness, postpartum breastfeeding duration and lactational amenorrhea, infertility treatment-seeking, and availability and use of infertility treatment.

4.3 Policy and programmatic implications

Valid and reliable prevalence estimates are needed to understand the burden of infertility and to inform policies, advocacy, service provision, and monitoring of fertility care. Having the right data is essential for generating people-centred and evidence-based policies and services to mitigate the impact of infertility, and would enable fulfillment of the rights of individuals to found a family and decide the number, timing and spacing of their children. These infertility prevalence estimates clearly show that a large number of people in different regions of the world experience infertility and require infertility prevention, diagnosis and treatment.

Currently, there are policy and programmatic challenges related to the low availability, accessibility, and quality of interventions to address infertility in most countries. Prevention, diagnosis and treatment of infertility is often not prioritized in national population and development policies, reproductive health strategies, or health financing. These estimates improve our understanding of the prevalence and burden of infertility, and they also provide a basis for the formulation of policies and services to advance universal access to fertility care.

More needs to be done to:

Estimate infertility prevalence by country

Disaggregate infertility estimates by cause (male factor, female factor, both male and female factors, and unexplained factors) and by age

Develop a set of questions that can be used in nationally representative demographic health and population surveys to generate infertility prevalence

Promote and ensure consistency in definitions and measures used in infertility research

Enhance inclusion of infertility in health policies, services, and financing, and achieve universal access to fertility care for all

4.4 Conclusion

Human health and gender equality are central elements of the Sustainable Development Goals, which call on governments to ensure universal access to sexual and reproductive health and rights. Fertility care is a core part of sexual and reproductive health, and responding to infertility can mitigate gender inequality. The drive to achieve the Sustainable Development Goals therefore must encompass actions to respond more effectively to the needs of people with infertility. The estimates presented in this report show high prevalence of infertility globally and regionally, and can be used to support the development of policies and practices that will help more individuals and couples achieve their desired family size. Findings also provide insight into how the estimation of infertility prevalence can be improved in order to obtain more actionable data, including data that allow for more meaningful comparisons across settings and time.

References

1. Thoma M, Fledderjohann J, Cox C, Kantum Adageba R. Biological and Social Aspects of Human Infertility: A Global Perspective. 2021. In: Oxford Encyclopedia of Sexual and Reproductive Health Oxford University Press, Oxford [Internet]. Oxford University Press.(https://doi.org/10.1093/acrefore/9780190632366.013.184, accessed on March 30, 2023).

2. Wang Y, Fu Y, Ghazi P, Gao Q, Tian T, Kong F, et al. Prevalence of intimate partner violence against infertile women in low-income and middle-income countries: a systematic review and meta-analysis. Lancet Glob Health. 2022;10(6):e820-e30.(https://doi.org/10.1016/S2214-109X(22)00098-5, accessed on March 30, 2023).

3. International Covenant on Economic, Social Cultural Rights (CESCR). New York: United Nations General Assembly; 1966.

4. Convention on the Elimination of All Forms of Discrimination Against Women, Treaty Series, vol. 1249, Part IV; Article 16. New York: United Nations General Assembly; 1979.

5. The Universal Declaration of Human Rights (UDHR). New York: United Nations. General Assembly; 1948.(https://www.un.org/sites/un2.un.org/files/2021/03/udhr.pdf, accessed on March 30, 2023).

6. Starrs AM, Ezeh AC, Barker G, Basu A, Bertrand JT, Blum R, et al. Accelerate progress-sexual and reproductive health and rights for all: report of the Guttmacher-Lancet Commission. Lancet. 2018;391(10140):2642-92.(https://doi.org/10.1016/S0140-6736(18)30293-9, accessed on March 30, 2023).

7. Thonneau P, Spira A. Prevalence of infertility: international data and problems of measurement. Eur J Obstet Gynecol Reprod Biol. 1991;38(1):43-52.(https://doi.org/10.1016/0028-2243(91)90206-z, accessed on March 30, 2023).

8. Schmidt L, Münster K. Infertility, involuntary infecundity, and the seeking of medical advice in industrialized countries 1970-1992: a review of concepts, measurements and results. Hum Reprod. 1995;10(6):1407-18.(https://doi.org/10.1093/humrep/10.6.1407, accessed on March 30, 2023).

9. Guzick DS, Swan S. The decline of infertility: apparent or real? Fertil Steril. 2006;86(3):524-6.(https://doi.org/10.1016/j.fertnstert.2006.05.027, accessed on March 30, 2023).

10. Olive DL, Pritts EA. Estimating infertility: the devil is in the details. Fertil Steril. 2006;86(3):529-30.(https://doi.org/10.1016/j.fertnstert.2006.05.026, accessed on March 30, 2023).

11. Gurunath S, Pandian Z, Anderson RA, Bhattacharya S. Defining infertility — a systematic review of prevalence studies. Hum Reprod Update. 2011;17(5):575-88.(https://doi.org/10.1093/humupd/dmr015, accessed on March 30, 2023).

12. Stanford JB. What is the true prevalence of infertility? Fertil Steril. 2013;99(5):1201-2.

13. Thoma M. Measuring infertility: searching for consensus. J Womens Health (Larchmt). 2015;24(7):541-3.(https://doi.org/10.1089%2Fjwh.2015.5399, accessed on March 30, 2023).

14. International Classification of Diseases, 11th Revision (ICD-11) Geneva: World Health Organization; 2018. (https://www.who.int/classifications/icd/en/, accessed on July 18, 2022).

15. Zegers-Hochschild F, Adamson GD, Dyer S, Racowsky C, De Mouzon J, Sokol R, et al. The international glossary on infertility and fertility care, 2017. Hum Reprod. 2017;32(9):1786-801.(https://doi.org/10.1093/humrep/dex234, accessed on March 30, 2023).

16. Joffe M, Key J, Best N, Keiding N, Scheike T, Jensen TK. Studying time to pregnancy by use of a retrospective design. Am J Epidemiol. 2005;162(2):115-24.(https://doi.org/10.1093/aje/kwi172, accessed on March 30, 2023).

17. Bonde JP, Joffe M, Sallmén M, Kristensen P, Olsen J, Roeleveld N, et al. Validity issues relating to time-to-pregnancy studies of fertility. Epidemiol. 2006;17(4):347-9.(https://doi.org/10.1097/01.ede.0000210239.80406.46, accessed on March 30, 2023).

18. Dyer SJ. International estimates on infertility prevalence and treatment seeking: potential need and demand for medical care. Hum Reprod. 2009;24(9):2379-80; author reply 80-3.(https://doi.org/10.1093/humrep/dep219, accessed on March 30, 2023).

19. Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS Med. 2012;9(12):e1001356.(https://doi.org/10.1371/journal.pmed.1001356, accessed on March 30, 2023).

20. Rutstein SO, Shah IH. Infecundity, Infertility, and Childlessness in Developing Countries. DHS Comparative Reports No. 9. Calverton, Maryland, USA: ORC Macro and the World Health Organization; 2004.(https://dhsprogram.com/pubs/pdf/cr9/cr9.pdf, accessed on March 30, 2023).

21. Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Hum Reprod. 2007;22(6):1506-12.(https://doi.org/10.1093/humrep/dem046, accessed on March 30, 2023).

22. Direkvand MA, Delpisheh A, Sayehmiri K. An investigation of the worldwide prevalence of infertility as a systematic review. Qom Univ Med Sci J. 2016;10(1):76-87.(https://journal.muq.ac.ir/article-1-443-en.html, accessed on March 30, 2023).

23. Stevens GA, Alkema L, Black RE, Boerma JT, Collins GS, Ezzati M, et al. Guidelines for Accurate and Transparent Health Estimates Reporting: the GATHER statement. Lancet (London, England). 2016;388(10062):e19-e23.(https://doi.org/10.1016/s0140-6736(16)30388-9, accessed on March 30, 2023).

24. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ (Clinical research ed). 2021;372:n71.(https://doi.org/10.1136/bmj.n71, accessed on March 30, 2023).

25. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000;283(15):2008-12.

26. Cox C, Thoma M, Tchangalova N, Mburu G, Kiarie J. Infertility estimates and their methods of estimation from 1990 - 2020: a systematic review and meta-analysis protocol. 2020. (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=211704; accessed on July 18, 2022).

27. World Bank. Countries and economies [Internet]. Washington DC: World Bank; 2021. (https://data.worldbank.org/country, accessed on July 18, 2022).

28. Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. J Clin Epidemiol. 2012;65(9):934-9.(https://doi.org/10.1016/j.jclinepi.2011.11.014, accessed on March 30, 2023).

29. Rücker G, Schwarzer G, Carpenter JR, Schumacher M. Undue reliance on I(2) in assessing heterogeneity may mislead. BMC Med Res Methodol. 2008;8:79.(https://doi.org/10.1186/1471-2288-8-79, accessed on March 30, 2023).

30. StataCorp. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC; 2019.

31. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-6.(https://doi.org/10.1136/bmj.39489.470347.ad, accessed on March 30, 2023).

32. Iorio A, Spencer FA, Falavigna M, Alba C, Lang E, Burnand B, et al. Use of GRADE for assessment of evidence about prognosis: rating confidence in estimates of event rates in broad categories of patients. BMJ (Clinical research ed). 2015;350:h870.(https://doi.org/10.1136/bmj.h870, accessed on March 30, 2023).

33. Basso O, Juul S, Olsen J. Time to pregnancy as a correlate of fecundity: differential persistence in trying to become pregnant as a source of bias. Int J Epidemiol. 2000;29(5):856-61.(https://doi.org/10.1093/ije/29.5.856, accessed on March 30, 2023).

34. Olsen J, Rachootin P. Invited commentary: monitoring fecundity over time--if we do it, then let's do it right. Am J Epidemiol. 2003;157(2):94-7.(https://doi.org/10.1093/aje/kwf178, accessed on July 18, 2022)

35. Larsen U. Primary and secondary infertility in sub-Saharan Africa. Int J Epidemiol. 2000;29(2):285-91.(https://doi.org/10.1093/ije/29.2.285, accessed on March 30, 2023).

36. Sharma S, Mittal S, Aggarwal P. Management of infertility in low resource countries. BJOG. 2009;116 Suppl 1:77-83.(https://doi.org/10.1111/j.1471-0528.2009.02311.x, accessed on March 30, 2023).

37. Chemaitelly H, Majed A, Abu-Hijleh F, Blondeel K, Matsaseng TC, Kiarie J, et al. Global epidemiology of Neisseria gonorrhoeae in infertile populations: systematic review, meta-analysis and metaregression. Sex Transm Infect. 2021;97(2):157-69.(https://doi.org/10.1136/sextrans-2020-054515, accessed on March 30, 2023).

38. Geelhoed DW, Nayembil D, Asare K, Schagen van Leeuwen JH, van Roosmalen J. Infertility in rural Ghana. Int J Gynaecol Obstet. 2002;79(2):137-42.(https://doi.org/10.1016/s0020-7292(02)00237-0, accessed on July 18, 2022).

39. Eric SN, Justine B, Jean NP. Prevalence of the Infertility among couples in ouagadougou (Burkina Faso): a population-based survey. The Open Public Health J. 2016;9(1).(http://dx.doi.org/10.2174/1874944501609010088, accessed on March 30, 2023).

40. White L, McQuillan J, Greil AL. Explaining disparities in treatment seeking: the case of infertility. Fertil Steril. 2006;85(4):853-7.(https://doi.org/10.1016/j.fertnstert.2005.11.039, accessed on March 30, 2023).

41. Greil AL, Slauson-Blevins KS, Tiemeyer S, McQuillan J, Shreffler KM. A new way to estimate the potential unmet need for infertility services among women in the United States. J Womens Health (Larchmt). 2016;25(2):133-8.(https://doi.org/10.1089/jwh.2015.5390, accessed on March 30, 2023).

42. Slama R, Ballester F, Casas M, Cordier S, Eggesbø M, Iniguez C, et al. Epidemiologic tools to study the influence of environmental factors on fecundity and pregnancy-related outcomes. Epidemiol Rev. 2014;36(1):148-64.(https://doi.org/10.1093/epirev/mxt011, accessed on March 30, 2023).

43. Larsen U. Research on infertility: which definition should we use? Fertil Steril. 2005;83(4):846-52.(https://doi.org/10.1016/j.fertnstert.2004.11.033, accessed on July 18, 2022).

44. Crawford S, Fussman C, Bailey M, Bernson D, Jamieson DJ, Murray-Jordan M, et al. Estimates of lifetime infertility from three states: the behavioral risk factor surveillance system. J Womens Health (Larchmt). 2015;24(7):578-86.(https://doi.org/10.1089%2Fjwh.2014.5102, accessed on March 30, 2023).

45. Jacobson MH, Chin HB, Mertens AC, Spencer JB, Fothergill A, Howards PP. "Research on Infertility: Definition Makes a Difference" Revisited. Am J Epidemiol. 2018;187(2):337-46.(https://doi.org/10.1093/aje/kwx240, accessed on March 30, 2023).

46. Sterne JA, Egger M. Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. J Clin Epidemiol. 2001;54(10):1046-55. (https://doi.org/10.1016/s0895-4356(01)00377-8, accessed on March 30, 2023).

Annexes

Annex 1. Risk of bias assessment

The Risk of Bias Tool is designed to assess the risk of bias in population-based prevalence studies. It was initially developed by Leboeuf-Yde and Lauritsen (1995) and then modified by Hoy et al. (2012). We slightly modified the Hoy et al. (2012) tool to align with the purpose of our study as shown below.

ITEM #	RISK OF BIAS ITEM	CRITERIA FOR ANSWERS	ADDITIONAL NOTES AND EXAMPLES
External validity			
1	**Was the sampling frame a true or close representation of the target population?**	• **Yes (LOW RISK):** The sampling frame was a true or close representation of the target population. • **No (HIGH RISK):** The sampling frame was NOT a true or close representation of the target population.	The sampling frame is a list of the sampling units in the target population and the study sample is drawn from this list. Clinic-based sampling frames are considered high risk given that they only represent those individuals seeking care. **Examples:** • The sampling frame was a list of almost every individual within the target population. The answer is: Yes (LOW RISK). • The cluster sampling method was used and the sample of clusters/villages was drawn from a list of all villages in the target population. The answer is: Yes (LOW RISK). • The sampling frame was a list of just one particular ethnic group within the overall target population, which comprised many groups. The answer is: No (HIGH RISK). • The sampling frame included all eligible patients attending a primary care clinic that serves the target population over a 12-month period. The answer is No (HIGH RISK). • The sampling frame included pregnant women only. The answer is: No (HIGH RISK).

ITEM #	RISK OF BIAS ITEM	CRITERIA FOR ANSWERS	ADDITIONAL NOTES AND EXAMPLES
2	**Was some form of random selection used to select the sample, OR, was a census undertaken?**	• **Yes (LOW RISK):** A census was undertaken, OR, some form of random selection was used to select the sample (e.g., simple random sampling, stratified random sampling, cluster sampling, systematic sampling). • **No (HIGH RISK):** A census was NOT undertaken, AND some form of random selection was NOT used to select the sample.	A census collects information from every unit in the sampling frame. Clinic-based studies that recruit all eligible patients within a time period of 12 months or longer are considered a census. In a survey, only part of the sampling frame is sampled. In these instances, random selection of the sample helps minimize study bias. **Examples:** • The sample was selected using simple random sampling. The answer is: Yes (LOW RISK). • The target population was the village and every person in the village was sampled. The answer is: Yes (LOW RISK). • A census of the patient population was taken at a clinic by sampling all eligible patients over a 12-month period. The answer is: Yes (LOW RISK). • The target population was a region within a country but only the nearest villages to the capital city were selected in order to save on the cost of fuel. The answer is: No (HIGH RISK). • In a case-control study, controls were selected to match the cases on certain characteristics such as age. The answer is: No: (HIGH RISK)
3	**Was the likelihood of non-response bias minimal?**	• **Yes (LOW RISK):** The response rate for the study was >/=75%, OR, an analysis was performed that showed no significant difference in relevant demographic characteristics between responders and no responders OR authors applied weighting methods to account for differences between responders and non-responders. • **No (HIGH RISK):** The response rate was <75%, and if any analysis comparing responders and non-responders was done, it showed a significant difference in relevant demographic characteristics between responders and non-responders.	**Examples:** • The response rate was 83%. The answer is : Yes (LOW RISK). • The response rate was 68%; however, the researchers did an analysis and found no significant difference between responders and non-responders in terms of age, sex, occupation and or socioeconomic status. The answer is: Yes (LOW RISK). • The response rate was 68%; however, the researchers applied weighting methods to account for differences between responders and non-responders in terms of age, sex, occupation and or socioeconomic status. The answer is: Yes (LOW RISK). • The response rate was 65% and the researchers did NOT carry out an analysis to compare relevant demographic characteristics between responders and non-responders. The answer is: No (HIGH RISK). • The response rate was 69% and the researchers did an analysis and found a significant difference in age, sex and socio-economic status between responders and non-responders and no procedures were applied to account for differences. The answer is: No (HIGH RISK).
Internal validity			
4	**Were data collected directly from the subjects (as opposed to a proxy)?**	• **Yes (LOW RISK):** All data were collected directly from the subjects. • **No (HIGH RISK):** In some instances, data were collected from a proxy.	A proxy is a representative of the subject. **Examples:** • All eligible subjects in the household were interviewed separately. The answer is: Yes (LOW RISK). • A representative of the household was interviewed and questioned about the presence of infertility in at least one household member, including his or her partner. The answer is: No (HIGH RISK). • Medical records (proxy) are used to identify those with infertility. Some individuals with known infertility will not be captured in medical records since not all patients are asked about infertility. The answer is No (HIGH RISK).

ITEM #	RISK OF BIAS ITEM	CRITERIA FOR ANSWERS	ADDITIONAL NOTES AND EXAMPLES
5	**Was an acceptable case definition used in the study?**	• **Yes (LOW RISK):** An acceptable case definition was used. In instances where multiple definitions are used, at least one acceptable case definition was used. • **No (HIGH RISK):** An acceptable case definition was NOT used.	Acceptable case definitions of infertility include those that define infertility as a failure to achieve either a clinical pregnancy or live birth after > 12 months of regular unprotected intercourse overall or > 6 months for ages 35 and over, consistent with minimum clinical criterion for defining infertility (ACOG). Given that some studies avoid use of 12 months due to heaping, definitions >9 months will be considered acceptable. Intentions may or may not be included in the definition. Definitions that include menopausal women and surgically sterile men or women are not acceptable. **Examples:** • Clinical definition: failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse. The answer is: Yes (LOW RISK) • Epidemiological definition: failure to achieve a clinical pregnancy (or live birth) after 24 months or more of regular unprotected sexual intercourse. The answer is: Yes (LOW RISK) • Demographic definition: failure to achieve a live birth after 5 years or more of regular unprotected sexual intercourse. The answer is: Yes (LOW RISK) • Failure to achieve a clinical pregnancy after 6 months of regular unprotected sexual intercourse. The answer is: No (HIGH RISK). • Difficulty achieving a clinical pregnancy (no duration specified). The answer is: No (HIGH RISK)
6	**Was the study instrument/ items that measured the parameter of interest (e.g., prevalence of infertility) shown to have reliability and validity (if necessary)?**	• **Yes (LOW RISK):** The study instruments/items had been shown to have reliability and validity (if this was necessary), e.g., test-retest, piloting, validation in a previous study, etc. • **No (HIGH RISK):** The study instruments/items had NOT been shown to have reliability or validity (if this was necessary).	Self-reported time-to-pregnancy/ time-trying-to-conceive instruments (retrospective or prospective) are considered low risk given that several studies have shown these measures to be fairly reliable and valid (though not all). Binary self-reported instruments that include a duration are also considered low risk (i.e., 'Have you ever had a time, lasting 12 months or longer, when you and a partner were trying for a pregnancy but it didn't happen?'). Studies that use ICD codes to identify cases of infertility are acceptable. Instruments that do not specify a duration of time are considered high risk unless compared to a valid and reliable measure since the definition of infertility is duration-based and these types of measures have not been validated. Current duration measures are considered high risk since these measures have not been validated for measuring infertility. Studies that use the reproductive calendar to indirectly classify women as infertile are considered high risk. Studies that use proxy measures for unprotected sex are considered high risk (e.g., assume those that are married are having unprotected sex). **Examples:** • The authors used a reproductive calendar to determine time to pregnancy or live birth. The answer is: Yes (LOW RISK). • The authors ask participants if they ever tried for 12-months or longer to get pregnant. The answer is: Yes (LOW RISK). • The authors ask participants if they ever had difficulty conceiving and do not compare results to a valid and reliable measure. The answer is: No (HIGH RISK) • The authors use a reproductive calendar to estimate current duration at risk and do not compare to a valid and reliable measure. The answer is: No (HIGH RISK) • The authors don't explicitly state or sufficiently describe the question (or the ICD codes) used to determine infertility status of respondents. The answer is: No (HIGH RISK) • A reproductive calendar is used to indirectly determine whether a woman is classified as infertile (no direct questions on infertility). The answer is: No (HIGH RISK). • The authors assume that all married couples are having unprotected sex. The answer is: No (HIGH RISK).

ITEM #	RISK OF BIAS ITEM	CRITERIA FOR ANSWERS	ADDITIONAL NOTES AND EXAMPLES
7	**Was the same mode of data collection used for all subjects?**	• **Yes (LOW RISK):** The same mode of data collection was used for all subjects. • **No (HIGH RISK):** The same mode of data collection was NOT used for all subjects.	The mode of data collection is the method used for collecting information from the subjects. The most common modes are face-to-face interviews, telephone interviews and self-administered questionnaires. **Examples:** • All eligible subjects had a face-to-face interview. The answer is: Yes (LOW RISK). • Some subjects were interviewed over the telephone and some filled in postal questionnaires. The answer is: No (HIGH RISK).
8	**Were the numerator(s) and denominator(s) for the parameter of interest appropriate?**	• **Yes (LOW RISK):** The paper presented appropriate numerator(s) AND denominator(s) for the parameter of interest (e.g., the prevalence of infertility). • **No (HIGH RISK):** The paper did present numerator(s) AND denominator(s) for the parameter of interest but one or more of these were inappropriate.	There may be errors in the calculation and/or reporting of the numerator and/or denominator. **Examples:** • There were no errors in the reporting of the numerator(s) AND denominator(s) for the prevalence of infertility. The answer is: Yes (LOW RISK). • In reporting the overall prevalence of infertility in both men and women), the authors accidentally used the population of women as the denominator rather than the combined population. The answer is: No (HIGH RISK).
Summary assessment			
9	**Summary item on the overall risk of study bias**	• **LOW RISK OF BIAS:** Further research is very unlikely to change our confidence in the estimate. • **MODERATE RISK OF BIAS:** Further research is likely to have an important impact on our confidence in the estimate and may change the estimate. • **HIGH RISK OF BIAS:** Further research is very likely to have an important impact on our confidence in the estimate and is likely to change the estimate.	1-point is awarded to each item labeled as “yes (LOW RISK). Items 1 - 8 are summed and level of risk is determined by the following tertiles: • Low risk of bias: 6 - 8 • Moderate risk of bias: 3 - 5 • High risk of bias: 0 - 2

Annex 2. Studies included in the systematic review

Ahmadi Asr Badr Y, Madaen K, Haj Ebrahimi S, Ehsan Nejad AH, Koushavar H. Prevalence of infertility in Tabriz in 2004. *Urol J* 2006;**3**:87–91.

Ajrouche R, Rudant J, Orsi L, Petit A, Baruchel A, Nelken B, Pasquet M, Michel G, Bergeron C, Ducassou S, *et al.* Maternal reproductive history, fertility treatments and folic acid supplementation in the risk of childhood acute leukemia: the ESTELLE Study. *Cancer Causes Control* 2014;**25**:1283–1293.

Akhondi MM, Ranjbar F, Shirzad M, Ardakani ZB, Kamali K, Mohammad K. Practical difficulties in estimating the prevalence of primary infertility in Iran. *Int J Fertil Steril* 2019;**13**:113–117.

Akre O, Cnattingius S, Bergström R, Kvist U, Trichopoulos D, Ekbom A. Human fertility does not decline: evidence from Sweden. *Fertil Steril* 1999;**71**:1066–1069.

Albayrak E, Günay O. State and trait anxiety levels of childless women in Kayseri, Turkey. *Eur J Contracept Reprod Health Care* 2007;**12**:385–390.

Anyalechi GE, Hong J, Kreisel K, Torrone E, Boulet S, Gorwitz R, Kirkcaldy RD, Bernstein K. Self-reported infertility and associated pelvic inflammatory disease among women of reproductive age: National Health and Nutrition Examination Survey, United States, 2013-2016. *Sex Transm Dis* 2019;**46**:446–451.

Bach CC, Bech BH, Nohr EA, Olsen J, Matthiesen NB, Bossi R, Uldbjerg N, Bonefeld-Jørgensen EC, Henriksen TB. Serum perfluoroalkyl acids and time to pregnancy in nulliparous women. *Environ Res* 2015;**142**:535–541.

Balakrishnan TR, Fernando R. Infertility among Canadians: an analysis of data from the Canadian Fertility Survey (1984) and General Social Survey (1990). *The Prevalence of Infertility in Canada: Research Studies of the Royal Commission on New Reproductive Technologies* 1993;**6**:, p. 107–162. Minister of Supply and Services Canada Ottawa: Ottawa, Canada.

Barden-O'Fallon J. Associates of self-reported fertility status and infertility treatment-seeking in a rural district of Malawi. *Hum Reprod* 2005;**20**:2229–2236.

Bello B, Kielkowski D, Heederik D, Wilson K. Time-to-pregnancy and pregnancy outcomes in a South African population. *BMC Public Health* 2010;**10**:565–572.

Bernhard P, Makunde RW, Magnussen P, Lemnge MM. Genital manifestations and reproductive health in female residents of a wuchereria bancrofti-endemic area in Tanzania. *Trans R Soc Trop Med Hyg* 2000;**94**:409–412.

Bhattacharya S, Porter M, Amalraj E, Templeton A, Hamilton M, Lee AJ, Kurinczuk JJ. The epidemiology of infertility in the North East of Scotland. *Hum Reprod* 2009;**24**:3096–3107.

Björvang RD, Gennings C, Lin P-I, Hussein G, Kiviranta H, Rantakokko P, Ruokojärvi P, Lindh CH, Damdimopoulou P, Bornehag C-G. Persistent organic pollutants, pre-pregnancy use of combined oral contraceptives, age, and time-to-pregnancy in the SELMA cohort. *Environ Health* 2020;**19**:1–14.

Bolumar F, Olsen J, Boldsen J, European Study Group on Infertility Subfecundity. Smoking reduces fecundity: a European multicenter study on infertility and subfecundity. *Am J Epidemiol* 1996;**143**:578–587.

Boulet SL, Warner L, Adamski A, Smith RA, Burley K, Grigorescu V. Behavioral risk factor surveillance system state-added questions: leveraging an existing surveillance system to improve knowledge of women's reproductive health. *J Womens Health* 2016;**25**:565–570.

Brunetti P, Morabia A, Campana A, Marcus-Steiff J. Biometrical study of reproduction conditions in the general-population: method and initial results of surveys carried out in chambery-grenoble and martigny. *Population* 1994;**49**:27–60.

Buckett W, Bentick B. The epidemiology of infertility in a rural population. *Acta Obstet Gynecol Scand* 1997;**76**:233–237.

Bushnik T, Cook JL, Yuzpe AA, Tough S, Collins J. Estimating the prevalence of infertility in Canada. *Hum Reprod* 2012;**27**:738–746.

Cabrera-Leon A, Lopez-Villaverde V, Rueda M, Moya-Garrido MN, Cabrera-León A. Calibrated prevalence of infertility in 30- to 49-year-old women according to different approaches: a cross-sectional population-based study. *Hum Reprod* 2015;**30**:2677–2685.

Cai X, Song R, Long M, Wang S, Ma Y, Li X, Ai H, Shan X, Fu L, Liu Y. [A cross-sectional study on the current status of female infertility in three counties of Xinjiang Uygur Autonomous Region]. *Zhonghua Yi Xue Za Zhi* 2011;**91**:3182–3185.

Cairncross ZF, Ahmed SB, Dumanski S, Nerenberg K, Metcalfe A. Infertility and the risk of cardiovascular disease: findings from the Study of Women's Health Across the Nation (SWAN). *CJC Open* 2020;

Chandra A, Stephen EH. Infertility and impaired fecundity in the United States, 1982–2010: data from the National Survey of Family Growth. *Natl Health Stat Report* 2013;1–19.

Chauhan S, Kulkarni R, Agarwal D. Prevalence and factors associated with chronic obstetric morbidities in Nashik district, Maharashtra. *Indian J Med Res* 2015;**142**:479–488.

Chen J, Zhong C, Liang H, Yang Y, Zhang O, Gao E, Chen A, Yuan W, Wang J, Sun F, et al. The relationship between age at menarche and infertility among Chinese rural women. *Eur J Obstet Gynecol Reprod Biol* 2015;**194**:68–72.

Crawford S, Fussman C, Bailey M, Bernson D, Jamieson DJ, Murray-Jordan M, Kissin DM. Estimates of lifetime infertility from three states: the behavioral risk factor surveillance system. *J Womens Health* 2015;**24**:578–586.

Damone AL, Earnest A, Joham AE, Teede HJ, Moran LJ, Loxton D. Depression, anxiety and perceived stress in women with and without PCOS: a community-based study. *Psychol Med* 2019;**49**:1510–1520.

Datta J, Palmer MJ, Tanton C, Gibson LJ, Jones KG, Macdowall W, Glasier A, Sonnenberg P, Field N, Mercer CH, *et al.* Prevalence of infertility and help seeking among 15 000 women and men. *Hum Reprod* 2016;**31**:2108–2118.

Dovom MR, Tehrani FR, Abedini M, Amirshekari G, Hashemi S, Noroozzadeh M. A population-based study on infertility and its influencing factors in four selected provinces in Iran (2008-2010). *Iran J Reprod Med* 2014;**12**:561–566.

Dulberg CS, Stephens T. The prevalence of infertility in Canada, 1991–1992: analysis of three national surveys. *The Prevalence of Infertility in Canada: Research Studies of the Royal Commission on New Reproductive Technologies* 1993;**6**:, p. 61–106. Minister of Supply and Services Canada Ottawa: Ottawa, Canada.

Ekudayo O, Titilayo A, Anuodo O, Babalola O. Female genital cutting and infertility in marriage: a cross-sectional study among women in Nigeria. *Int J Educ Res* 2020;**8**:65–78.

Ericksen K, Brunette T. Patterns and predictors of infertility among African women: a cross-national survey of twenty-seven nations. *Soc Sci Med* 1996;**42**:209–220.

Esmaeilzadeh S, Delavar MA, Zeinalzadeh M, Mir M-RA. Epidemiology of infertility: a population-based study in Babol, Iran. *Women Health* 2012;**52**:744–754.

Eustache F, Auger J, Cabrol D, Jouannet P. Are volunteers delivering semen samples in fertility studies a biased population? *Hum Reprod* 2004;**19**:2831–2837.

Fledderjohann J, Johnson DR. Impaired fertility and perceived difficulties conceiving in Ghana: measurement problems and prospects. *J Biosoc Sci* 2016;**48**:431–456.

Fledderjohann J, Trinitapoli J, Billari F. Who seeks help? Responses to perceived fertility impairments in Malawi. *International Popular Conference* [Internet] 2017; International Union for the Scientific Study of Population (IUSSP). Available from: https://iussp.confex.com/iussp/ipc2017/meetingapp.cgi/Paper/3525.

Fuentes A, Devoto L. Infertility after 8 years of marriage: a pilot study. *Hum Reprod* 1994;**9**:273–278.

Geelhoed DW, Nayembil D, Asare K, Schagen van Leeuwen JH, Roosmalen J van. Infertility in rural Ghana. *Int J Gynaecol Obstet* 2002;**79**:137–142.

Gleason JL, Shenassa ED, Thoma ME. Stressful life events, the incidence of infertility, and the moderating effect of maternal responsiveness: a longitudinal study. *J Dev Orig Health Dis* 2020;1–9.

Gokler ME, Unsal A, Arslantas D. The prevalence of infertility and loneliness among women aged 18-49 years who are living in semi-rural areas in western Turkey. *Int J Fertil Steril* 2014;**8**:155–162.

Guldbrandsen K, Håkonsen LB, Ernst A, Toft G, Lyngsø J, Olsen J, Ramlau-Hansen CH. Age of menarche and time to pregnancy. *Hum Reprod* 2014;**29**:2058–2064.

Gunnell DJ, Ewings P. Infertility prevalence, needs assessment and purchasing. *J Public Health Med* 1994;**16**:29–35.

Győrffy Z, Dweik D, Girasek E. Reproductive health and burn-out among female physicians: nationwide, representative study from Hungary. *BMC Womens Health* 2014;**14**:121.

Hærvig KK, Kierkegaard L, Lund R, Bruunsgaard H, Osler M, Schmidt L. Is male factor infertility associated with midlife low-grade inflammation? A population based study. *Hum Fertil (Camb)* 2018;**21**:146–154.

Hallén M, Sandblom G, Nordin P, Gunnarsson U, Kvist U, Westerdahl J. Male infertility after mesh hernia repair: a prospective study. *Surgery* 2011;**149**:179–184.

Hassan KE. Prevalence of infertility and its impact on marital fertility, Egypt, 1993. 1997. Available from: http://www.zohry.com/dwb/khassan/pub/infertility.pdf.

He Y, Zheng D, Shang W, Wang X, Zhao S, Wei Z, Song X, Shi X, Zhu Y, Wang S, et al. Prevalence of oligomenorrhea among women of childbearing age in China: a large community-based study. *Womens Health* 2020;**16**:1-9.

Herbert D, Lucke J, Dobson A. Infertility, medical advice and treatment with fertility hormones and/or in vitro fertilisation: a population perspective from the Australian Longitudinal Study on Women's Health. *Aust N Z J Public Health* 2009a;**33**:358–364.

Herbert DL, Lucke JC, Dobson AJ. Infertility in Australia circa 1980: an historical population perspective on the uptake of fertility treatment by Australian women born in 1946-51. *Aust N Z J Public Health* 2009b;**33**:507–514.

Hoenderboom BM, Bergen JEAM van, Dukers-Muijrers NHTM, Götz HM, Hoebe CJPA, Vries HJC de, Broek IVF van den, Vries F de, Land JA, Sande MAB van der, *et al.* Pregnancies and time to pregnancy in women with and without a previous chlamydia trachomatis infection. *Sex Transm Dis* 2020;**47**:739–747.

Hollegaard S, Vogel I, Thorsen P, Jensen IP, Mordhorst C-H, Jeune B. Chlamydia trachomatis C-complex serovars are a risk factor for preterm birth. *In Vivo* 2007;**21**:107–112.

Hosseini J, Emadedin M, Mokhtarpour H, Sorani M. Prevalence of primary and secondary infertility in four selected provinces in Iran, 2010-2011. *Iran J Obstet Gynecol Infertil* 2012;**15**:1–7.

Hu P, Cai C, Vinturache A, Hu Y, Gao Y, Zhang J, Lu M, Gu H, Qiao J, Tian Y, et al. Maternal preconception body mass index and time-to-pregnancy in Shanghai Women, China. *Women Health* 2020;**60**:1014–1023.

Huang J -t, Tang Y -g. Incidence of infertility and its influencing factors among married residents in Guangdong province. *China Public Health = Zhongguo Gong Gong Wei Sheng* 2013;**29**:0194–0197.

Jacob MC, McQuillan J, Greil AL. Psychological distress by type of fertility barrier. *Hum Reprod* 2007;**22**:885–894.

Jacobson MH, Chin HB, Mertens AC, Spencer JB, Fothergill A, Howards PP. "Research on infertility: definition makes a difference" Revisited. *Am J Epidemiol* 2018;**187**:337–346.

Jensen TK, Slama R, Ducot B, Suominen J, Cawood EHH, Andersen AG, Eustache F, Irvine S, Auger S, Jouannet P, *et al.* Regional differences in waiting time to pregnancy among fertile couples from four European cities. *Hum Reprod* 2001;**16**:2697–2704.

Joffe M. Time trends in biological fertility in Britain. *Lancet* 2000;**355**:1961–1965.

Karmaus W, Juul S. Infertility and subfecundity in population-based samples from Denmark, Germany, Italy, Poland and Spain. *Eur J Public Health* 1999;**9**:229–235.

Katole A, Saoji A. Prevalence of primary infertility and its associated risk factors in urban population of central India: a community-based cross-sectional study. *Indian J Community Med* 2019;**44**:337–341.

Kazemijaliseh H, Ramezani Tehrani F, Behboudi-Gandevani S, Hosseinpanah F, Khalili D, Azizi F. The prevalence and causes of primary infertility in Iran: a population-based study. *Glob J Health Sci* 2015;**7**:226–232.

Keiding N, Ali MM, Eriksson F, Matsaseng T, Toskin I, Kiarie J. The use of time to pregnancy for estimating and monitoring human fecundity from demographic and health surveys. *Epidemiology* 2021;**32**:27–35.

Kirkegaard I, Uldbjerg N, Tabor A, Henriksen TB. Longer time-to-pregnancy in spontaneously conceived pregnancies is associated with lower PAPP-A and free [beta]-hCG in first trimester screening for Down syndrome. *Prenat Diagn* 2014;**34**:235–240.

Klemetti R, Raitanen J, Sihvo S, Saarni S, Koponen P. Infertility, mental disorders and well-being: a nationwide survey. *Acta Obstet Gynecol Scand* 2010;**89**:677–682.

Klouman E, Manongi R, Knut-Inge Klepp. Self-reported and observed female genital cutting in rural Tanzania: associated demographic factors, HIV and sexually transmitted infections. *Trop Med Int Health* 2005;**10**:105–1115.

Kreisel KM, Ikerdeu E, Cash HL, De Jesus SL, Kamb ML, Anderson T, Barrow RY, Sugiyama MS, Basilius K, Madraisau S. An evaluation of infertility among women in the Republic of Palau, 2016. *Hawaii J Health Soc Welf* 2020;**79**:7–15.

Küppers-Chinnow M, Karmaus W. Prävalenz von verminderter Fruchtbarkeit und Inanspruchnahme ärztlicher Hilfe. *Geburtshilfe Frauenheilkd* 1997;**57**:89–95.

Larsen U. Primary and secondary infertility in sub-Saharan Africa. *Int J Epidemiol* 2000;**29**:285–291.

Larsen U. Infertility in central Africa. *Trop Med Int Health* 2003;**8**:354–367.

Larsen U. Research on infertility: which definition should we use? *Fertil Steril* 2005;**83**:846–852.

Louis JF, Thoma ME, Sørensen DN, McLain AC, King RB, Sundaram R, Keiding N, Buck Louis GM. The prevalence of couple infertility in the United States from a male perspective: evidence from a nationally representative sample. *Andrology* 2013;**1**:741–748.

Magnus MC, Fraser A, Rich-Edwards JW, Magnus P, Lawlor DA, Håberg SE. Time-to-pregnancy and risk of cardiovascular disease among men and women. *Eur J Epidemiol* 2021;**36**:383–391.

Mascarenhas MN, Cheung H, Mathers CD, Stevens GA. Measuring infertility in populations: constructing a standard definition for use with demographic and reproductive health surveys. *Popul Health Metr* 2012a;**10**:17.

Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. *PLoS Med* 2012b;**9**:e1001356.

McQuillan J, Greil AL, White L, Jacob MC. Frustrated fertility: infertility and psychological distress among women. *J Marriage Fam* 2003;**65**:1007–1018.

Mena GP, Mielke GI, Brown WJ. Do physical activity, sitting time and body mass index affect fertility over a 15-year period in women? Data from a large population-based cohort study. *Hum Reprod* 2020;**35**:676–683.

Meng Q, Ren A, Zhang L, Liu J, Li Z, Yang Y, Li R, Ma L. Incidence of infertility and risk factors of impaired fecundity among newly married couples in a Chinese population. *Reprod Biomed Online* 2015;**30**:92–100.

Merritt MA, De Pari M, Vitonis AF, Titus LJ, Cramer DW, Terry KL. Reproductive characteristics in relation to ovarian cancer risk by histologic pathways. *Hum Reprod* 2013;**28**:1406–1417.

Miller-Fellows SC, Howard L, Kramer R, Hildebrand V, Furin J, Mutuku FM, Dunstan Mukoko, Ivy JA, King CH. Cross-sectional interview study of fertility, pregnancy, and urogenital schistosomiasis in coastal Kenya: documented treatment in childhood is associated with reduced odds of subfertility among adult women. *PLoS Negl Trop Dis* 2017;**11**:e0006101.

Mirzaei M, Namiranian N, Dehghani Firouzabadi R, Gholami S. The prevalence of infertility in 20-49 years women in Yazd, 2014-2015: a cross-sectional study. *Int J Reprod Biomed* 2018;**16**:683–688.

Muller A, Slama R, Labbé-Declèves C, Jouannet P, Bujan L, Mieusset R, Le Lannou D, Guerin J-F, Benchaib M, Spira A. Geographic variations in probability of pregnancy in four cities of France. *Rev Epidemiol Sante Publique* 2006;**54**:55–60.

Nasrabad HBR, Abbasi-Shavazi MJ, Hosseini-Chavoshi M, Karegar-Shoraki MR. Trend and patterns of childlessness in Iran. *Proceedings of the XXVII International Population Conference of the IUSSP*. 2013; pp. 26–31. Busan, Korea.

Nelson DB, Sammel MD, Patterson F, Lin H, Gracia CR, Freeman EW. Effects of reproductive history on symptoms of menopause: a brief report. *Menopause* 2011;**18**:1143–1148.

Nguyen RH, Wilcox AJ, Skjærven R, Baird DD. Men's body mass index and infertility. *Hum Reprod* 2007;**22**:2488–2493.

Oakley LL. The epidemiology of infertility: measurement, prevalence and an investigation of early life and reproductive risk factors. 2010; London School of Hygiene & Tropical Medicine.

Passey M, Mgone CS, Lupiwa S, Suve N, Tiwara S, Lupiwa T, Clegg A, Alpers MP. Community based study of sexually transmitted diseases in rural women in the highlands of Papua New Guinea: prevalence and risk factors. *Sex Transm Infect* 1998;**74**:120–127.

Pedersen KK, Hagen C, Eshoj O. Infertility and pregnancy outcome in women with insulin-dependent diabetes mellitus. An epidemiological study. *Ugeskr Laeger* 1994;**156**:6196–6200.

Philippov OS, Radionchenko AA, Bolotova VP, Voronovskaya NI, Potemkina TV. Estimation of the prevalence and causes of infertility in western Siberia. *Bull World Health Organ* 1998;**76**:183–187.

Pick WM, Obermeyer CM. Urbanization, household composition and the reproductive health of women in a South African city. *Soc Sci Med* 1996;**43**:1431–1441.

Polis CB, Cox CM, Tunçalp Ö, McLain AC, Thoma ME. Estimating infertility prevalence in low-to-middle-income countries: an application of a current duration approach to Demographic and Health Survey data. *Hum Reprod* 2017;**32**:1064–1074.

Priestley SR. Impaired fertility in Jamaica: evidence from fertility surveys. *West Indian Med J* 2012;**61**:716–725.

Purkayastha N, Sharma H. Prevalence and potential determinants of primary infertility in India: evidence from Indian demographic health survey. *Clin Epidemiol Glob Health* 2021;**9**:162–170.

Raatikainen K, Harju M, Hippeläinen M, Heinonen S. Prolonged time to pregnancy is associated with a greater risk of adverse outcomes. *Fertil Steril* 2010;**94**:1148–1151.

Rao N, Esber A, Turner A, Mopiwa G, Banda J, Norris A. Infertility and self-rated health among Malawian women. *Women Health* 2018;**58**:1081–1093.

Righarts A, Dickson NP, Ekeroma A, Gray AR, Parkin L, Gillett WR. The burden of infertility in New Zealand: a baseline survey of prevalence and service use. *Aust N Z J Obstet Gynaecol* 2021;**61**:439–447.

Righarts A, Dickson NP, Parkin L, Gillett WR. Infertility and outcomes for infertile women in Otago and Southland. *N Z Med J* 2015;**128**:43–53.

Risch HA, Marrett LD, Howe GR. Parity, contraception, infertility, and the risk of epithelial ovarian cancer. *Am J Epidemiol* 1994;**140**:585–597.

Roode T van, Dickson NP, Righarts AA, Gillett WR. Cumulative incidence of infertility in a New Zealand birth cohort to age 38 by sex and the relationship with family formation. *Fertil Steril* 2015;**103**:1053-1058.e2.

Rostad B, Schmidt L, Sundby J, Schei B. Has fertility declined from mid-1990s to mid-2000s? *Acta Obstet Gynecol Scand* 2013;**92**:1284–1289.

Rutstein SO, Shah IH. *Infecundity, infertility, and childlessness in developing countries* [Internet]. 2004; OCR Macro and World Health Organization. Available from: https://www.who.int/reproductivehealth/publications/infertility/DHS_9/en/.

Safarinejad MR. Infertility among couples in a population-based study in Iran: prevalence and associated risk factors. *Int J Androl* 2008;**31**:303–314.

Samarakoon S, Rajapaksa L, Seneviratne HR. Prevalence of primary and secondary infertility in the Colombo District. *Ceylon J Med Sci* 2007;**45**:83–91.

Sarac M, Koc I. Prevalence and risk factors of infertility in Turkey: evidence from demographic and health surveys, 1993-2013. *J Biosoc Sci* 2018;**50**:472–490.

Sharif SN, Azizi Kutenaee M, Darsareh F, Roozbeh N. Prevalence and risk factors of infertility in a southern port city of Iran. *Hormozgan Medical Journal* 2020;**24**: e99412.

Singh BP, Shukla U. Inability to conceive and treatment-seeking behaviour in Uttar Pradesh state in India. *Can Stud Popul* 2015;**42**:1–12.

Slama R, Ducot B, Carstensen L, Lorente C, La Rochebrochard E de, Leridon H, Keiding N, Bouyer J. Feasibility of the current-duration approach to studying human fecundity. *Epidemiology* 2006;**17**:440–449.

Slama R, Hansen OKH, Ducot B, Bohet A, Sorensen D, Giorgis Allemand L, Eijkemans MJC, Rosetta L, Thalabard JC, Keiding N, *et al.* Estimation of the frequency of involuntary infertility on a nation-wide basis. *Hum Reprod* 2012;**27**:1489–1498.

Soares S, Rodrigues T, Barros H. [Infertility prevalence in the city of Porto]. *Acta Med Port* 2011;**24**:699–706.

Somé EN, Boncoungou J, Poda JN. Prevalence of the infertility among couples in Ouagadougou (Burkina Faso): A population-based survey. *Open Public Health J* 2016;**9**:88-97.

Song S. Assessing the impact of in utero exposure to famine on fecundity: evidence from the 1959-61 famine in China. *Popul Stud* 2013;**67**:293–308.

Sundby J, Mboge R, Sonko S. Infertility in the Gambia: frequency and health care seeking. *Soc Sci Med* 1998;**46**:891–899.

Sundby J, Schei B. Infertility and subfertility in Norwegian women aged 40-42: prevalence and risk factors. *Acta Obstet Gynecol Scand* 1996;**75**:832–837.

Taponen S, Ahonkallio S, Martikainen H, Koivunen R, Ruokonen A, Sovio U, Hartikainen A-L, Pouta A, Laitinen J, King V, et al. Prevalence of polycystic ovaries in women with self-reported symptoms of oligomenorrhoea and/or hirsutism: Northern Finland Birth Cohort 1966 Study. *Hum Reprod* 2004;**19**:1083–1088.

Taylor GM, Faragher EB, Chantler E, Seif MW. Fecundity in the modern city: a comparison of couples attending antenatal clinics in Manchester (UK) and Melbourne (Australia). *J Obstet Gynaecol* 1999;**19**:489–495.

Terävä A-N, Gissler M, Hemminki E, Luoto R. Infertility and the use of infertility treatments in Finland: prevalence and socio-demographic determinants 1992–2004. *Eur J Obstet Gynecol Reprod Biol* 2008;**136**:61–66.

Thoma ME, McLain AC, Louis JF, King RB, Trumble AC, Sundaram R, Buck Louis GM. Prevalence of infertility in the United States as estimated by the current duration approach and a traditional constructed approach. *Fertil Steril* 2013;**99**:1324–1331.

Toft G, Axmon A, Giwercman A, Thulstrup AM, Rignell-Hydbom A, Pedersen HS, Ludwicki JK, Zvyezday V, Zinchuk A, Spano M, *et al.* Fertility in four regions spanning large contrasts in serum levels of widespread persistent organochlorines: a cross-sectional study. *Environ Health* 2005;**4**:26.

Udgiri R, Patil VV. Comparative study to determine the prevalence and socio-cultural practices of infertility in rural and urban field practice area of tertiary care hospital, Vijayapura, Karnataka. *Indian J Community Med* 2019;**44**:129–133.

Unisa S. Childlessness in Andhra Pradesh, India: treatment-seeking and consequences. *Reprod Health Matters* 1999;**7**:54–64.

Vahidi S, Ardalan A, Mohammad K. Prevalence of primary infertility in the Islamic Republic of Iran in 2004-2005. *Asia Pac J Public Health* 2009;**21**:287–293.

Van der Avoort IAM, Van Golde RJT, Tuerlings JHAM, Kiemeney LA, Meuleman EJH, Braat DDM, Kremer JAM. Underestimation of subfertility among relatives when using a family history: taboo bias. *J Androl* 2003;**24**:285–288.

Walraven G, Scherf C, West B, Ekpo G, et al. The burden of reproductive-organ disease in rural women in the Gambia, West Africa. *Lancet* 2001;**357**:1161–1167.

Wang B, Zhou W, Zhu W, Chen L, Wang W, Tian Y, Shen L, Zhang J. Associations of female exposure to bisphenol A with fecundability: evidence from a preconception cohort study. *Environ Int* 2018;**117**:139–145.

Weiss HA, Troisi R, Rossing MA, Brogan D, Coates RJ, Gammon MD, Potischman N, Swanson CA, Brinton LA. Fertility problems and breast cancer risk in young women: a case-control study in the United States. *Cancer Causes Control* 1998;**9**:331–339.

Woodall PA, Kramer MR. Schistosomiasis and infertility in East Africa. *Am J Trop Med Hyg* 2018;**98**:1137.

Wu S, Tian J, Wang M, Pan B, Lü H, Wang Z, Li H. [The effect of cadmium pollution on reproductive health in females]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2004;**25**:852–855.

Wulff M, Högberg U, Stenlund H. Infertility in an industrial setting: a population-based study from Northern Sweden. *Acta Obstet Gynecol Scand* 1997;**76**:673–679.

Xingping G, Yu W, Qiufang H. Prevalence of infertility in rural areas of Shanxi Province. *Chin J Fam Plan* 2006;**14**:358.

Yang F, Li L, Chen J-P, Liu X-Q, Zhong C-L, Yang Y, Ren Y-F, Yuan W, Liang H, Miao M-H. Couple's infertility in relation to male smoking in a Chinese rural area. *Asian J Androl* 2017;**19**:311–315.

Yang Y-Q, Shen H, Chen J, Chen Z-W. [A prevalence survey of infertility in Beijing, China]. *Zhonghua Yi Xue Za Zhi* 2011;**91**:313–316.

Zargar AH, Wani AI, Masoodi SR, Laway BA, Salahuddin M. Epidemiologic and etiologic aspects of primary infertility in the Kashmir region of India. *Fertil Steril* 1997;**68**:637–643.

Zhang H, Wang S, Zhang S, Wang T, Deng X. Increasing trend of prevalence of infertility in Beijing. *Chin Med* J 2014;**127**:691–695.

Zhang X -h, Zhang R. Analysis on infertility prevalence and its affecting factors in Gansu province. *Reprod Contracept* 2013;**33**:184–192.

Zhou Z, Zheng D, Wu H, Li R, Xu S, Kang Y, Cao Y, Chen X, Zhu Y, Chen Z, et al. Epidemiology of infertility in China: a population-based study. *BJOG* 2018;**125**:432–441.

Annex 3. Summary of included studies by region

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
AFRICAN REGION											
Somé et al. (2016)	Burkina Faso	Cross-sectional	Households: 480	Women: 18 - 45 Men: 18 - 55	Retrospective Time-to-Pregnancy (TTP) Design	Childbearing age women/men who have never born a child and who had been seeking a child for more than 12 months	All women/men in union/living with partner	Lifetime	12	Infertility - women Primary infertility Secondary infertility Infertility - men Primary infertility Secondary infertility	10.4 (7.9-13.5) 6.8 (4.8-9.4) 3.6 (2.2-5.7) 9.3 (7.0-12.2) 4.8 (3.2-7.2) 4.4 (2.9-6.7)
Sundby et al. (1998)	Gambia	Cross-sectional	3 000	15 - 49	Self-reported infertility measure (Direct)	Women with no pregnancy or live children born despite being married and not having used family planning for at least a year	All women	Period	12	Infertility Primary infertility	9.5 3.3
						Women who are married, not using contraceptives and not breastfeeding and have had no birth of a child for the last three years.	All women	Period	36	Secondary subfertility	6.2
Walraven et al. (2001)	Gambia	Cross-sectional	871	< 45 years	Self-reported infertility measure (Direct)	Women trying to conceive for at least one year without success despite regular (one time per week) sexual intercourse, no use of contraception, postmenarchal and premenopausal.	Married women not using contraception, postmenarchal and premenopausal	Period	12	Infertility	9·8 (8·2–11·6)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Geelhoed et al. (2002)	Ghana	Cross-sectional	Women: 1073 Men: 1064	Reproductive age	Self-reported infertility measure (Direct)	Women/men who experienced failure to achieve conception after at least one year of exposure	All women/men	Lifetime	12	Infertility - women Primary infertility Secondary infertility Infertility - men Primary infertility Secondary infertility	11.8 0.6 11.2 15.8 6.8 9.0
Fledderjohann and Johnson (2016)	Ghana	Cohort	1 350	15 - 49	Self-reported infertility measure (Direct)	Women reporting difficulties conceiving (takes a long time to get pregnant when they want to and/or can no longer become pregnant) Unadjusted: Does not account for contraceptive use or fertility desires Adjusted: Women who desire a child and are not currently using modern contraception	Married or in union women	Period	No duration	Self-assessed difficulties conceiving: Unadjusted Adjusted	 65.0 20.0
					Constructed infertility measure (Indirect)	Woman without a birth after 12/24/60/84 months Unadjusted: Does not account for contraceptive use or fertility desires Adjusted: Women who desire a child and are not currently using modern contraception	Women in union	Period	12 24 60 80 12 24 60 80	Infertility - Unadjusted Adjusted	69.0 64.0 35.0 24.0 17.0 15.0 7.0 4.0
Miller-Fellows et al. (2017)	Kenya	Cross-sectional	160	15 - 45	Self-reported infertility measure (Direct)	Women who were in a sexual union and not using contraception for at least 5 years and did not have a live birth and/or women who reported a period of over one year without a pregnancy with regular, unprotected sexual intercourse	Women who had ever been married or in a co-residing sexual union, were currently pregnant, and/or had given birth to at least one child.	Lifetime	60 or 12	Subfertility Primary infertility Secondary infertility	44.0 (37.0 – 52.0) 2.0 (0.3 – 5.0) 42.0 (35.0 – 51.0)
Barden-O'Fallon (2005)	Malawi	Cohort	Women: 678 Men: 362	Women: 15 - 34 Men: 20 - 44	Self-reported infertility measure (Direct)	Women/men who said they ever experienced difficulty becoming pregnant	Women/men who had ever been pregnant or tried to become pregnant	Lifetime	No duration	Perceived infertility: Women Men	 19.6 19.6

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Fledderjohann et al. (2017)	Malawi	Cross-sectional	116	15 - 25	Self-reported infertility measure (Direct)	Women who reported that they had a lot or some difficulty conceiving and/or carrying a pregnancy	All women	Lifetime	No duration	Impaired fertility	12.8
Rao et al. (2018)	Malawi	Cross-sectional	915	15 - 39	Self-reported infertility measure (Direct)	Women who had ever tried and failed to conceive a pregnancy for 2 years or longer	All women	Lifetime	24	Infertility	20.0
Polis et al. (2017)	Nigeria	Cross-sectional	6 340	18 - 44	Current Duration Design	Couples not yet pregnant by 12/24/36 months (estimated)	Women at risk of pregnancy (18–44 years, married or cohabitating, sexually active within the past 4 weeks and not currently using contraception and had not been sterilized)	Period	12 24 36	Infertility Primary infertility Secondary infertility Infertility Primary infertility Secondary infertility Infertility Primary infertility Secondary infertility	31.1(27.9 - 34.7) 17.4 (12.9 - 23.8) 34.1 (30.3 - 39.3) 17.7 (15.7 - 20) 10.0 (7.0 - 14.3) 19.2 (17.1 - 22.1) 11.5 (10.2 - 13.0) 6.8 (4.6 - 10) 12.3 (11.0 - 14.1)
Ekudayo (2020)	Nigeria	Cross-sectional	16 922	15 - 49	Constructed infertility measure (Indirect)	Women who reported 0 as the total number of children ever born, who were not pregnant at the time of the survey and were not presently using contraception	Married women or women living with a partner who reported at least 1 child or who were presently pregnant (unclear if contraceptive users were included)	Period	24	Infertility	3.1
Bello et al. (2010)	South Africa	Cross-sectional	482	18 - 49	Retrospective Time-to-Pregnancy (TTP) Design	Women with a TTP greater than 6/12/24 months for the most recent pregnancy or current pregnancy attempt (if pregnancy has not been achieved)	Women who had been pregnant and planned their most recent pregnancies and women who had never been pregnant but were trying	Period	6 12 24	TTP > 6 months TTP > 12 months TTP > 24 months	50.0 32.0 17.0
Pick and Obermeyer (1996)	South Africa	Cross-sectional	298	15+	Self-reported infertility measure (Direct)	Women not using any form of contraception at the time of the survey who reported difficulty in becoming pregnant	Women who were not using any form of contraception at the time of the survey	Lifetime	No duration	Infertility	19.0

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
						Women with no pregnancy in the preceding five years who reported difficulty in becoming pregnant and were not using contraception at the time of the survey	Women who were not using any form of contraception at the time of the survey	Period	60	Infertility	10.0
Larsen (2005)	United Republic of Tanzania	Cross-sectional	993	20 - 44	Retrospective Time-to-Pregnancy (TTP) Design	Women who have been having intercourse without using contraception or trying in any way to delay or avoid getting pregnant for at least two years without conceiving	Women in first union (married or consensual union) for at least two years	Period	24	Infertility Primary infertility Secondary infertility	12.1 (9.4 - 14.8) 2.5 (1.5 - 3.5) 9.6 (7.3 - 11.9)
						Women who have tried to conceive for at least two years	Women in first union (married or consensual union) for at least two years	Period	24	Infertility Primary infertility Secondary infertility	6.9 (5.2 - 8.6) 1.8 (0.9 - 2.7) 5.0 (3.5 - 6.5)
			1 120	20 - 44	Self-reported infertility measure (Direct)	Women who report ever having problems getting pregnant	Women in first union (married or consensual union)	Lifetime	No duration	Infertility Primary infertility Secondary infertility	10.3 (8.4 - 12.2) 2.9 (1.9 - 3.9) 7.4 (6.0 - 8.8)
			720	20 - 44	Constructed infertility measure (Indirect)	Women who have had no births at least 5 years subsequent to last birth or marriage, if childless.	Women in first union (married or consensual union) for at least five years	Period	60	Infertility Secondary infertility	11.5 (9.2 - 13.7) 11.1 (9.8 - 12.6)
						Women who have had no births at least 5 years subsequent to last birth or marriage, if childless despite confirming that she wants a(nother) child	Women in first union (married or consensual union) for at least five years	Period	60	Infertility Secondary infertility	5.5 (3.9 - 7.1) 4.8 (3.9 - 5.7)
						Women married at least five/ seven years without ever having a child	Women in first union (married or consensual union) for at least five/ seven years	Lifetime	60 84	Primary infertility	3.5 (2.3 - 4.7) 1.9 (0.8 - 3.0)
Bernhard et al. (2000)	United Republic of Tanzania	Cross-sectional	530	> 15	Self-reported infertility measure (Direct)	Women with unsuccessful attempt to conceive for more than 6 months	All women	Lifetime	6	Primary infertility Secondary infertility	1.5 5.1
Klouman et al. (2005)	United Republic of Tanzania	Cross-sectional	636	15 - 44	Undetermined	Women who were unable to become pregnant within a year of living with their partners	All women	Period	12	Infertility Primary infertility Secondary infertility	10.3 3.1 7.2

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Larsen (2003)	Cameroon, Central African Republic, Gabon, and Chad	Cross-sectional	Cameroon: 3091 CAR: 3783 Chad: 5068 Gabon: 3205	15 - 49	Constructed infertility measure (Indirect)	Childless women married for at least five years	Women married for at least five years (current contraceptive users classified as fertile)	Period	60	Primary infertility (range)	3.1 - 6.9
						Childless women married for at least five years	Women married for at least five years (contraceptive use not taken into account)	Period	60	Primary infertility (range)	3.2 - 7.0
			Cameroon: 2819 CAR: 3219 Chad: 4418 Gabon: 3134	20 - 44		Ever-married, parous women who have had no live births during the last 5 years before the interview	Ever-married women who had at least one child and had been observed at least 5 years subsequent to the birth date of their first child (contraceptive users classified as fertile)	Period	60	Secondary infertility (range)	18.9 - 26.3
						Ever-married, parous women who have had no live births during the last 5 years before the interview	Ever-married women who had at least one child and had been observed at least 5 years subsequent to the birth date of their first child (contraceptive use not taken into account)	Period	60	Secondary infertility (range)	19.1 - 29.4
Larsen (2000)	Multiple countries (22 countries with data in or after 1990)	Cross-sectional	Range: 1361 - 5869	20 - 44	Constructed infertility measure (Indirect)	Women who have had no livebirths during the last 5 (secondary)/7 (primary) years before censoring (i.e., the month of survey or the month of last sexual intercourse, whichever came first)	Ever-married women (contraceptive users classified as fertile)	Period	60/84 60	Infertility: Range Secondary: Range	7.0 - 28.0 7.0 - 25.0
						Women who have had no livebirths during the last 5 (secondary)/7 (primary) years before censoring (i.e., the month of survey or the month of last sexual intercourse, whichever came first)	Ever-married women (contraceptive use not taken into account)	Period	60/84 84 60	Infertility: Range Primary: Range Secondary: Range	7.0 - 29.0 1.0 - 6.0 7.0 - 26.0

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Ericksen and Brunette (1996)	Multiple countries (12 countries with data in or after 1990)	Cross-sectional	Range: 1499 - 6206	20 - 41	Constructed infertility measure (Indirect)	Women who had been married or sexually experienced without a birth for at least 5/7years	All women exposed to conception	Period	60 84	Infertility: Range	8.9 - 16.6 12.0 - 20.8
Woodall and Kramer (2018)	Ethiopia, Kenya, United Republic of Tanzania, and Uganda	Cross-sectional	17 547	15 - 49	Constructed infertility measure (Indirect)	Women with no live birth within the last 5 years who have been married or in union for at least five years, are not using contraception, and are not currently pregnant	Women married or in union for at least 5 years, not using a contraceptive, and not presently pregnant	Period	60	Infertility Primary infertility	35.0 3.0
REGION OF THE AMERICAS											
Bushnik et al. (2012)	Canada	Cross-sectional	3 225 900	18-44	Constructed infertility measure (Indirect)	Couples who did not become pregnant after exposure to the risk of conception during the previous 12 months	Couples not using any form of birth control within the past 12 months	Period	12	Infertility Primary infertility	15.7 (14.2 - 17.4) 20.6 (17.8 - 23.7)
			3 176 900			Couples who did not become pregnant after exposure to the risk of conception during the previous 12 months	Couples who did not use any form of birth control within the past 12 months and reported having sexual intercourse in the past 12 months	Period	12	Infertility Primary infertility	14 (12.6 - 15.6) 18.7 (15.9 - 21.7)
						Couples who did not become pregnant after exposure to the risk of conception during the previous 12 months	Couples who did not use any form of birth control within the past 12 months, reported having sexual intercourse in the past 12 months, and reported ever having tried to become pregnant with their current partner	Period	12	Infertility Primary infertility	11.5 (10.2 - 12.9) 10.2 (8.3 - 12.5)
Risch et al. (1994)	Canada	Case-control	564	35 - 79	Self-reported infertility measure (Direct)	Women who ever had an interval of time when pregnancy was attempted without success	All women (control group)	Lifetime	No duration	Secondary infertility	7.6

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Dulberg and Stephens (1993)	Canada	Cross-sectional	1 413 (12-month) 1 350 (24-month)	18 - 44	Constructed infertility measure (Indirect)	Women and their husband/ partner who did not use any contraceptive method (non-surgical or surgical) and was not pregnant during 12/24 months prior to the interview.	Women who had been married or cohabitating for at least 12/24 months prior to the survey	Period	12 24	Infertility	8.5 (7.0 - 9.9) 7.0 (5.6 - 8.4)
Balakrishnan and Maxim (1993)	Canada	Cross-sectional	7 765	16 - 49	Self-reported infertility measure (Direct)	Women who believe she or her partner are incapable of having children	All women in union	Period	No duration	Perceived infertility Primary infertility Secondary infertility	3.19 5.22 2.79
			9 267		Constructed infertility measure (Indirect)	Women who reported that neither they nor their partner were sterilized, had not used any form of contraception in the year prior to the survey, and were not currently pregnant or post-partum mothers	All women in union	Period	12	Inferred infertility Primary infertility Secondary infertility	6.66 11.23 5.31
			7 765			Women classified as perceived infertile (direct question) and/or inferred infertile (indirect questions)	All women in union	Period	12 or no duration	Aggregate infertility Primary infertility Secondary infertility	7.74 11.68 6.72
Fuentes and Devoto (1994)	Chile	Cross-sectional	365	15 - 45	Self-reported infertility measure (Direct)	Women married for one year failing to achieve pregnancy after one or more years of unprotected sexual intercourse	Women at risk of pregnancy in their first year of marriage (i.e., having unprotected intercourse).	Period	12	Infertility (prevalence)	10.14 (9.15 - 11.05)
			270			Women married for eight years failing to achieve pregnancy after one or more years of unprotected sexual intercourse	Women at risk of pregnancy in their eighth year of marriage (i.e., having unprotected intercourse).	Period	12	Infertility (prevalence) Primary infertility Secondary infertility	7.04 3.33 (2.74 - 3.72) 3.71 (3.28 - 4.14)
			474			Women married for one year failing to achieve pregnancy after one or more years of unprotected sexual intercourse	Married women	Period	12	Infertility (frequency)	7.8
						Women married for eight years failing to achieve pregnancy after one or more years of unprotected sexual intercourse	Married women	Period	12	Infertility (frequency)	4.01

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
						Women suffering from infertility at some point in their lives disregarding whether they are currently infertile or not	Married women	Lifetime	12	Infertility	25.74 (+/- 3.9)
Priestley (2012)	Jamaica	Cross-sectional	8 180	15 - 49	Constructed infertility measure (Indirect)	Sexually experienced non-contracepting women who are non-surgically sterile, subfecund (women who think pregnancy is difficult), or have a long interval without contraception (more than 24 months without the use of contraception)	Sexually experienced women	Period	24	Impaired fecundity Primary Secondary	31 12.2 36.1
Jacobson et al. (2018)	United States of America	Cross-sectional	1 014	22 - 45	Retrospective Time-to-Pregnancy (TTP) Design	Women who did not get pregnant after 6/12/24 months of regular (>3 times per month) unprotected sex	Women who were at risk of becoming pregnant	Lifetime	6 12 24	Infertility	42.6 35.3 23.5
						Women who did not get pregnant after 6/12/24 months of regular (>3 times per month) unprotected sex while actively trying to become pregnant	Women who were at risk of becoming pregnant	Lifetime	6 12 24	Infertility	25.5 19.7 11.2
						Women who did not get pregnant after 12 months of regular (>3 times per month) unprotected intercourse for those <35 years old or after 6 months for those ≥35 years old	Women who were at risk of becoming pregnant	Lifetime	12 (6 ≥35yrs)	Infertility	35.9
						Women who did not get pregnant after 12 months of regular (>3 times per month) unprotected intercourse for those <35 years old or after 6 months for those ≥35 years old while actively trying to become pregnant	Women who were at risk of becoming pregnant	Lifetime	12 (6 ≥35yrs)	Infertility	20.5

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Crawford et al. (2015)	United States of America	Cross-sectional	Florida: 1 285 MA: 1 302 Michigan: 3 360	18 - 50	Self-reported infertility measure (Direct)	Those who ever tried to get pregnant for a year or longer and were unable to do so	All adults	Lifetime	12	Infertility Florida Massachusetts Michigan	 9.7 (7.6–11.8) 6.0 (4.6–7.5) 4.2 (3.5–5.0)
			Florida: 736 MA: 1 246 Michigan: 2 742			Those who ever tried to get pregnant for a year or longer and were unable to do so	All adults who ever tried to get pregnant	Lifetime	12	Florida Massachusetts Michigan	25.3 9.9 5.8
Thoma et al. (2013)	United States of America	Cross-sectional	277	15-44	Current Duration Design	Women who want to become pregnant with a TTP greater than 12 months (estimated)	Women at risk of pregnancy at time of interview (not using a method of contraception nor pregnant but were sexually active at the time of interview AND responded "Yes" to the question ‘‘Is the reason you are not using a method of birth control now because you, yourself, want to become pregnant as soon as possible?’’)	Period	12	TTP > 12 months Primary	15.5 (8.6 - 27.5) 24.30 (12.4-43.5)
			222			Women who want to become pregnant with a TTP greater than 12 months (estimated)	Women at risk of pregnancy at time of interview (not using a method of contraception nor pregnant but were sexually active at the time of interview AND responded "Yes" to the question ‘‘Is the reason you are not using a method of birth control now because you, yourself, want to become pregnant as soon as possible?’’) AND did not report use of current infertility treatment	Period	12	TTP > 12 months Primary	12.6 (7.6-21.4) 18.3 (11.0-30.9)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
			3 812		Constructed infertility measure (Indirect)	Married or cohabiting respondents who had been in a continuous relationship for 12 months or more with no use of contraception, but sexually active every month for the past 12 months, and did not have a pregnancy	All married or cohabiting respondents	Period	12	Infertility Primary infertility Secondary infertility	7.0 (6.2 - 7.8) 13.2 (11.2 - 15.2) 5.3
			Not reported			Married or cohabiting respondents who had been in a continuous relationship for 12 months or more with no use of contraception, but sexually active every month for the past 12 months, and did not have a pregnancy AND did not report current use of infertility treatment	All married or cohabiting respondents who did not report current use of infertility treatment.	Period	12	Infertility Primary infertility	6.6 (5.8-7.5) 11.9 (9.9-13.9)
Louis et al. (2013)	United States of America	Cross-sectional	157	15-45	Current Duration Design	Men who are in a relationship and trying to become pregnant with a TTP > 12 months (estimated)	Men at risk of pregnancy at time of interview (sexually active in the past year with a female partner and currently trying to get pregnant)	Period	12	Infertility Primary infertility	12.0 (7.0 - 23.2) 14.0 (6.0 - 25.6)
			Not reported			Men who are in a relationship and trying to become pregnant with a TTP > 12 months (estimated)	Men at risk of pregnancy at time of interview (sexually active in the past year with a female partner and currently trying to get pregnant) and who reported not having sought infertility treatment during their current pregnancy attempt.	Period	12	Infertility	9.4 (5.2-17.2)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Chandra et al. (2013)	United States of America	Cross-sectional	61 755 (Weighted population size) 12 279 (unweighted sample size)	15-44	Hybrid* Primary: Self-reported infertility measure (Direct) Secondary: Constructed infertility measure (Indirect)	Women with impaired fecundity (i.e. non-surgically sterile (self or partner), subfecund (self or partner), and/or long interval (36 or more months) without conception)	All women	Period	No duration or 36	Impaired fecundity Primary infertility Secondary infertility	10.9 (SE = 0.4) 11.2 (SE = 0.7) 10.6 (SE = 0.6)
			25 605 (Weighted population size) 3 971 (unweighted sample size)			Women with impaired fecundity (i.e. non-surgically sterile (self or partner), subfecund (self or partner), and/or long interval (36 or more months) without conception)	Married women	Period	No duration or 36	Impaired fecundity Primary infertility Secondary infertility	12.1 (SE = 0.8) 21.2 (SE = 2.0) 9.9 (SE = 0.8)
			62 128 (Weighted population size)		Self-reported infertility measure (Direct)	Men who are nonsurgically sterile (self or partner) or subfertile	All men	Period	No duration	Infertility	9.4 (SE = 0.5)
			5 422 (unweighted sample size)		Constructed infertility measure (Indirect)	Women and their partner who, during the previous 12 months or longer, were continuously married, were sexually active each month, had not used contraception, and had not become pregnant.	Married women	Period	12	Infertility Primary infertility Secondary infertility	6.0 (SE = 0.5) 14.0 (SE = 1.6) 4.0 (SE = 0.5)
Boulet et al. (2016)	United States of America	Cross-sectional	8 691	18-50	Self-reported infertility measure (Direct)	Women who reported difficulty becoming or staying pregnant	All women	Lifetime	No duration	Perceived infertility	13.20 (11.3-15.2)
Nelson et al. (2011)	United States of America	Cross-sectional	291	35 - 47	Self-reported infertility measure (Direct)	Women who ever tried to get pregnant for over one year without being able to	All women	Lifetime	12	Infertility	20.0

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
McQuillan et al. (2003)	United States of America	Cross-sectional	580	25 - 50	Self-reported infertility measure (Direct)	Women who have (a) tried for longer than 12 months to conceive any of their pregnancies, (b) sought medical help to conceive any of their pregnancies, (c) ever tried to get pregnant for more than 12 months without success, and/or (d) ever had regular unprotected intercourse for more than a year without pregnancy.	All women	Lifetime	12	Subfecundity (medically defined infertility)	35.0
Weiss et al. (1998)	United States of America	Cross-sectional	1 989	Seattle and New Jersey: 20 - 44 Atlanta: 20 - 54	Self-reported infertility measure (Direct)	Women who report difficulty in either becoming pregnant or maintaining a pregnancy.	All women	Lifetime	No duration	Infertility Primary infertility	19.0 31.0
Merritt et al. (2013)	United States of America	Case-control	2 100	Not reported	Self-reported infertility measure (Direct)	Women who had tried to become pregnant without success or had seen a doctor about having difficulties in getting pregnant or carrying a pregnancy to term.	All women (control group)	Lifetime	No duration	Infertility	20.8
Jacob et al. (2007)	United States of America	Cross-sectional	580	25 - 50	Self-reported infertility measure (Direct)	Women who experienced 12 months of regular unprotected intercourse without conception at some time in their lives	All women	Lifetime	12	Infertility	28.0
Gleason et al. (2020)	United States of America	Cohort	1 652	29 - 35	Self-reported infertility measure (Direct)	Women who reported regular sexual intercourse over at least 12 months without the use of contraception and without conceiving a child and ever tried to get pregnant	Women who ever tried to get pregnant	Lifetime	12	Infertility	24.1
Anyalechi et al. (2019)	United States of America	Cross-sectional	2 628	18-49	Self-reported infertility measure (Direct)	Women who had ever had sexual intercourse with a male partner and attempted to get pregnant for 12 months without becoming pregnant	Women who ever had intercourse with a male partner	Lifetime	12	Infertility	13.80 (12.3-15.3)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Cairncross et al. (2020)	United States of America	Cross-sectional	2 809	42 - 52	Self-reported infertility measure (Direct)	Women unable to achieve a clinical pregnancy for a period of > 12 months of trying to conceive or who used fertility medications for > 1 month	Women who had ever attempted to conceive	Lifetime	12 or fertility medication for > 1 month	Infertility	24.7
SOUTH-EAST ASIA REGION											
Zargar et al. (1997)	India	Cross-sectional	10 063	15 - 44	Self-reported infertility measure (Direct)	Couples who conceived more than one year after marriage or had not yet conceived at the time of the survey despite unprotected sexual intercourse for more than one year after marriage	Couples married for one year or more	Period	12	Primary Infertility	15.07
						Couples who had not yet conceived at the time of the survey despite unprotected sexual intercourse for more than one year after marriage	Couples married for one year or more	Period	12	Unresolved Primary Infertility	4.66
Unisa (1999)	India	Cross-sectional	Not reported	20 - 49	Constructed infertility measure (Indirect)	Women who have been married for three or more years without a live birth	Women who have been married for three or more years	Period	36	Childlessness (3 or more years)	5.0
Katole and Saoji (2019)	India	Cross-sectional	570	15 - 49	Self-reported infertility measure (Direct)	Women at risk of becoming pregnant (not pregnant, sexually active, not using contraception, and not lactating) who report trying unsuccessfully for a pregnancy for 2 years or more	All married women	Period	24	Primary infertility	8.9
Udgiri and Patil (2019)	India	Cross-sectional	693 (Rural) 419 (Urban)	20 - 49	Self-reported infertility measure (Direct)	Women at risk of becoming pregnant who report trying unsuccessfully for a pregnancy for 2 years or more	Women at risk of becoming pregnant	Period	24	Infertility Rural Urban Primary infertility Rural Urban Secondary infertility Rural Urban	 7.6 8.8 5.3 5.7 2.3 3.1

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Singh and Shukla (2015)	India	Cross-sectional	44 415	20 - 34	Self-reported infertility measure (Direct)	Women who ever had a problem getting pregnant despite cohabitation and exposure to pregnancy for two or more years	All women married for at least two years	Lifetime	24	Infertility Primary infertility	10.7 8.4
						Women who never had a live birth up to the interview date, and reported problems conceiving for the first time (failure to conceive despite two years of cohabitation and exposure to pregnancy)	All women married for at least two years	Period	24	Primary infertility	2.6
			21 583			Women who never had a live birth up to the interview date, and reported problems conceiving for the first time (failure to conceive despite two years of cohabitation and exposure to pregnancy)	Women married for at least two years and not using contraception	Period	24	Primary infertility	2.3
Purkayastha (2020)	India	Cross-sectional	499 627	15 - 49	Constructed infertility measure (Indirect)	Currently married women who are married for five years or more, not currently pregnant, never used contraceptives, have no terminated pregnancies, and have zero children ever born	Currently married women	Period	60	Primary infertility	1.79
Chauhan et al. (2015)	India	Cross-sectional	1 167	15+	Undetermined	Women who failed to conceive following a previous pregnancy or abortion despite cohabitation and exposure to pregnancy in absence of contraception for one or more years	Ever married women	Period	12	Secondary infertility	1.7
Samarakoon et al. (2007)	Sri Lanka	Cross-sectional	2 000	Women: 15 - 48 Men: 17 - 53	Undetermined	Women who have never conceived in spite of cohabitation and exposure to pregnancy for a period of 12 months	All married women	Period	12	Primary infertility	4.05 (3.2 - 4.9)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
			1 907			Women who have previously conceived but have been unable to conceive subsequently despite cohabitation and exposure to pregnancy for a period of 24 months (exposure to pregnancy was from the end of the period of lactation amenorrhea for women who breast fed the previous infant).	All married women who have had a pregnancy	Period	24	Secondary infertility	16 (14.39 - 17.60)
EUROPEAN REGION											
Bach et al. (2015)	Denmark	Cross-sectional	1 372	Not reported	Retrospective Time-to-Pregnancy (TTP) Design	Nulliparous women with a TTP greater than 12 months or infertility treatment prior to the studied pregnancy	Nulliparous women who planned or partly planned their pregnancy and gave birth to a singleton	Period	12	Primary infertility	21
Guldbrandsen et al. (2014)	Denmark	Cohort	73 107	Not reported	Retrospective Time-to-Pregnancy (TTP) Design	Pregnant women with planned pregnancies and a TTP greater than 6/12 months	Pregnant women with a planned pregnancy	Period	6 12	Subfecundity	32.0 16.0
Hollegaard et al. (2007)	Denmark	Cross-sectional	2 927	18 +	Retrospective Time-to-Pregnancy (TTP) Design	Pregnant women with a TTP greater than 12 months	Pregnant women	Period	12	Subfertility	17.3
Kjaer Pedersen et al (1994) Translation	Denmark	Case-control	247	18 - 49	Undetermined	Women who failed to conceive after trying for more than 12 months	All women (controls)	Lifetime	12	Infertility	12.0 (8.0 - 17.0)
			182			Women who failed to conceive after trying for more than 12 months	Women who had attempted and/or achieved pregnancy (controls)	Lifetime	12	Infertility	17.0 (12.0 - 23.0)
Hærvig et al (2018)	Denmark	Cross-sectional	2 140	50 - 51	Self-reported infertility measure (Direct)	Men who ever tried to achieve a pregnancy, without success during the first 12 months	All men	Lifetime	12	Infertility	17.9

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Kirkegaard et al. (2014)	Denmark	Cross-sectional	9 507	Not reported	Retrospective Time-to-Pregnancy (TTP) Design	Women with spontaneous planned pregnancy with TTP of 12/24 or more months	Women with spontaneous planned pregnancies	Period	12 24	Subfertility	9.9 3.1
Raatikainen et al. (2010)	Finland	Cross-sectional	17 114	Not reported	Retrospective Time-to-Pregnancy (TTP) Design	Pregnant women who reported a TTP > 36 months	Pregnant women not using contraception at the time of pregnancy	Period	36	TTP >36 months	2.2
Terävä et al. (2008)	Finland	Cross-sectional	4 371	25 - 64	Self-reported infertility measure (Direct)	Women who experienced a time period when they had tried to become pregnant, but had not conceived or conception took more than 12 months	All women	Lifetime	12	Subfertility	16.0
Klemetti et al (2010)	Finland	Cross-sectional	Women: 1198 Men: 1093	30 - 44	Self-reported infertility measure (Direct)	Women/men who made unsuccessful attempts to conceive a child over a period of 12 months or longer	All women/men	Lifetime	12	Infertility - women Men	20.0 9.0
Taponen et al. (2004)	Finland	Case-control	60	31	Self-reported infertility measure (Direct)	Women who reported that Infertility has ever (earlier or at this moment) been a problem	Women not using oral contraceptives or IUD devices (control group)	Lifetime	No duration	Infertility	10.0
Slama et al. (2006)	France	Cross-sectional	69	18-44	Current Duration Design	Couples not yet pregnant after 12/24 months of unprotected intercourse (estimated)	Women at risk of pregnancy (18 to 44 years at interview, declared not to be pregnant, currently had a male partner, had had sexual intercourse within the last 2 months, did not use any birth control method (including sterilization of either partner), and had not given birth to a live- or stillborn baby in the 3 months before the interview)	Period	12 24	TTP > 12 months TTP > 24 months	34.0 (15.0 - 54.0) 16.0 (4.0 - 29.0)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
			53			Estimated proportion of couples not yet pregnant after 6/12/24 months who were trying to become pregnant	Women at risk of pregnancy (as defined above) and reported they were currently willing to become pregnant or that they had stopped contraception to become pregnant, even if they declared that they did not desire to become pregnant currently	Period	6 12 24	TTP > 6 months TTP > 12 months TTP > 24 months	47.0 (28.0 - 66.0) 26.0(10.0 - 42.0) 10.0 (2.0 - 18.0)
Slama et al. (2012)	France	Cross-sectional	867 (overall) 360 (primary)	18-44	Current Duration Design	Couples with no detected pregnancy during the first 6/12/24 months of unprotected intercourse (estimated)	Women at risk of pregnancy defined as not using any birth control method, had a male partner and had been sexually active in the previous month.	Period	6 12 24	Infertility Primary infertility Infertility Primary infertility Infertility Primary infertility	46.0 (36.0-35.0) 47.0 (26.0 - 68.0) 24.0 (19.0 - 30.0) 26.0 (15.0 - 36.0) 11.0 (8.0 - 14.0) 11.0 (7.0 - 16.0)
						Couples who declared that they had stopped using birth control methods in order to obtain a pregnancy and had no detected pregnancy conceived during the first 6/12/24 months of unprotected intercourse (estimated)	Women at risk of pregnancy defined as not using any birth control method, had a male partner and had been sexually active in the previous month AND declared that they had stopped using birth control methods in order to obtain a pregnancy	Period	6 12 24	Infertility	45.0 (34.0 - 55.0) 23.0 (18.0 - 28.0) 10.0 (8.0- 12.0)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
						Couples who declared that they had stopped using birth control methods in order to obtain a pregnancy and had no detected pregnancy conceived during the first 6/12/24 months of unprotected intercourse (estimated)	Women at risk of pregnancy defined as not using any birth control method, had a male partner and had been sexually active in the previous month AND declared that they had stopped using birth control methods in order to obtain a pregnancy AND who did not use infertility treatments over the CDUI period	Period	6 12 24	Infertility	43.0 (34.0 - 53.0) 20.0 (16.0 - 25.0) 8.0 (6.0 - 10.0)
Eustache et al. (2004)	France	Cross-sectional	390	Male partner: 20–45	Retrospective Time-to-Pregnancy (TTP) Design	Pregnant couples who took more than 12 months to conceive and whose male partner did not provide a semen sample	Pregnant couples whose male partner did not provide a semen sample	Period	12	TTP > 12 months	5.0 (3.2–7.3)
Muller et al. (2006)	France	Cross-sectional	Total: 894 Range: 178 - 273	Men: 20 - 45	Retrospective Time-to-Pregnancy (TTP) Design	Pregnant women with a TTP greater than 12 months	Pregnant women not using contraception at the start of pregnancy	Period	12	TTP > 12 mo: Range	5.0 - 11.0
Ajrouche et al (2014)	France	Case-control	1 167	Not reported	Self-reported infertility measure (Direct)	Women who took more than a year to conceive the index child and/or needed to consult a doctor and/or needed for the mother or father to undergo fertility treatment	Women with a child (control group)	Period	12	Difficulty becoming pregnant	18.0
Kuppers-Chinnow and Karmaus (1997) Translation	Germany	Cross-sectional	1 216	25 - 45	Retrospective Time-to-Pregnancy (TTP) Design	Women who have ever in their lifetime experienced a time of unprotected intercourse (TUI) (with or without the onset of pregnancy) of more than 12 months	Women who have ever been at risk of becoming pregnant (i.e., had unprotected sexual intercourse)	Lifetime	12	Subfecundity	31.8 (29.4 - 34.6)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Datta et al. (2016)	United Kingdom	Cross-sectional	Women: Unweighted: 8 066 Weighted: 7 052 Men: Unweighted: 5 553 Weighted: 6 811	16 - 74	Self-reported infertility measure (Direct)	Women/men who ever had a time, lasting 12 months or longer, when they and their partner were trying for a pregnancy, but it didn't happen	All women/men who reported having experience of heterosexual sex	Lifetime	12	Infertility - women Men	12.5 (11.7–13.3) 10.1 (9.2–11.1)
Joffe (2000)	United Kingdom	Cross-sectional	1 540	16-59	Retrospective Time-to-Pregnancy (TTP) Design	Individuals with time to pregnancy greater than 12 months for first pregnancy	All individuals whose first pregnancy was a birth and was not due to a contraceptive failure	Period	12	TTP >12 months (Primary)	15.0
Gyorffy et al. (2014)	Hungary	Cross-sectional	1 069	24+	Self-reported infertility measure (Direct)	Participants whose time-to-pregnancy had been longer than one year in case of any of their pregnancies.	All women (control group)	Lifetime	12	TTP > 12 months	9.8
Van der Avoort et al. (2003)	Netherlands (Kingdom of the)	Cross-sectional	243	25 - 40	Self-reported infertility measure (Direct)	Male respondents who reported a lack of conception after at least 12 months of unprotected intercourse	All men	Period	12	Subfertility	8.6
			137			Male respondents who reported a lack of conception after at least 12 months of unprotected intercourse	Men at risk for fertility problems	Period	12	Subfertility	15.3
Hoenderboom et al. (2020)	Netherlands (Kingdom of the)	Cohort	2 377	16 - 39	Retrospective Time-to-Pregnancy (TTP) Design	Women with an attempted time to first pregnancy of > 12 months	Women who had ever attempted to conceive	Period	12	Primary infertility (Time to first planned pregnancy)	16.7
Sundby and Schei (1996)	Norway	Cross-sectional	4 034	40 - 42	Self-reported infertility measure (Direct)	Women who tried to become pregnant for more than a year without succeeding	All Women	Lifetime	12	Infertility	10.3
						Women who tried to become pregnant for more than a year without succeeding and had never given birth to a child	Married women not using contraception, postmenarchal and premenopausal	Lifetime	12	Permanent Infertility	2.6

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
						Women who tried to become pregnant for more than a year without succeeding and had given birth to at least one child	Married women not using contraception, postmenarchal and premenopausal	Lifetime	12	Subfertility	7.7
Rostad et al. (2013)	Norway	Cross-sectional	4 951	50 - 59	Self-reported infertility measure (Direct)	Women who have ever tried for more than a year to get pregnant regardless of any subsequent birth	All women	Lifetime	12	Infertility	12.7
Nguyen et al. (2007)	Norway	Cross-sectional	26 303	18 - 39	Retrospective Time-to-Pregnancy (TTP) Design	Couples who planned their pregnancy and that took more than 12 months to achieve pregnancy or received infertility treatment	Couples who planned their pregnancy	Period	12	Infertility	12.0
Magnus et al. (2021)	Norway	Cohort	64 064	27 - 62	Hybrid* Primary Retrospective Time-to-Pregnancy (TTP) Design Secondary: Self-reported infertility measure (Direct)	Women with a planned pregnancy and a TTP > 12 or reported use of assisted reproductive technologies	Women who had a planned pregnancy	Period	12	Time to pregnancy	12.3
Soares et al. (2011) Translation	Portugal	Cross-sectional	1 540	18+	Self-reported infertility measure (Direct)	Women who reported ever trying to get pregnant for more than a year without success	All women	Lifetime	12	Infertility	11.9 (10.4-13.7)
Philippov et al. (1998)	Russian Federation	Cross-sectional	2 000	18 - 45	Undetermined	Women who had not conceived after 12 months or more of unprotected intercourse	Married women	Lifetime	12	Infertility Primary infertility Secondary infertility	16.7 3.8 12.9
Bhattacharya et al. (2009)	United Kingdom	Cross-sectional	4 066 (12-month) 4 049 (24-month)	31-50	Self-reported infertility measure (Direct)	Women who had unsuccessfully attempted conception for 12/24 months or longer	Women whose fertility had been tested	Lifetime	12	Infertility Primary infertility Secondary infertility Experienced both	17.5 (16.3–18.6) 10.5 (9.5–11.4) 5.3 (4.7–6.0) 1.7 (1.3–2.0)
									24	Infertility Primary infertility Secondary infertility Experienced both	9.1 (8.2–10.0) 5.9 (5.2–6.6) 2.9 (2.4–3.4) 0.3 (0.2–0.5)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
						Women who had unsuccessfully attempted conception for 12/24 months or longer and/or had sought medical help with conception	Women whose fertility had been tested	Lifetime	12	Infertility Primary infertility Secondary infertility Experienced both	19.3 (18.1–20.5) 9.8 (8.9–10.7) 7.0 (6.2–7.8) 2.5 (2.0–2.9)
									24	Infertility Primary infertility Secondary infertility Experienced both	11.8 (10.8–12.8) 5.7 (5.0–6.4) 5.2 (4.5–5.9) 0.9 (0.6–1.1)
Cabrera-Leon et al. (2015)	Spain	Cross-sectional	443	30 - 49	Retrospective Time-to-Pregnancy (TTP) Design	Women who did not achieve pregnancy after having had sexual intercourse with vaginal penetration and no contraception for one year or more.	All women	Lifetime	12	Infertility Huelva City Spain Primary infertility Huelva City Spain Secondary infertility Huelva City Spain	 17.79 17.58 (17.57–17.59) 6.14 6.12 (6.12–6.12) 11.64 11.33 (11.32–11.37)
						Women with biological children who spent more than 6/12/24 months trying to become pregnant with any of their biological children	All women	Lifetime	6 12 24	Subfertility Huelva City Spain Huelva City Spain Huelva City Spain	 21.00 19.98 (19.97–20.0) 11.62 11.21 (11.2–11.22) 4.59 4.36 (4.35–4.37)
					Self-reported infertility measure (Direct)	Women who perceived having or having had difficulty in getting pregnant	All women	Lifetime	No duration	Subjective Infertility: Huelva City Spain	 9.41 8.22 (8.21–8.23)
Akre et al. (1999)	Sweden	Cross-sectional	401 653	20 +	Retrospective Time-to-Pregnancy (TTP) Design	Primiparous women who did not become pregnant after more than one year	Primiparous women	Period	12	Primary subfertility	8.3
Wulff et al. (1997)	Sweden	Cross-sectional	534	25-44	Self-reported infertility measure (Direct)	Women who experienced a period of infertility (inability to conceive within 12 months of unprotected intercourse) at some point in life	All women	Lifetime	12	Infertility ever	24.3

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
						Couples who were unable to get pregnant (again) after having tried for 12 months	All women	Period	12	Primary infertility Secondary infertility	6.2 2.8
Hallen (2011)	Sweden	Cross-sectional	201	18 - 55	Self-reported infertility measure (Direct)	Men reporting a period of 1 or more years of involuntary childlessness during the last five years	All men (control group)	Period	12	Involuntary childlessness	7.0 (3.4–10.5)
Björvang et al (2020)	Sweden	Cross-sectional	818	Not reported	Retrospective Time-to-Pregnancy (TTP) Design	Women with planned pregnancies who had a TTP greater than 12 months	Pregnant women with planned pregnancies	Period	12	Infertility	9.7
Brunetti et al. (1994) Translation	Switzerland	Cross-sectional	216	29	Retrospective Time-to-Pregnancy (TTP) Design	Women exposed to fertilisation (i.e. women wishing to have children, with a stable partner and a regular sex life) for 24 or more months who have never conceived by the age of 29	Women exposed to fertilisation before their 28th birthday (i.e. women wishing to have children, with a stable partner, a regular sex life, and presence of 24 months of unprotectedness)	Lifetime	24	Primary infertility (unresolved)	2.8
			212			Women aged 29 who waited at least once for more than a year before obtaining a conception	Women who have conceived	Lifetime	12	Unintentionally delayed motherhood (hypofertility; resolved subfertility)	10.0
Gokler et al. (2014)	Türkiye	Cross-sectional	570	18 - 49	Self-reported infertility measure (Direct)	Women who have the inability to become pregnant despite regular sexual intercourse during the last year	All married women	Period	12	Infertility Primary (% of total) Secondary (% of total)	12.8 38.4 61.6
Sarac and Koc (2018)	Türkiye	Cross-sectional	5 947	15 - 49	Constructed infertility measure (Indirect)	Women who have been married for at least five years, have not used any birth control methods during that time, and have not given birth	Women who have been married for at least five years	Period	60	Primary infertility	1.8

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
			6 835			Women who have been married for at least one year, have not used any contraception during the last year and who have not become pregnant in the last year	Women who have been married for at least one year	Period	12	Infertility	8.1
			5 860	18 - 44		Women who were at risk of pregnancy in the first 12 months of the total 5-year period	Women who are at risk of exposure to pregnancy	Period	12	Infertility	8.6
Albayrak and Günay (2007)	Türkiye	Cross-sectional	2 400	15 - 49	Undetermined	Women who had never been able to conceive, although they had been married at least 12 months, were living with their husband and had a desire for a baby	Married women	Period	12	Primary infertility (Childless women)	6.3
Gunnell and Ewings (1994)	United Kingdom	Cross-sectional	2 377	36 - 50	Retrospective Time-to-Pregnancy (TTP) Design	Women who failed to become pregnant after 12/24 months of regular unprotected intercourse	All women	Lifetime	12	Infertility Primary infertility Secondary infertility	26.4 (24.6 - 28.2) 16.1 (14.6 - 17.6) 15.8 (14.3 - 17.3)
									24	Infertility Primary infertility Secondary infertility	12.9 7.4 6.6
						Women with primary unresolved infertility and women who became pregnant but remained involuntarily childless	All women	Lifetime	12	Involuntary Childlessness	3.0
Buckett and Bentick (1997)	United Kingdom	Cross-sectional	728	45 - 55	Retrospective Time-to-Pregnancy (TTP) Design	Women who tried to conceive for more than 12/24 months	All women	Lifetime	12	Infertility Primary infertility Secondary infertility	17.3 (14.6 - 20.0) 10.6 (8.4-12.8) 6.7 (4.9 - 8.5)
									24	Infertility	12 (9.6 - 14.4)
						Women with primary or secondary infertility who never conceived	All women	Lifetime	12	Unresolved involuntary infertility	4.3 (2.8 - 5.8)
Oakley et al. (2010)	United Kingdom	Cross-sectional	7 702	18-55	Self-reported infertility measure (Direct)	Women who reported having problems getting pregnant	Women who had become pregnant or ever tried to get pregnant	Lifetime	No duration	Self-reported infertility	19.5 (18.6-20.4)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
						Women with at least 1 planned pregnancy with a TTP > 12 months	Women who had become pregnant or ever tried to get pregnant and reported the pregnancy was planned	Lifetime	12	TTP > 12 months	16.0 (15.1-16.9)
			6 584	40 - 55		Women with no pregnancy despite trying	Women who had become pregnant or ever tried to get pregnant	Lifetime	No duration	Primary unresolved infertility	2.4 (2.0-2.8)
						Women with no live birth despite trying	Women who had become pregnant or ever tried to get pregnant	Lifetime	No duration	Primary unresolved infertility	4.3 (3.8-4.8)
Bolumar et al. (1997)	Denmark, Germany, Italy, Poland, and Spain	Cross-sectional	3 187	25 - 44	Retrospective Time-to-Pregnancy (TTP) Design	Women who had planned their pregnancies and reported a TTP greater than 12 months for their first pregnancy	Women who had stopped using birth control and had planned their pregnancy	Period	12	Primary infertility	12.0
Karmaus and Juul (1999)	Denmark, Germany, Italy, Poland, and Spain	Cross-sectional	932	25 - 44	Retrospective Time-to-Pregnancy (TTP) Design	Women with a time of unprotected intercourse (TUI) greater than 12/24 months for first TUI with a starting date less than 5 years before the interview	Time of unprotected intercourse (TUI) for first TUI with a starting date less than 5 years before the interview, among women at risk	Period	12 24	Primary Subfecundity: Total Range Total Range	 23.4 14.8 - 33.3 17.6 10.1 - 26.8
						Women planning their pregnancies with a time of unprotected intercourse (TUI) greater than 12/24 months for first TUI with a starting date less than 5 years before the interview	Time of unprotected intercourse (TUI) for first TUI with a starting date less than 5 years before the interview, among women at risk and planning pregnancy	Period	 12 24	Primary Subfecundity: Total Range Total Range	 18.7 12.1 - 30.2 13.6 8.1 - 24.1
Toft et al. (2005)	Greenland, Poland and Ukraine	Cross-sectional	Warsaw: 376 Kharkiv: 307 Greenland: 520	18+ (Greenland) Not reported for other sites	Retrospective Time-to-Pregnancy (TTP) Design	Married women with a TTP greater than 12 months	Married women not using contraception	Period	12	TTP > 12 months Warsaw Kharkiv Greenland	 19.0 27.0 15.0

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Jensen et al. (2001)	Denmark, Finland, France, and United Kingdom	Cross-sectional	Range: 191 - 302	Male partner: 20–45	Retrospective Time-to-Pregnancy (TTP) Design	Pregnant couples who took more than 6/12 months to conceive and whose male partner provided a semen sample	Pregnant couples whose male partner provided a semen sample	Period	6 12	TTP > 6/12 mo: Range	16.9 - 20.9 7.5 - 10.1
EASTERN MEDITERRANEAN REGION											
Hassan (1997)	Egypt	Cross-sectional	20 002	< 50 years	Constructed infertility measure (Indirect)	Women who have been exposed to or at risk of pregnancy for successive 12 months or more without conceiving	Married women	Period	12	Infertility Primary infertility Secondary infertility	12.0 4.3 7.7
Kazemijaliseh et al. (2015)	Iran (Islamic Republic of)	Cross-sectional	1067	18 - 57	Retrospective Time-to-Pregnancy (TTP) Design	Women failing to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse	Married women willing to become pregnant	Lifetime	12	Primary infertility	17.3
Nasrabad et al. (2013)	Iran (Islamic Republic of)	Cross-sectional	90 141	15 - 49	Constructed infertility measure (Indirect)	Couples of reproductive age who are having sexual intercourse without contraception and are unable to establish a pregnancy within one year	Ever-married women	Period	12	Primary infertility	2.3
						Sexually active women who are not using a contraception but are unable to have a live birth for five or more years	Ever-married women	Period	60	Primary infertility	2.6
Esmaeilzadeh et al. (2012)	Iran (Islamic Republic of)	Cross-sectional	1 081	20 - 45	Self-reported infertility measure (Direct)	Women who have experienced a delay in conception for least 12 months of unprotected intercourse at some time in their life	Women who attempted conception	Lifetime	12	Infertility Primary infertility Secondary infertility Experienced both	15.5 (13.5 - 17.5) 12.2 1.9 1.5
						Women who were currently experiencing a delay in conception for least 12 months of unprotected intercourse and had not previously given birth to a child	Women who attempted conception	Period	12	Primary Infertility	4.3 (2.3 - 6.3)

Infertility prevalence estimates, 1990–2021

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Mirzaei et al. (2018)	Iran (Islamic Republic of)	Cross-sectional	2 611	20 - 49	Self-reported infertility measure (Direct)	Women who have failed to achieve clinical pregnancy after 12 months or more unprotected coitus	All married, divorced, or widowed women	Period	12	Infertility Primary infertility Secondary infertility	5.2(4.3 - 6.1) 2.68 (2.4 - 3.8) 2.15 (1.89 - 3.4)
Safarinejad (2008)	Iran (Islamic Republic of)	Cross-sectional	11 441	15-50	Undetermined	Women who did not conceive despite cohabitation and exposure to pregnancy for two years	Women who ever cohabitated for at least two years	Lifetime	24	Infertility Primary infertility Secondary infertility	8.0 (3.2 - 15.0) 4.6 (3.6 - 5.2) 3.4 (2.4 - 5.1)
Vahidi et al. (2009)	Iran (Islamic Republic of)	Cross-sectional	10 662	19-49	Constructed infertility measure (Indirect)	Ever-married women who have experienced of infertility (no pregnancy) despite one year of unprotected intercourse	Ever-married women	Lifetime	12	Primary infertility	24.9 (23.5-26.2)
			10 873			Women who meet the definition of lifetime primary infertility and have not conceived up to the study time	Ever-married women	Period	12	Primary infertility	3.4 (3.0-3.8.0)
Ahmadi Asr Badr et al. (2006)	Iran (Islamic Republic of)	Cross-sectional	3 183	Not reported	Retrospective Time-to-Pregnancy (TTP) Design	Women with no conception during marriage after at least 12 months' period of intercourse without using contraception	Women married for at least one year	Lifetime	12	Infertility Primary infertility Secondary infertility	3.27 2.04 1.23
			2 623	15-49		Women with no conception during marriage after at least 12 months' period of intercourse without using contraception	Women ages 15 - 49 years married for at least one year	Lifetime	12	Infertility Primary infertility Secondary infertility	3.35 2.05 1.30
Akhondi et al. (2019)	Iran (Islamic Republic of)	Cross-sectional	17 178	20-40	Constructed infertility measure (Indirect)	Women who are sexually active, do not use any contraception, and do not have a live birth after 12/24/36/48/60 months	Married women	Lifetime	12 24 36 48 60	Primary infertility	20.2 (SE = 0.2) 12.5 10.3 9.6 9.20
Dovom et al. (2014)	Iran (Islamic Republic of)	Cross-sectional	888	18 - 49	Retrospective Time-to-Pregnancy (TTP) Design	Women who have not become pregnant after at least 1 year of unprotected intercourse	Women who had attempted to get pregnant for at least one year, not use a contraceptive method, and have regular unprotected sexual intercourse	Period	12	Primary Infertility	6.4 (4.8 - 8.0)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
			681			Women who failed to achieve a second clinical pregnancy after 12 months or more of regular unprotected sexual intercourse whether or not having the second child	Women who had attempted to get pregnant for the second time for at least one year, not use a contraceptive method, and have regular unprotected sexual intercourse	Lifetime	12	Secondary Infertility	7.8 (6.0 - 9.6)
			888			Women with any delay of more than one year to get pregnant during their life regardless of whether or not they have a child now	Women married for at least one year who have ever had a willingness for pregnancy	Lifetime	12	Infertility	21.2 (18.4 - 23.8)
Hosseini et al. (2012)	Iran (Islamic Republic of)	Cross-sectional	2 296	18 - 49	Self-reported infertility measure (Direct)	Couples with lack of pregnancy after one year of continuous unprotected sex during the ovulation point of menstrual cycle	Married women at risk of pregnancy	Period	12	Primary infertility Secondary infertility	3.2 1.7
Sharif et al. (2020)	Iran (Islamic Republic of)	Cross-sectional	1 469	18 - 45	Self-reported infertility measure (Direct)	Couples who had not achieved pregnancy in the past 12 months	All women of childbearing age and in union	Period	12	Infertility	15.24 (14.7-15.4)
WESTERN PACIFIC REGION											
Herbert et al. (2009a)	Australia	Cohort	13 715	45 - 50	Self-reported infertility measure (Direct)	Women who have tried unsuccessfully to get pregnant for 12 months or more, have been diagnosed as infertile by a doctor (self or partner), and/or had treatment for infertility in lifetime (self or partner)	Women born between 1946 - 1951	Lifetime	12	Infertility	11.0
Herbert et al. (2009b)	Australia	Cohort	1 031	28 - 33	Self-reported infertility measure (Direct)	Women who had tried to conceive for 12 or more months unsuccessfully	Women who had tried to conceive or had been pregnant	Lifetime	12	Infertility	17.3
Mena et al. (2020)	Australia	Cohort	6 130	Time 1: 22 - 27 Final time: 37 - 42	Self-reported infertility measure (Direct)	Women who reported ever having problems with infertility (tried unsuccessfully to get pregnant for 12 months or more) with a current or previous partner	Women who ever tried to get pregnant	Period	12	Infertility (Cumulative incidence)	15.4 (14.5 - 16.4)

Infertility prevalence estimates, 1990–2021

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Damone et al. (2019)	Australia	Cross-sectional	8 612	28 - 33	Self-reported infertility measure (Direct)	Couples who ever had problems with fertility (tried unsuccessfully for 12 months or more to get pregnant)	All women in union (currently or previously)	Lifetime	12	Infertility	11.1
Zhou et al. (2018)	China	Cross-sectional	17 275	20 - 49	Retrospective Time-to-Pregnancy (TTP) Design	Women who wanted to become pregnant in the previous year, who had unprotected sexual intercourse at least once a month, and who were trying to achieve pregnancy longer than 12 months	Women exposed to the risk of pregnancy (not using contraception and had not lived separated longer than three months)	Period	12	Infertility Primary infertility Secondary infertility	15.5 9.5 6
			10 742			Women who wanted to become pregnant in the previous year, who had unprotected sexual intercourse at least once a month, and who were trying to achieve pregnancy longer than 12 months	Women attempting to become pregnant (not using contraception, had not lived separated longer than three months, and willing to become pregnant)	Period	12	Infertility Primary infertility Secondary infertility	25 15.3 9.7
Xingping et al. (2006) Translation	China	Cross-sectional	5 325 844	< 49	Undetermined	Women who failed to achieve pregnancy after one year of regular sexual intercourse without contraception	Married women of childbearing age	Period	12	Infertility Primary (% of total) Secondary (% of total)	1.57 82.4 17.6
Zhang et al. (2014)	China	Cross-sectional	12 342	27 - 57	Self-reported infertility measure (Direct)	Married couples who failed to achieve a clinical pregnancy after 12 months of regular unprotected sexual intercourse	All married couples who had regular unprotected intercourse for at least 12 months prior to the date of interview	Period	12	Infertility Primary infertility Secondary infertility	4.2 3.1 1.1
Yang et al. (2011) Translation	China	Cross-sectional	5 631	20 - 49	Undetermined	Couples who had a desire to have children, had normal cohabitation for two years, had regular sexual intercourse, and were not pregnant without contraception	All couples	Period	24	Infertility Primary (% of total) Secondary (% of total)	1.72 58.76 41.24
Wu et al. (2004) Translation	China	Cross-sectional	274	Reproductive age	Undetermined	Married women who did not use contraception within two years after marriage and did not become pregnant	Married women	Period	24	Infertility	1.1

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Cai et al. (2011) Translation	China	Cross-sectional	1 835	20 - 49	Self-reported infertility measure (Direct)	Married women with an absence of pregnancy after 1 year of normal sexual intercourse without the use of contraception under the conditions of exposure to pregnancy	Married women	Period	12	Infertility Primary infertility Secondary infertility	15.2 7.5 7.7
Zhang and Zhang (2013) Translation	China	Cross-sectional	2 187	20-49	Undetermined	Couples who had a desire to have children, normal sexual activity for more than one year and have not used contraception, but still fail to conceive	Married women willing to have a child and not using contraception during a specified one-year period	Period	12	Primary Infertility Secondary infertility	13.08 35.25
Song (2013)	China	Cross-sectional	3 110	37 - 38	Retrospective Time-to-Pregnancy (TTP) Design	Women with no child after 24/84 months of marriage	All married women	Period	24 84	Sterility	14.24 1.67
Wang et al. (2018)	China	Cohort	700	20 - 40	Prospective Time-to-Pregnancy (TTP) Design	Couples in a committed relationship and planning to conceive with a TTP greater than 12 months	Couples in a committed relationship planning to conceive	Period	12	Infertility	28.0
Yang et al. (2017)	China	Cross-sectional	7 025	18 - 49	Retrospective Time-to-Pregnancy (TTP) Design	Couples whose waiting time to pregnancy was 12 or more months for the first pregnancy or couples who had never been pregnant and time trying to conceive was 12 or more months	Couples who had been married for more than 12 months	Period	12	Infertility	11.4
Huang and Tang (2013) Translation	China	Cross-sectional	18 893	Women: 18 - 49	Undetermined	Married couples who had regular sexual intercourse and did not take contraceptive measures, but had not conceived after cohabitation for more than 12 months	Couples married in 2007 who did not use contraceptive measures within one year after marriage	Period	12	Infertility	13.3
Meng et al. (2015)	China	Cohort	1 627 (12-month) 936 (24-month)	Not reported	Prospective Time-to-Pregnancy (TTP) Design	Newly married couples who failed to achieve a clinical pregnancy after 12/24 months or more of regular unprotected sexual intercourse	Newly married couples exposed to the risk of pregnancy	Period	12 24	Infertility Primary infertility Secondary infertility Infertility Primary infertility Secondary infertility	13.6 (11.9 - 15.3) 14.0 (12.2 - 15.8) 11.2 (7.2 - 15.2) 8.5 (6.7 - 10.3) 8.7 (6.7 - 10.7) 7.9 (3.6 - 12.2)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Hu et al. (2020)	China	Cohort	820	24-46	Prospective Time-to-Pregnancy (TTP) Design	Couples who engaged in regular unprotected intercourse and had a TTP greater than 12 months	Couples who engaged in regular unprotected intercourse and achieved pregnancy during follow-up	Period	12	Infertility	26.2
He et al. (2020)	China	Cross-sectional	12 364	18 - 49	Undetermined	Women who failed to achieve a clinical pregnancy after one year or more of unprotected sexual intercourse, despite having a desire to get pregnant	All married and cohabitating women	Lifetime	12	Infertility	10.11
			2 486			Women who failed to achieve a clinical pregnancy after one year or more of unprotected sexual intercourse, despite having a desire to get pregnant	Married and cohabitating women not using contraception	Lifetime	12	Infertility	20.92
Chen et al. (2015)	China	Cross-sectional	6 906	> 21	Retrospective Time-to-Pregnancy (TTP) Design	Couples with TTP greater than or equal to12 months or being unable to conceive after trying for at least 12 months for their first pregnancy	Married couples who ever tried for pregnancy	Period	12	Primary Infertility	11.97
Righarts et al. (2015)	New Zealand	Cross-sectional	974	25 - 50	Hybrid* Primary: Self-reported infertility measure (Direct) Secondary: Constructed infertility measure (Indirect)	Women who ever tried to conceive for 12/24 months or more	All women who had ever conceived or had tried to conceive	Lifetime	12 24	Infertility	21.7 (19.1 - 24.2) 12.8 (10.7 - 15.2)
						Women who ever tried to conceive for 12 months or more and/or sought help to conceive	All women who had ever conceived or had tried to conceive	Lifetime	12	Infertility	25.3 (22.6 - 28.1)
			476			Women ages 40 years or more with no previous births, whose infertility was not resolved with a live birth	Women ages 40 years or more who had ever tried to become or had been pregnant.	Lifetime	12	Primary unresolved infertility	1.9 (0.9 - 3.6)

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
van Roode et al. (2015)	New Zealand	Cohort	Men: 386 Women: 396	32 and 38	Self-reported infertility measure (Direct)	Men/women who, with a partner, had ever tried for 12 months or more to get pregnant without success	Men/women who ever reported or attempted pregnancy	Lifetime	12	Infertility - men women	17.9 (14.2 - 22.1) 25.0 (20.8 - 29.6)
						Men/women who, with a partner, had ever tried for 12 months or more to get pregnant without success OR who sought medical help to get pregnant	Men/women who ever reported or attempted pregnancy	Lifetime	12	Infertility - men women	21.8 (17.7-26.2) 26.0 (21.8-30.6)
			Not reported			Men/women who, with a partner, had ever tried for 12 months or more to get pregnant without success OR who sought medical help to get pregnant	All men/women	Lifetime	12	Infertility - men women	18.2 (14.8 - 22.1) 22.5 (18.7 - 26.6)
Righarts et al. (2021)	New Zealand	Cross-sectional	Men: 3 744 Women: 5 222	16 - 74	Self-reported infertility measure (Direct)	Men/women who ever had a time, lasting 12 months or longer, when they or a partner were trying for a pregnancy but it didn't happen	All men/women who had heterosexual intercourse	Lifetime	12	Infertility- men women	8.2 (7.1-9.4) 12.5 (11.3-13.8)
			Fertility-tested women: 3 792			Men/women who ever had a time, lasting 12 months or longer, when they or a partner were trying for a pregnancy but it didn't happen	Fertility-tested women (ever conceived or tried unsuccessfully to conceive for 12 months or longer)	Lifetime	12	Infertility	15.4 (14.0-16.9)
			Men: 3 744 Women: 5 222			Men/women who ever had a time, lasting 12 months or longer, when they or a partner were trying for a pregnancy but it didn't happen OR they believed they or their partner were infertile.	All men/women who had heterosexual intercourse	Lifetime	12 and/ or no duration (self-perceived)	Infertility- men women	11.4 (10.1-12.8) 13.4 (12.2-14.7)
			Fertility-tested women: 3 792			Men/women who ever had a time, lasting 12 months or longer, when they or a partner were trying for a pregnancy but it didn't happen OR they believed they or their partner were infertile.	Fertility-tested women (ever conceived or tried unsuccessfully to conceive for 12 months or longer)	Lifetime	12 and/ or no duration (self-perceived)	Infertility	16.3 (14.8-17.8)

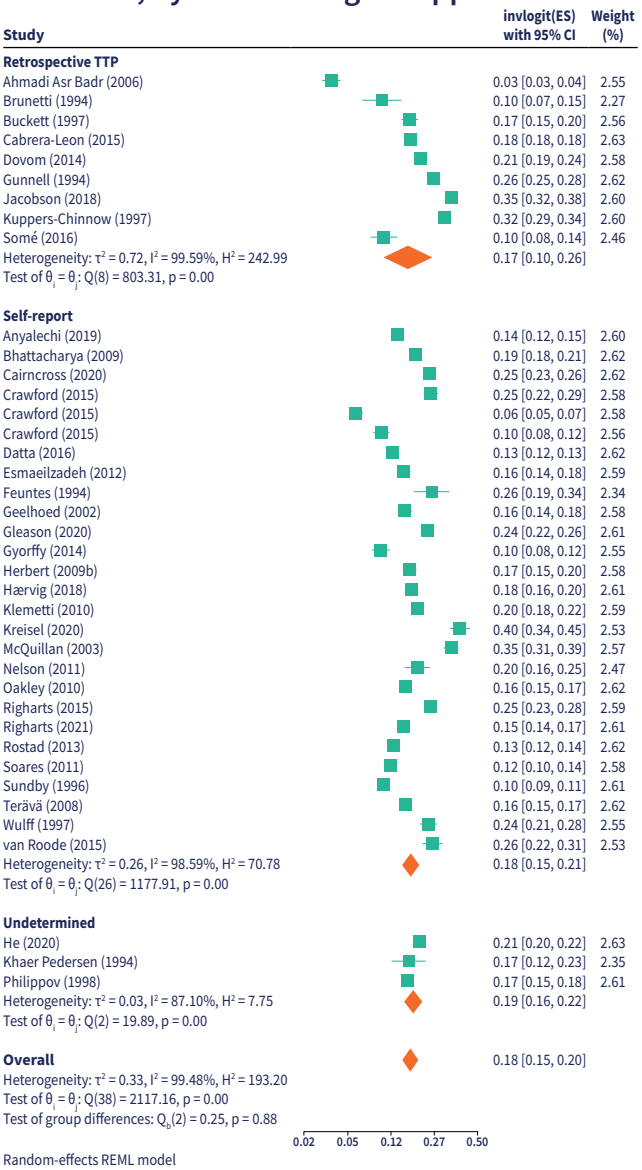
AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
Kreisel et al. (2020)	Palau	Cross-sectional	315	>17	Self-reported infertility measure (Direct)	Women who have tried unsuccessfully to become pregnant for 12 or more months	Women who reported ever trying to become pregnant	Lifetime	12	Infertility	39.7 (34.2 - 45.3)
Passey et al (1998)	Papua New Guinea	Cross-sectional	201	15 - 45	Self-reported infertility measure (Direct)	Women who reported that they wanted more children, were trying to conceive, and had had unprotected intercourse for 2 or more years	All women	Period	24	Infertility	29.6
MULTIPLE REGIONS											
Rutstein and Shah (2004)	Multiple	Cross-sectional	Less Developed Countries (China excluded): 939 796.7	25 - 49	Constructed infertility measure (Indirect)	Women who have been married for the past five years, who ever had sexual intercourse, who did not use contraception during the past five years, and who did not have any births in the past five years	Ever-married women	Period	60	Infertility Range Primary infertility Range Secondary infertility Range	25.7 16.0 - 30.0 2.5 1.5 - 2.8 23.8 13.6 - 28.2
Keiding et al. (2021)	Benin, Nigeria, Senegal, United Republic of Tanzania, Indonesia, Philippines, Dominican Republic, and Colombia	Cross-sectional	Range: 211 - 1 183	18 - 44	Current Duration Design	Nulliparous women not yet pregnant by 12 months (estimated) *Initiation of attempt estimated by date of cohabitation with partner	Women at risk of conception at the time of the survey (18 and 44 years, only one partner, currently married or living with a partner, had sex in the last 4 weeks, never had a live birth, menstruating and not currently pregnant, not menopausal, had not had a hysterectomy, and was not contracepting at the time of interview)	Period	12	Primary Infertility: Range	24.0 - 85.0
Mascarenhas et al. (2012a)	Global	Cross-sectional	Range: 337 - 62 785	20-44, > 30 (countries with data on women in union only)	Constructed infertility measure (Indirect)	Women who desire a child and have been in a union for at least five years, during which they have not used any contraceptives, and who have not had a live birth	Women in both infertile and fertile unions, where women in a fertile union have successfully had at least one live birth and have been in the union for at least five years at the time of the survey	Period	60	Primary infertility: World Range	 1.9 (1.8 - 2.2) 0.8 - 4.0

AUTHORS (YEAR)	GEOGRAPHIC LOCATION	TYPE OF STUDY	ANALYTIC SAMPLE SIZE	AGE RANGE	METHODOLOGIC APPROACH	NUMERATOR	DENOMINATOR	PERIOD OR LIFETIME MEASURE	DURATION (MONTHS)	RATIO MEASURED	ESTIMATE % (95% CI)
						Women who desire a child and have been in a union for at least five years, during which they have not used any contraceptives, and who have not had a live birth	All women (calculated as the product of the prevalence of infertility among child-seeking women and the proportion who are exposed to the risk of pregnancy)	Period	60	Primary infertility: World Range	 1.5 (0.3 - 1.7) 0.5 - 3.0
			China excluded			Women who desire a child and have been in a union for at least five years since their last birth, during which they have not used any contraceptives, and who have not had another live birth	Women in both infertile and fertile unions, where women in a fertile union have successfully had at least one live birth and, at the time of the survey, have been in the union for at least five years following their first birth	Period	60	Secondary infertility: World Range	 10.2 (9.2 - 11.4) 3.8 - 22.2
						Women who desire a child and have been in a union for at least five years since their last birth, during which they have not used any contraceptives, and who have not had another live birth.	All women (calculated as the product of the prevalence of infertility among child-seeking women and the proportion who are exposed to the risk of pregnancy)	Period	60	Secondary infertility: World Range	 2.9 (2.6 - 3.2) 0.8 - 10.5
Mascarenhas et al. (2012b)	26 countries	Cross-sectional	Range: 532 - 71 095 (primary) Range: 190 - 22 740 (secondary)	20 - 49	Constructed infertility measure (Indirect)	Women that have been in a union for at least five years (secondary infertility: since the partner's last live birth) without a live birth, during which neither partner used contraception, and where the female partner expresses a desire for a(nother) child.	Women in union for at least five years (secondary infertility: following their first live birth) at the time of the survey	Period	60	Primary: Range Secondary: Range	0.8 - 3.4 8.7 - 32.6
Taylor et al. (1999)	United Kingdom and Australia	Cross-sectional	Melbourne: 929 Manchester: 960	Not reported	Retrospective Time-to-Pregnancy (TTP) Design	Women who failed to conceive current pregnancy within 12 months of unprotected intercourse	Pregnant women	Period	12	Subfecundity Melbourne Manchester	 20.2 14.5

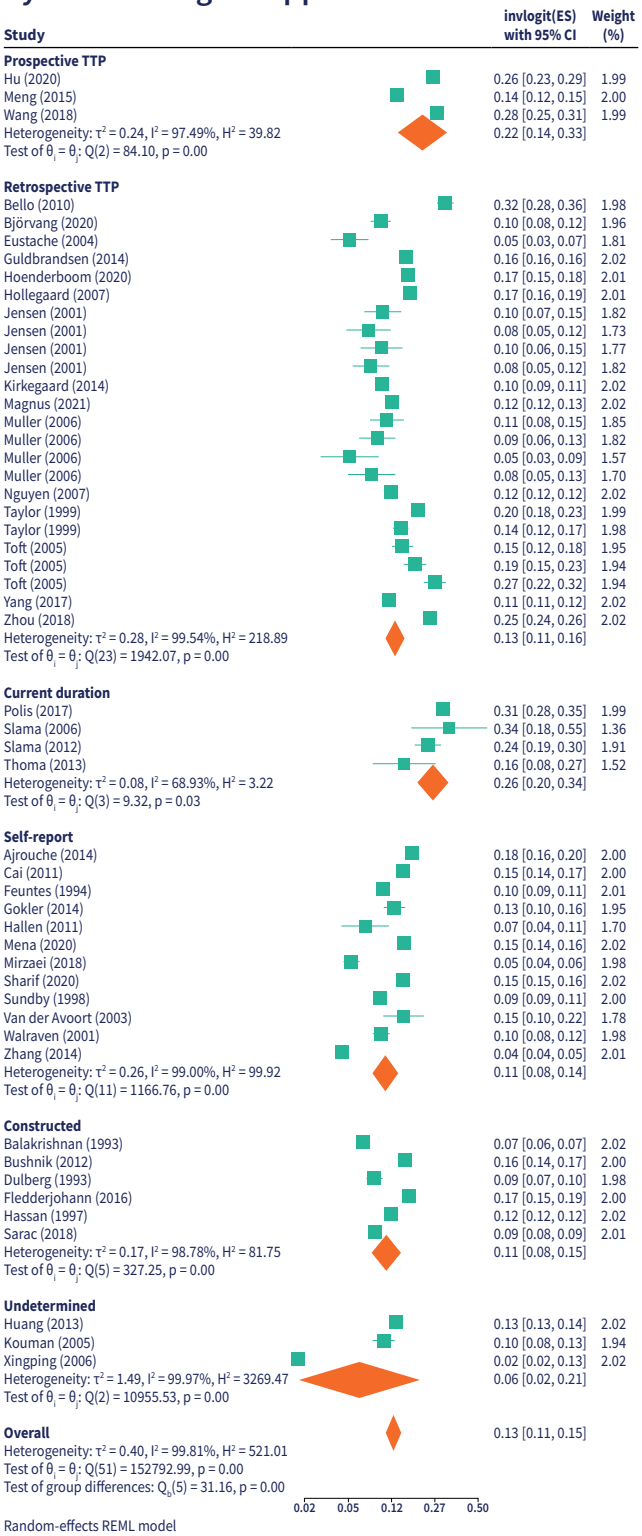
* Hybrid approach includes studies that combined two approaches to generate a single infertility estimate

Annex 4. Pooled lifetime and period infertility prevalence estimates, by methodological approach

Pooled lifetime infertility prevalence estimates, by methodological approach



Pooled period infertility prevalence estimates, by methodological approach



Annex 5. Certainty of estimates

Table A5.1 Certainty rating for 12-month infertility estimates (lifetime)

№ of studies	Quality assessment						Effect	Certainty
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Rate (95% CI)	
Infertility (12 months cross section; assessed with: Prevalence per 100 patients)								
37	Observational	Not serious[a]	Serious[b]	Not serious[c]	Not serious[d]	Publication bias: not detected	Prevalence 18 (15 to 20 per 100 persons)	⨁⨁⨁◯ MODERATE

[a] 77.4% of studies were at overall low risk of bias. 21.1% were at moderate risk of bias. Only 1.5% were at high risk of bias.
[b] Considerable heterogeneity was observed. This was based on visual inspection of point estimates and 95% CI reported on the forest plots. Individual study estimates ranged from 2% to 32%. None of the hypothesized subgroup analyses (geographic region or measurement approach) explained the observed heterogeneity.
[c] All individual studies addressed a question that was very similar, if not the same, as the review question in these estimates.
[d] Although a clear threshold for judging imprecision was not set, the width of the confidence interval was judged as sufficiently narrow. For the given assessment, the confidence interval was judged as sufficiently narrow and may not lead to completely different decisions. That is, whether the upper or lower bound of the 95% CI represents the truth, the reactions to the estimates will probably be the same.

Table A5.2 Certainty rating for pooled 12-month infertility estimates (period prevalence)

№ of studies	Quality assessment						Effect	Certainty
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Rate (95% CI)	
Infertility (12 months cross section; assessed with: Prevalence per 100 patients)								
43	Observational	Not serious[a]	Serious[b]	Not serious[c]	Not serious[d]	Publication bias: not detected	prevalence 13 (11 to 15 per 100 persons)	⨁⨁⨁◯ MODERATE

[a] 77.4% of studies were at overall low risk of bias. 21.1% were at moderate risk of bias. Only 1.5% were at high risk of bias.
[b] Considerable heterogeneity was observed. This was based on visual inspection of point estimates and 95% CI reported on the forest plots. Individual study estimates ranged from 2% to 32%. None of the hypothesized subgroup analyses (geographic region or measurement approach) explained the observed heterogeneity.
[c] All individual studies addressed a question that was very similar, if not the same, as the review question addressed in this review.
[d] Although a clear threshold for judging imprecision was not set, the width of the confidence interval was judged as being sufficiently narrow. For the given assessment, the confidence interval was judged as sufficiently narrow and may not lead to completely different decisions. That is, whether the upper or lower bound of the 95% CI represents the truth, the reactions to the estimates will likely be the same.

Table A5.3 Certainty rating for primary 12-month infertility estimates (lifetime)

№ of studies	Quality assessment						Effect	Certainty
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Rate (95% CI)	
Infertility (12 months cross section; assessed with: Prevalence per 100 patients)								
12	Observational	Not serious[a]	Serious[b]	Not serious[c]	Not serious[d]	Publication bias: not detected	Prevalence 10 (6 to 14 per 100 persons)	⨁⨁⨁◯ MODERATE

[a] 77.4% of studies were at overall low risk of bias. 21.1% were at moderate risk of bias. Only 1.5% were at high risk of bias.
[b] Considerable heterogeneity was observed. This was based on visual inspection of point estimates and 95% CI reported on the forest plots. Individual study estimates ranged from 2% to 25%. None of the hypothesized subgroup analyses (geographic region or measurement approach) explained the observed heterogeneity.
[c] All individual studies addressed a question that was very similar, if not the same, as the review question addressed in these estimates.
[d] Although a clear threshold for judging imprecision, the width of the confidence interval was judged as sufficiently narrow. For the given assessment, the confidence interval was judged as sufficiently narrow and may not lead to completely different decisions. That is, whether the upper or lower bound of the 95% CI represents the truth, the reactions to the estimates will likely be the same.

Table A5.4 Certainty rating for primary 12-month infertility estimates (period prevalence)

№ of studies	Quality assessment						Effect	Certainty
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Rate (95% CI)	
Infertility (12 months cross section; assessed with: Prevalence per 100 patients)								
33	Observational	Not serious[a]	Serious[b]	Not serious[c]	Not serious[d]	None	Prevalence 9 (7 to 12 per 100 persons)	⨁⨁⨁◯ MODERATE

[a] 77.4% of studies were at overall low risk of bias. 21.1% were at moderate risk of bias. Only 1.5% were at high risk of bias.
[b] Considerable heterogeneity was observed. This was based on visual inspection of point estimates and 95% CI reported on the forest plots. Individual study estimates ranged from 1% to 38%. None of the hypothesized subgroup analyses (geographic region or measurement approach) explained the observed heterogeneity.
[c] All individual studies addressed a question that was very similar, if not the same, as the review question addressed in these estimates.
[d] Although a clear threshold for judging imprecision was not set, the confidence interval was judged as sufficiently narrow. For the given assessment, the confidence interval was judged as sufficiently narrow and may not lead to completely different decisions. That is, whether the upper or lower bound of the 95% CI represents the truth, the reactions to the estimates will probably be the same.

Table A5.5 Certainty rating for secondary 12-month infertility estimates (lifetime)

№ of studies	Quality assessment						Effect	Certainty
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Rate (95% CI)	
Infertility (12 months cross section; assessed with: Incidence per 100 patients)								
10	Observational	Not serious[a]	Serious[b]	Not serious[c]	Not serious[d]	None	Prevalence 7 (4 to 11 per 100 persons)	⨁⨁⨁◯ MODERATE

[a] 77.4% of studies were at overall low risk of bias. 21.1% were at moderate risk of bias. Only 1.5% were at high risk of bias.
[b] Considerable heterogeneity was observed. This was based on visual inspection of point estimates and 95% CI reported on the forest plots. Individual study estimates ranged from 1% to 16%. None of the hypothesized subgroup analyses (geographic region or measurement approach) explained the observed heterogeneity.
[c] All individual studies addressed a question that was very similar, if not the same, as the review question addressed in these estimates.
[d] Although a set any clear threshold for judging imprecision was not set, the width of the confidence interval was judged as sufficiently narrow. For the given assessment, the confidence interval was judged as sufficiently narrow and may not lead to completely different decisions. That is, whether the upper or lower bound of the 95% CI represents the truth, the reactions to the estimates will probably be the same.

Table A5.6 Certainty rating for secondary 12-month infertility estimates (period prevalence)

№ of studies	Quality assessment						Effect	Certainty
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Rate (95% CI)	
Infertility (12 months cross section; assessed with: Prevalence per 100 patients)								
17	Observational	Not serious[a]	Serious[b]	Not serious[c]	Not serious[d]	None	Prevalence 5 (3 to 9 per 100 persons)	⨁⨁⨁◯ MODERATE

[a] 77.4% of studies were at overall low risk of bias. 21.1% were at moderate risk of bias. Only 1.5% were at high risk of bias.
[b] We observed considerable heterogeneity was observed. This was based on visual inspection of point estimates and 95% CI reported on the forest plots. Individual study estimates ranged from 0% to 35%. None of the hypothesized subgroup analyses (geographic region or measurement approach) explained the observed heterogeneity.
[c] All individual studies addressed a question that was very similar, if not the same, as the review question addressed in these estimates
[d] Although a clear threshold for judging imprecision was not set, the width of the confidence interval was judged as sufficiently being narrow. For the given assessment, the confidence interval was judged as sufficiently narrow and may not lead to completely different decisions. That is, whether the upper or lower bound of the 95% CI represents the truth, the reactions to the estimates will probably be the same.

For further information please contact:

Department of Sexual and Reproductive Health and Research
World Health Organization

Avenue Appia 20
CH-1211, Geneva 27
Switzerland

email: srhcfc@who.int
https://www.who.int/health-topics/infertility

9789240068315