Reproductive Health

RESEARCH

Open Access

Epidemiological characteristics of infertility, 1990–2021, and 15-year forecasts: an analysis based on the global burden of disease study 2021

Jiale Feng[1†], Qingguo Wu[1†], Yangbing Liang[1], Yiwen Liang[1] and Qin Bin[1*]

Abstract

Background Infertility, defined as the inability to achieve pregnancy after 1 year of regular unprotected intercourse, affects approximately 186 million people globally, with consistent prevalence across different income levels. Globally, the rising infertility rates are impacting population growth and individual quality of life. Infertility is not just a personal issue but also a public health concern, with social and economic implications, including stigmatization, marital discord, and mental strain. The COVID-19 pandemic has further exacerbated mental health issues among individuals with infertility, underscoring the need for research into the mental health impacts and access to fertility services. Economically, infertility poses a significant financial burden, especially in regions where Assisted Reproductive Technology (ART) costs can be up to 200% of the GDP per capita. Understanding the complexities and spread of infertility is essential for guiding policy decisions and program rollouts, with studies analyzing infertility issues based on the Global Burden of Disease (GBD) database.

Methods The study leverages data from the GBD 2021, encompassing 371 conditions or injuries and 88 risk factors across 204 nations. It examines prevalence, disability-adjusted life years (DALYs), age-standardized prevalence rate (ASPR), and age-standardized DALYs rate (ASDR) for infertility, categorized by sex, age, regions, and nations. The Social and Demographic Index (SDI), reflecting socio-economic levels, is used to analyze its correlation with infertility burden. The study employs decomposition analysis and frontier analysis methods to assess changes in infertility prevalence and DALYs, and Spearman's rank correlation coefficient to confirm relationships between age-standardized rates (ASRs) and SDI. The estimated annual percentage change (EAPC) of rates, with 95% confidence intervals (CIs), was calculated.

Results In 2021, it was calculated that the global ASPR for male infertility stood at 1354.76 cases per 100,000 individuals, with a 95% Uncertainty Interval ranging from 802.12 to 2174.77 cases per 100,000 individuals. For female infertility, the ASPR was recorded at 2764.62 per 100,000 individuals (95% UI: 1476.33–4862.57 per 100,000 individuals). Between 1990 and 2021, the EAPC in ASPR was observed to be 0.5% (95% CI 0.36–0.64) for males and 0.7% (95% CI 0.53–0.87) for females. In that same year, the global ASDR attributed to male infertility was 7.84 per 100,000 individuals (95% UI: 2.85–18.56 per 100,000 individuals), while for female infertility, it amounted to 15.12 per 100,000 individuals (95% UI: 5.35–36.88 per 100,000 individuals). The EAPC for ASDR linked to male and female infertility from 1990 to 2021

†Jiale Feng and Qingguo Wu have contributed equally to this work.

*Correspondence:
Qin Bin
qbin081@126.com

was assessed at 0.51% (95% CI 0.38–0.65) and 0.71% (95% CI 0.54–0.88), respectively. Among the 204 countries and territories in 2021, India ranked first in both the prevalence of cases and DALYs associated with male and female infertility, followed by China and Indonesia. Additionally, the investigation revealed a slight negative correlation between the ASPR and ASDR of infertility and the SDI. Decomposition analysis indicated that approximately 65% of the rise in the global burden of infertility could be attributed to population growth. Frontier analysis suggested that the variations in efficiency frontiers across specific SDI levels diminish as the SDI increases. Looking forward, the study projects a global rise in ASPR and ASDR for infertility between 2022 and 2036.

Conclusions The worldwide prevalence of infertility has substantially increased between 1990 and 2021, largely as a result of population growth. This trend highlights the pressing necessity for better strategies concerning prevention, diagnosis, and treatment, particularly in low and middle-income nations. Strengthening healthcare infrastructures, enhancing access to high-quality medical services, and raising awareness about infertility are vital measures to tackle this issue. The results of the study offer essential information to help policymakers and health officials formulate targeted strategies for the prevention and management of infertility.

Keywords Infertility, Global burden of disease 2021, Epidemiological, Prevalence, Disability-adjusted life years

Introduction

Infertility is defined as the failure to achieve pregnancy after engaging in unprotected sexual intercourse regularly for a year or longer [1]. Infertility impacts approximately 186 million people worldwide [2]. Around 17% of individuals will face infertility at some stage in their lives, with prevalence rates showing consistency across nations, irrespective of their income levels—17.8% of individuals in high-income nations and 16.5% of individuals in low- or middle-income nations experience infertility, respectively [3]. The second most populous nation, China, is also the largest emerging economy. It has witnessed a decrease in fertility rates and is now facing an aging demographic. Infertility is a significant factor hindering population growth. With Social and Demographic Index (SDI) of 0.719, China is categorized as a high-middle SDI country, holding the largest population in its region. In China, the incidence of infertility has increased from 12 to 18% from 2007 to 2020, as noted in the report "70 Years of Women's Reproductive, Maternal, Newborn, Child, and Adolescent Health in China," published by The Lancet [4]. Similarly, the United States, as the world's largest economy and the largest developed country, is an immigrant nation with cultural and racial diversity, ranking third in global population size, and also faces the same troubles. A study carried out by the National Survey of Family Growth from 2006 to 2010 revealed that 6% of married women within the age range of 15–44 in the United States are categorized as infertile, while 12% exhibit diminished fecundity [5]. It significantly affects individuals' quality of life across genders, creating difficulties not only for human fertility and birth rates, notably in areas where the desire for children is low, but also giving rise to various social challenges such as stigmatization, marital discord, and mental strain [6]. The situation is severe in African countries, where fertility is considered to have significant social importance [7, 8]. In many of these environments, couples facing infertility often experience social ostracism, with marriages affected by this issue frequently culminating in divorce [1, 6]. Furthermore, individuals facing infertility often experience emotional distress, including anxiety and depression, which can affect their relationships and overall quality of life [9]. This emotional toll is particularly pronounced during crises, such as the COVID-19 pandemic, which has exacerbated mental health issues among individuals with infertility [9, 10]. The pandemic has underscored the need for robust research into the mental health impacts of infertility and the importance of maintaining access to fertility services during public health crises [11, 12].

Economically, a systematic review highlighted that Assisted Reproductive Technology (ART) costs in some regions, particularly in Africa and Southeast Asia, can be up to 200% of the GDP per capita, indicating a severe financial barrier to accessing necessary medical interventions [13]. In high income countries, delaying childbearing, led to a growing demand for ART services, which, while providing solutions, also raises questions about the sustainability of healthcare systems in accommodating this demand [14].

In low- and middle-income countries, the lack of government-funded infertility treatments and insurance coverage further limits access, leaving many couples to pay out of pocket, which can lead to significant financial hardship [13]. Individuals may experience job loss or reduced work capacity due to the stress and health issues associated with infertility, further impacting their economic stability [15, 16]. The economic burden of infertility is not only a personal issue but also a public health concern that requires attention from policymakers to ensure equitable access to fertility treatments and support services.

A deep understanding of the complexities and spread of infertility is essential for gauging progress in combating this health issue and guiding policy decisions and program rollouts. There are studies that have analyzed infertility issues based on the Global Burden of Disease (GBD) database. Specifically, seven studies were based on the GBD2019 database [17–23], while two studies were based on the GBD2017 database [24, 25]. Among these seven studies based on the GBD2019 database, six studies focused solely on the global burden of disease trends for female infertility [17–22], and one study focused on the global burden of disease trends for male infertility [23]. Although the study based on the GBD2017 database attempted to analyze both male and female infertility issues, its analysis was relatively limited in depth [24, 25]. This study is the first to conduct an in-depth analysis of infertility issues using the GBD2021 database. Not only have we conducted a more comprehensive and in-depth analysis, but we have also introduced decomposition analysis and frontier analysis methods for the first time in the study of the disease burden of infertility.

In addition, in the Forecast analysis, we mainly observed that the varying prediction timeframes in the GBD database are influenced by a combination of factors, including the inherent characteristics of the diseases, the quality and availability of data, the methodologies used for forecasting, socio-demographic factors, and the anticipated impact of public health interventions, all of which contribute to the complexity of predicting disease burden across varying time horizons [26–30]. Different diseases' distinct epidemiological characteristics determine their prediction timeframes, with chronic conditions like diabetes or cardiovascular diseases often predicted over longer periods, such as 30 years, due to their long-term implications, while infectious diseases or those with potential for rapid control or eradication may have shorter prediction horizons, like 10 or 15 years, reflecting the potential for significant changes in incidence and management strategies within that timeframe [26, 30, 31]. Infertility patients seeking medical help experience changes, and the infertility population improves significantly in the short term due to public health interventions, hence the prediction of the disease burden of infertility tends to favor short-term forecasts to capture these changes [32].

This research seeks to characterize the epidemiological aspects of infertility in different regions, nations, and areas from 1990 to 2021. It offers crucial foundational data that facilitates the investigation of the epidemiological traits associated with infertility. The findings highlight the urgent need for implementing preventive and therapeutic interventions for infertility within the context of global health and serve as a scientific foundation for creating effective public health policies and strategies to address the increasing prevalence of infertility cases.

Methods

Data source

The GBD 2021 Study conducted an extensive and rigorous assessment of the impacts of various diseases, injuries, and risk factors across different age groups and genders worldwide. The study presented data on 371 distinct conditions or injuries and 88 risk factors, based on information collected from 204 nations and regions over the timeframe from 1990 to 2021 [33, 34]. We obtained annual data regarding prevalence, Disability-Adjusted Life Years (DALYs), age-standardized prevalence rate (ASPR), and age-standardized DALYs rate (ASDR), along with their corresponding 95% uncertainty interval (UI) for infertility, categorized by sex, age, regions, and nations during the timeframe of 1990–2021. The SDI is a comprehensive development indicator for countries or regions, reflecting socio-economic levels through a combination of metrics such as per capita income, average education level, and fertility rate, and is strongly correlated with health outcomes [34]. Socio-economic factors, including access to healthcare and education, play a critical role in the prevalence and management of infertility [35]. The correlation analysis of the SDI indicators in the burden of infertility disease reveals the complex interplay between factors affecting reproductive health outcomes. Understanding these correlations is crucial for developing targeted interventions and policies aimed at reducing the burden of infertility, especially in areas with limited access to education and healthcare [35]. Addressing these socio-demographic factors can improve reproductive health outcomes and reduce the prevalence of infertility across different populations. The research utilized the Disease Modeling-Bayesian meta-regression software (version 2.1), which aims to estimate the years of life lost due to disability using epidemiological data [36]. The authors affirm their compliance with the ethical standards set forth by the journal, as outlined on its author guidelines page. Since the research relied solely on publicly accessible data, no ethical approval was necessary.

Definition

Infertility is divided into primary infertility and secondary infertility [37]. Primary male infertility pertains to a man who has never initiated a clinical pregnancy and is classified as infertile, while primary female infertility pertains to a woman who has never been diagnosed with a clinical pregnancy and is classified as having infertility [37]. Secondary infertility in males refers to a man who cannot initiate a clinical pregnancy despite having done so before, while in females, it refers to a woman who is unable to establish a clinical pregnancy after having previously been diagnosed with one [37]. The stress and emotional burden of infertility can lead to a decline in overall health, such as increased risks of severe maternal morbidity, cancer, and chronic diseases [11, 18, 38]. This can potentially increase the years lived with disability (YLDs), thereby contributing to the overall DALY metric, which combines years of life lost (YLLs) due to premature mortality and YLDs [11, 18]. For the purpose of standardizing based on population size and demographic distribution, age-standardized rates (ASRs) were computed, using rates per 100,000 individuals aligned with the updated standard population age framework established by GBD 2021 [39]. The SDI scores, ranging from 0.00 to 1.00, were adjusted by a factor of 100 to classify nations and regions into quintiles of development stages: low (below 0.46), low-middle (0.46–0.60), middle (0.61–0.69), high-middle (0.70–0.81), and high (above 0.81) [33, 34]. Additionally, due to their similar socioeconomic characteristics and geographic locations, the 204 countries and territories were grouped into 21 distinct regions defined by the GBD.

Statistical analyses

The impact of diseases associated with infertility was evaluated by utilizing ASPR and ASDR, while also recording the statistics for both prevalence and DALYs. The data, which includes ASRs for every 100,000 individuals across the full spectrum of age categories and specific rates for certain age brackets, was derived from the Global Burden of Disease 2021 database, with the outcomes displayed as 95% confidence interval-accompanied estimates [33, 34]. To thoroughly examine the trends, the EAPC was computed for the years from 1990 to 2021. An EAPC estimate with a 95% CI that does not include zero indicates a statistically significant trend. A linear regression model was employed, represented as $y=\alpha+\beta x+\varepsilon$, where y denotes the natural logarithm of (ASR), x stands for the calendar year, and ε represents an independent, normally distributed error term [40]. More specifically, if the lower bound of the 95% CI is above zero, it suggests a significant upward trend for the specified period. In contrast, if the upper bound of the 95% CI is below zero, it indicates a considerable downward trend. To gain a deeper understanding of the factors contributing to the changes in infertility prevalence and DALYs from 1990 to 2021, we conducted a decomposition analysis based on age structure, population size, and epidemiological changes, and performed frontier analysis to determine the attainable minimum prevalence and DALYs [41]. To confirm the relationships between ASRs and the SDI, Spearman's rank correlation coefficient was utilized. The combined influences of age, period, and cohort were analyzed using the Bayesian age-period-cohort model with conventional parameters [42, 43]: $\eta ij=\mu+\alpha i+\beta j+\gamma k$. Here, ηij denotes the ASR, μ is the baseline value, and αi and γk signify the impacts of age and period, as well as cohort, respectively. All additional statistical analyses were performed using R software (version 4.4.1, R Foundation for Statistical Computing, Vienna, Austria). A *p*-value lower than 0.05 was considered statistically significant.

Results

Burden of infertility at global and regional level

In the year 2021, the global ASPR for male infertility stood at 1354.76 per 100,000 individuals (95% UI: 802.12–2174.77 per 100,000 individuals, Table 1). Conversely, for female infertility, the ASPR was recorded at 2764.62 per 100,000 individuals (95% UI: 1476.33–4862.57 per 100,000 individuals, Table 1). Between 1990 and 2021, the globally ASPR of infertility for both genders demonstrated a variable upward trajectory (Fig. 1). Notably, after 2010, there has been a marked rise in this rate (Fig. 1). Furthermore, the EAPC for male and female infertility ASPRs from 1990 to 2021 was 0.5% (95% CI 0.36–0.64) and 0.7% (95% CI 0.53–0.87, Table 1), respectively. In 2021, the total number of individuals affected by male infertility was 55,000,818 (95%UI: 32,611,257–88,727,953), while the number for female infertility was 110,089,459 (95% UI: 58,608,815–195,025,585, Table 1). From 1990 to 2021, there has been an increasing trend in infertility prevalence, with female facing infertility issues at nearly double the rate of male (Fig. 2). The ASPR for infertility among females exceeded that of males (Table 1 and Fig. 1). In 2021, the high-middle SDI region reported the highest ASPR for both gender infertility, whereas the high SDI region recorded the lowest ASPR (Table 1).

In 2021, the highest ASPR of infertility among females and males was observed in East Asia and Eastern Europe, respectively (Table 1). Conversely, Australasia reported the lowest ASPR for both female and male infertility (Table 1). When compared to 1990, regions that saw an increase in ASPR for female infertility included Andean Latin America, South Asia, and High-income North America (Table 1). Conversely, a decrease in the ASPR for female infertility was noted in Oceania and Eastern Sub-Saharan Africa (Table 1). As for male infertility, regions like Andean Latin America and Tropical Latin America recorded an increase in ASPR compared to 1990 (Table 1). On the contrary, the regions where the ASPR for male infertility fell included Eastern Sub-Saharan Africa and Oceania (Table 1).

Table 1 The number of prevalence cases and ASPR (per 100,000 individuals) of infertility in 2021, and percentage change of ASPR were analyzed across the GBD regions

Location	Male infertility			Female infertility		
	Num_2021	**ASPR_2021 per 100,000**	**EAPC_CI 1990–2021**	**Num_2021**	**ASPR_2021 per 100,000**	**EAPC_CI 1990–2021**
Global	55,000,818 (32,611,257–88,727,953)	1354.76 (802.12–2174.77)	0.5% (0.36–0.64)	110,089,459 (58,608,815–195025585)	2764.62 (1476.33–4862.57)	0.7% (0.53–0.87)
Andean Latin America	232,367 (128,537–402,807)	655.75 (363.35–1142.51)	2.14% (1.77–2.51)	180,844 (18,126–574,607)	504.63 (50.37–1593.83)	8.22% (6.7–9.76)
Australasia	94,399 (53,292–163,037)	622.98 (350.36–1073.96)	0.25% (0.21–0.29)	23,946 (5824–97,727)	152.74 (37.22–604.18)	0.86% (0.71–1.01)
Caribbean	320,709 (202,005–504649)	1331.15 (838.46–2090.09)	− 0.09% (− 0.2–0.01)	589,496 (342,122–997,994)	2406.71 (1390.62–4061.59)	− 0.11% (− 0.28–0.06)
Central Asia	482,054 (278,127–809,038)	933.06 (541.89–1535.07)	0.38% (0.24–0.53)	798,112 (353,395–1,591,761)	1540.98 (693.02–3004.33)	0.89% (0.63–1.14)
Central Europe	751,761 (408,846–1337049)	1371.77 (748.4–2424.41)	0.62% (0.51–0.73)	1,334,989 (617,168–2,521,006)	2528.33 (1205.28–4746.56)	0.88% (0.74–1.02)
Central Latin America	1,366,956 (804,646–2251065)	1049.57 (618.04–1736.39)	0.51% (0.27–0.75)	2,270,205 (933,287–4,395,051)	1637.03 (676.33–3179.79)	1.19% (0.8–1.58)
Central Sub-Saharan Africa	842,776 (472,132–1,354,804)	1411.72 (789.07–2271.46)	− 0.38% (− 0.79–0.04)	1,705,616 (872,692–3,067,605)	2865.53 (1445.2–5372.44)	− 0.17% (− 0.78–0.45)
East Asia	12,167,667 (6,670,101–21239731)	1575.7 (880.94–2675.46)	0% (− 0.05–0.06)	30,097,127 (14,985,652–53,555,149)	4102.68 (2124.47–7170.94)	0.01% (− 0.04–0.05)
Eastern Europe	2,041,839 (1,134,417–3,432,078)	2058.13 (1120.2–3444.23)	0.26% (0.15–0.36)	3,640,758 (1,828,022–6714993)	3604.24 (1850.66–6527.52)	0.6% (0.48–0.73)
Eastern Sub-Saharan Africa	1,481,393 (872,091–2357013)	777.87 (459.72–1236.42)	− 1.19% (− 1.41–0.96)	3,960,451 (2,299,441–6,526,195)	1966.79 (1124.46–3295.26)	− 1.25% (− 1.52–0.98)
High-income Asia Pacific	797,761 (429,920–1382800)	898.57 (491.48–1481.48)	− 0.2% (− 0.29–0.11)	555,824 (51,072–1751423)	605.07 (61.02–1892.11)	− 0.39% (− 0.65–0.13)
High-income North America	1,752,539 (954,878–2,959,535)	1010.31 (546.66–1701.88)	0.83% (0.19–1.47)	1,478,922 (218,891–3,682,781)	848.73 (128–2124.44)	3.01% (1.61–4.43)
High-middle SDI	10,194,899 (5,795,901–17173215)	1472.79 (851.46–2414.28)	0.13% (0.11–0.14)	21,200,266 (10,465,956–38450758)	3180.18 (1643.03–5750.65)	0.26% (0.24–0.28)
High SDI	5,890,821 (3,376,658–10,016,230)	1071.23 (617.22–1766.67)	0.63% (0.51–0.75)	7,476,943 (2,888,374–14,892,481)	1415.8 (542.85–2854.67)	1.43% (1.28–1.58)
Low-middle SDI	14,297,089 (8,370,702–22875418)	1395.96 (813.3–2252.12)	1% (0.61–1.4)	30,053,933 (16,629,265–51,679,485)	2940.52 (1623.86–5103.43)	1.24% (0.69–1.79)
Low SDI	6,427,824 (3,885,082–9979635)	1269.37 (770.19–1959.84)	− 0.17% (− 0.45–0.12)	12,249,744 (6,801,478–20619052)	2333.95 (1299.03–3969.36)	0.1% (− 0.28–0.5)
Middle SDI	18,151,666 (10,796,198–29302986)	1387.96 (819.52–2230.9)	0.6% (0.52–0.69)	39,038,802 (20,324,320–70133766)	3027.65 (1579.65–5404.99)	0.58% (0.46–0.7)
North Africa and Middle East	4,150,567 (2,458,605–6611301)	1154.32 (681.51–1863.21)	0.8% (0.63–0.98)	6,357,159 (3,075,148–10825896)	1928.83 (931.82–3266.23)	1.19% (0.89–1.49)
Oceania	50,725 (35,213–72,464)	712.44 (498.04–1011.41)	− 0.96% (− 1.17–0.75)	75,092 (42,007–115416)	1068.87 (593.82–1647.74)	− 1.58% (− 1.85–1.3)
South Asia	15,223,186 (8,656,105–25000575)	1464.33 (835.34–2404.5)	1.52% (0.96–2.09)	35,555,258 (19,863,521–60,335,282)	3523.38 (1963.94–5994.84)	1.95% (1.2–2.71)

Table 1 (continued)

Location	Male infertility			Female infertility		
	Num_2021	**ASPR_2021 per 100,000**	**EAPC_CI 1990–2021**	**Num_2021**	**ASPR_2021 per 100,000**	**EAPC_CI 1990–2021**
Southeast Asia	5,370,095 (3,092,324–8839732)	1399.74 (805.71–2309.49)	1.59% (1.3–1.88)	11,004,744 (5,574,141–19,376,109)	2919.2 (1477.11–5150.66)	1.68% (1.34–2.02)
Southern Latin America	361,275 (206,015–615642)	1014.36 (577.04–1717.53)	−0.05% (−0.12–0.03)	387,109 (94,046–864584)	1060.26 (260.27–2339.84)	−0.25% (−0.33–0.16)
Southern Sub-Saharan Africa	320,676 (168,458–598,876)	718.21 (382.24–1327.36)	−0.68% (−1.22–0.13)	782,508 (260,859–1743635)	1715.36 (578.85–3827.21)	−0.75% (−1.49–0)
Tropical Latin America	1,384,604 (780,681–2299828)	1110.32 (629.61–1860.19)	1.83% (1.41–2.26)	2,215,723 (943,705–4309763)	1697 (729.23–3288.91)	1.71% (1.13–2.29)
Western Europe	1,933,592 (1,070,793–3257464)	972.43 (540.33–1653.86)	0.95% (0.75–1.14)	2,492,439 (748,783–5,485,462)	1224.48 (367.65–2644.73)	1.48% (1.2–1.76)
Western Sub-Saharan Africa	3,873,874 (2,374,489–5,892,117)	1918.52 (1198.23–2948.44)	−0.62% (−0.88–0.36)	4,583,137 (2,061,353–8923482)	2057.2 (894.15–4060.81)	−0.32% (−0.6–0.04)

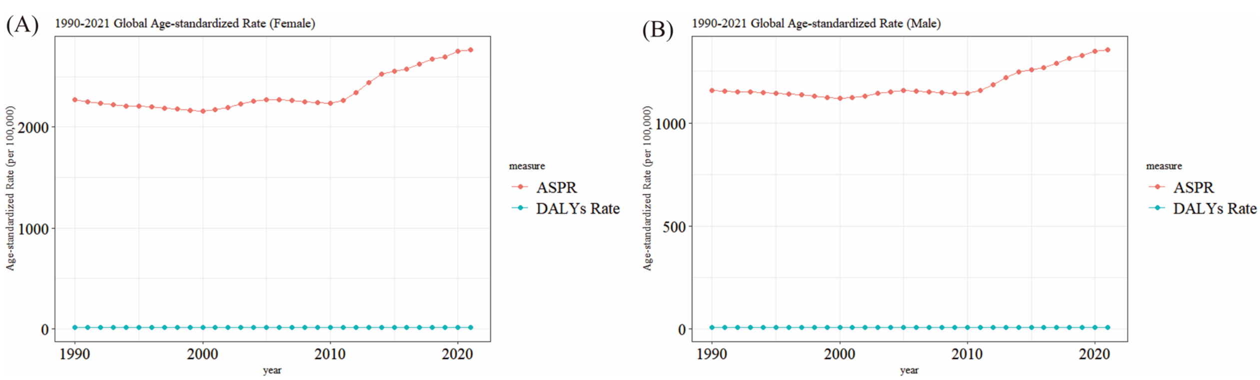

Fig. 1 Global ASRs of Infertility. **a** Global ASRs of female infertility; **b** Global ASRs of male infertility. ASRs, age-standardized rates

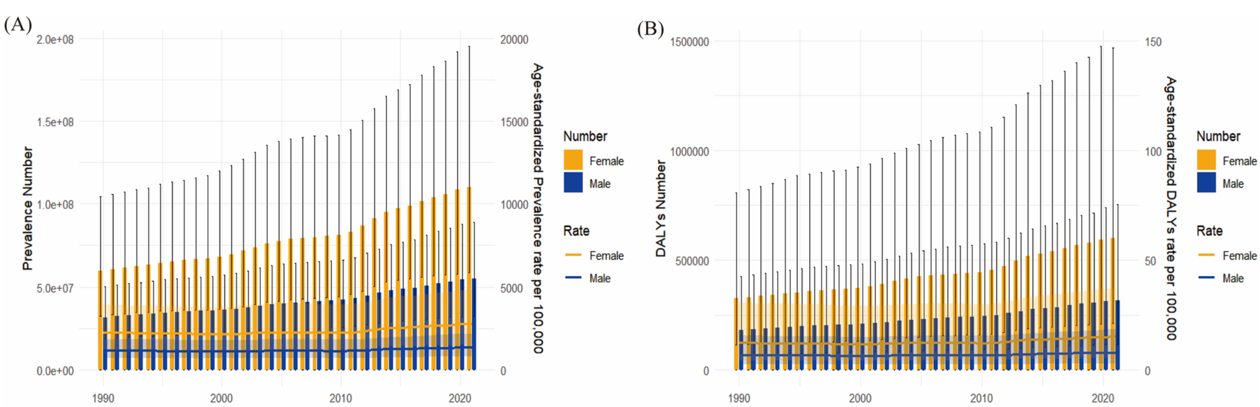

Fig. 2 Burden of infertility by sex and year groups. **a** The number of Prevalence and ASPR by sex during 1990–2021; **b** The number of Disability-adjusted life years and ASDR by sex during 1990–2021. ASPR, age-standardised prevalence rate; ASDR, age-standardised DALYs rate

In the year 2021, the ASDR for male infertility was reported at 7.84 per 100,000 individuals (95% UI: 2.85–18.56 per 100,000 individuals, Table 2). Conversely, female infertility exhibited an ASDR of 15.12 per 100,000 individuals (95% UI: 5.35–36.88 per 100,000 individuals, Table 2). Additionally, during the time frame from 1990 to 2021, the EAPC in ASDR was recorded at 0.51% (95% CI 0.38–0.65) for male and 0.71% (95% CI 0.54–0.88) for female (Table 2). In the same year, the DALYs attributed to male infertility amounted to 317,614 individuals (95% UI: 116,288–752,758), while the figure for female infertility reached 601,134 individuals (95%UI: 213, 158–1,468,475, Table 2). Furthermore, among the five SDI regions in 2021, the high-middle SDI region reported the greatest ASPR for both male and female infertility, contrasting with the lowest ASIR which was documented in the high SDI region (Table 2).

In 2021, Eastern Europe reported the highest ASDR for male infertility, while East Asia recorded the highest ASDR for female infertility (Table 2). An analysis of data spanning from 1990 to 2021 showed marked increases in ASDR relating to male infertility in regions such as Andean Latin America, Central Asia, Central Europe, Central Latin America, High-income North America, South Asia, North Africa and the Middle East, Southeast Asia, Tropical Latin America, and Western Europe (Table 2). In contrast, decreases in ASDR for male infertility were observed in regions like Eastern Sub-Saharan Africa, Southern Sub-Saharan Africa, Western Sub-Saharan Africa, and Oceania in 2021 (Table 2). Female infertility likewise experienced rising ASDR across the majority of the 21 regions analyzed, with particularly notable increases occurring in Andean Latin America and High-income North America (Table 2).

Burden of infertility at national level

In 2021, India held the top position among 204 countries and territories for both genders infertility prevalence cases and DALYs, with China and Indonesia following closely (Table S1 and S2). Between 1990 and 2021, most countries and territories experienced a rise in male infertility prevalence, though some exceptions were observed in Russia and nations within the Balkan Peninsula, Mediterranean area, and Eastern Europe (Table S1 and Fig. 3a). Likewise, during this same timeframe, a similar upward trend was noted for female infertility across most countries and territories, with the aforementioned regions being the exceptions (Table S1 and Fig. 3c).

In 2021, the ASPR for female infertility varied between 308.22 and 5751.56 per 100,000 individuals (Table S1). Significantly, the highest rates were observed in the Central African Republic (5751.56 per 100,000 individuals, 95% UI: 3585.62–9238.57), Djibouti (5304.56 per 100,000 individuals, 95% UI: 3029.58–8632.08), and Gabon (5072.46 per 100,000 individuals, 95% UI: 2842.85–8423.78) (Table S1 and Fig. 3b). In a similar fashion, the ASPR for male infertility ranged from 286.34 to 2804.1 per 100,000 individuals (Table S1). Noteworthy cases include Liberia (2804.1 per 100,000 individuals, 95% UI: 1612.32–4491.78), the Central African Republic (2803.4 per 100,000 individuals, 95% UI: 1618.38–4341.94), and Mauritania (2707.04 per 100,000 individuals, 95% UI: 1625.71–4341.97), which recorded the highest ASPRs (Table S1 and Fig. 3d). Countries such as the Central African Republic, India, China, and Indonesia urgently require the attention of international health agencies concerning the critical public health challenge of infertility.

Ecuador, Peru, and the Plurinational State of Bolivia exhibited the most significant rising trends in the ASPR for female infertility, recording increases of 9.33% (95% UI: 7.27–11.42), 7.12% (95% UI: 5.52–8.74), and 6.7% (95% UI: 3.89–9.57), respectively (Table S1 and Fig. 3e). In contrast, the Philippines, Morocco, and Slovenia displayed the highest increasing trends in the ASPR for male infertility, with rates of 5.33% (95% UI: 3.27–7.44), 2.79% (95% UI: 1.97–3.61), and 2.73% (95% UI: 2.21–3.26), respectively (Table S1 and Fig. 3f).

Between 1990 and 2021, the number of DALYs attributed to male infertility rose in the majority of nations and regions, with the exceptions being Russia and areas within the Balkan Peninsula, the Mediterranean, and Eastern Europe (Table S2 and Figure S1a). Likewise, the number of DALYs related to female infertility also increased across most countries and territories, excluding Russia and regions in the Balkan Peninsula, the Mediterranean, North America, South Africa, and Eastern Europe (Table S2 and Figure S1a).

In 2021, the highest ASDR for male infertility was reported in Cameroon, the Central African Republic, and Mauritania (Table S2 and Figure S1a). Conversely, the lowest ASDR for male infertility was recorded in Burundi, Malawi, and Uganda (Table S2 and Figure S1a). As for female infertility, the Central African Republic, Djibouti, and Gabon exhibited the highest ASDR in 2021 (Table S2 and Figure S1a); meanwhile, Australia, Colombia, and New Zealand were observed to have the lowest ASDR for female infertility (Table S2 and Figure S1a). From 1990 to 2021, both Ecuador and Peru experienced a significant increase in ASDR for female infertility, with EAPC of 9.15% (95% CI 7.13–11.20) and 7.08% (95% CI 5.54–8.65), respectively (Table S2 and Figure S1a). Similarly, substantial upward trends in ASDR for male infertility were noted in the Philippines and Morocco, with EAPC values of 5.28% (95% CI 3.29–7.30) and 2.74% (95% CI 1.92–3.57), respectively (Table S2 and Figure S1a).

Table 2 The number of DALY cases and ASDR (per 100,000 individuals) of infertility in 2021, and percentage change of ASDR were analyzed across the GBD regions

Location	Male infertility			Female infertility		
	Num_2021	ASDR_2021 per 100,000	EAPC_CI 1990–2021	Num_2021	ASDR_2021 per 100,000	EAPC_CI 1990–2021
Global	317,614 (116,288–752,758)	7.84 (2.85–18.56)	0.51% (0.38–0.65)	601,134 (213,158–1,468,475)	15.12 (5.35–36.88)	0.71% (0.54–0.88)
Andean Latin America	1308 (457–3074)	3.69 (1.29–8.74)	2.06% (1.72–2.4)	970 (83–3433)	2.71 (0.23–9.58)	8.11% (6.62–9.62)
Australasia	566 (208–1403)	3.76 (1.37–9.32)	0.26% (0.22–0.3)	135 (22–593)	0.87 (0.14–3.67)	0.83% (0.69–0.97)
Caribbean	1865 (701–4268)	7.74 (2.89–17.77)	−0.12% (−0.21–0.03)	3230 (1194–8225)	13.19 (4.88–33.64)	−0.13% (−0.28–0.03)
Central Asia	2798 (1071–6651)	5.44 (2.08–12.78)	0.34% (0.21–0.48)	4353 (1393–10,832)	8.44 (2.67–20.74)	0.83% (0.59–1.07)
Central Europe	4209 (1490–10604)	7.77 (2.74–19.83)	0.58% (0.48–0.68)	7124 (2268–18,324)	13.6 (4.29–34.98)	0.84% (0.71–0.98)
Central Latin America	7737 (2830–17728)	5.93 (2.18–13.66)	0.49% (0.26–0.72)	12,076 (3458–32,018)	8.71 (2.5–23.2)	1.17% (0.79–1.55)
Central Sub-Saharan Africa	4740 (1668–11,334)	7.86 (2.75–19.15)	−0.35% (−0.75–0.05)	9141 (2975–21,605)	15.23 (4.7–35.74)	−0.13% (−0.73–0.47)
East Asia	65,671 (22,295–160,100)	8.57 (2.94–20.87)	0.02% (−0.04–0.09)	157,326 (51,989–406,568)	21.55 (7.4–54.1)	0.02% (−0.03–0.07)
Eastern Europe	11,889 (4220–29847)	12.2 (4.27–30.22)	0.26% (0.16–0.37)	20,006 (6812–52,654)	20.11 (7.05–51.09)	0.58% (0.45–0.7)
Eastern Sub-Saharan Africa	8420 (3013–19823)	4.37 (1.59–10.17)	−1.17% (−1.39–0.95)	21,486 (7752–50,131)	10.57 (3.79–25.04)	−1.23% (−1.49–0.97)
High-income Asia Pacific	4516 (1588–11,264)	5.17 (1.8–12.84)	−0.19% (−0.27–0.11)	2963 (191–11,210)	3.24 (0.24–12.55)	−0.4% (−0.65–0.15)
High-income North America	10,826 (3847–26,993)	6.26 (2.19–15.78)	0.76% (0.12–1.41)	8507 (1021–26836)	4.9 (0.58–15.3)	2.91% (1.51–4.33)
High-middle SDI	57,219 (21,039–141093)	8.35 (3.02–20.74)	0.14% (0.13–0.16)	112,846 (38,219–282,874)	17.04 (5.87–41.71)	0.27% (0.24–0.29)
High SDI	34,878 (12,752–84,167)	6.4 (2.3–15.53)	0.6% (0.48–0.72)	41,101 (11,612–110,625)	7.83 (2.2–21.41)	1.41% (1.25–1.56)
Low-middle SDI	84,065 (30,521–196576)	8.18 (2.98–19.2)	0.95% (0.57–1.33)	167,400 (58,563–403,460)	16.34 (5.7–39.57)	1.19% (0.65–1.73)
Low SDI	37,248 (13,729–85,517)	7.28 (2.7–16.88)	−0.16% (−0.44–0.12)	67,696 (24,767–161,485)	12.8 (4.73–31.1)	0.11% (−0.28–0.5)
Middle SDI	103,980 (38,249–249,703)	7.98 (2.9–19.24)	0.66% (0.58–0.75)	211,708 (75,088–517044)	16.47 (5.84–39.99)	0.62% (0.5–0.74)
North Africa and Middle East	25,132 (9234–57,501)	7.02 (2.56–16.24)	0.73% (0.55–0.91)	35,930 (11,008–89848)	10.93 (3.36–27.16)	1.09% (0.78–1.4)
Oceania	292 (110–676)	4.08 (1.55–9.43)	−0.94% (−1.13–0.74)	416 (144–1001)	5.9 (2.05–14.25)	−1.53% (−1.8–1.26)
South Asia	90,312 (32,227–209,136)	8.67 (3.11–20.15)	1.43% (0.89–1.96)	199,476 (71,920–470290)	19.74 (7.09–46.79)	1.85% (1.13–2.57)
Southeast Asia	31,369 (11,255–73,878)	8.19 (2.93–19.24)	1.55% (1.28–1.82)	60,681 (21,015–150690)	16.11 (5.57–40.33)	1.66% (1.33–1.98)
Southern Latin America	2142 (776–5318)	6.02 (2.19–14.98)	−0.04% (−0.1–0.03)	2160 (370–6141)	5.93 (1.01–17.1)	−0.26% (−0.34–0.18)
Southern Sub-Saharan Africa	1819 (619–4609)	4.08 (1.39–10.21)	−0.72% (−1.26–0.18)	4197 (1096–11247)	9.21 (2.42–24.57)	−0.8% (−1.54–0.06)
Tropical Latin America	8117 (2920–19585)	6.53 (2.37–15.72)	1.76% (1.34–2.18)	12,166 (3807–32977)	9.35 (3–25.33)	1.62% (1.05–2.21)
Western Europe	11,857 (4236–29,090)	6.03 (2.13–14.95)	0.93% (0.74–1.12)	14,102 (3264–39,770)	6.99 (1.63–19.39)	1.44% (1.17–1.72)
Western Sub-Saharan Africa	22,028 (8143–51,657)	10.78 (3.94–25.15)	−0.6% (−0.87–0.34)	24,687 (7276–61,455)	10.97 (3.17–27.28)	−0.3% (−0.57–0.03)

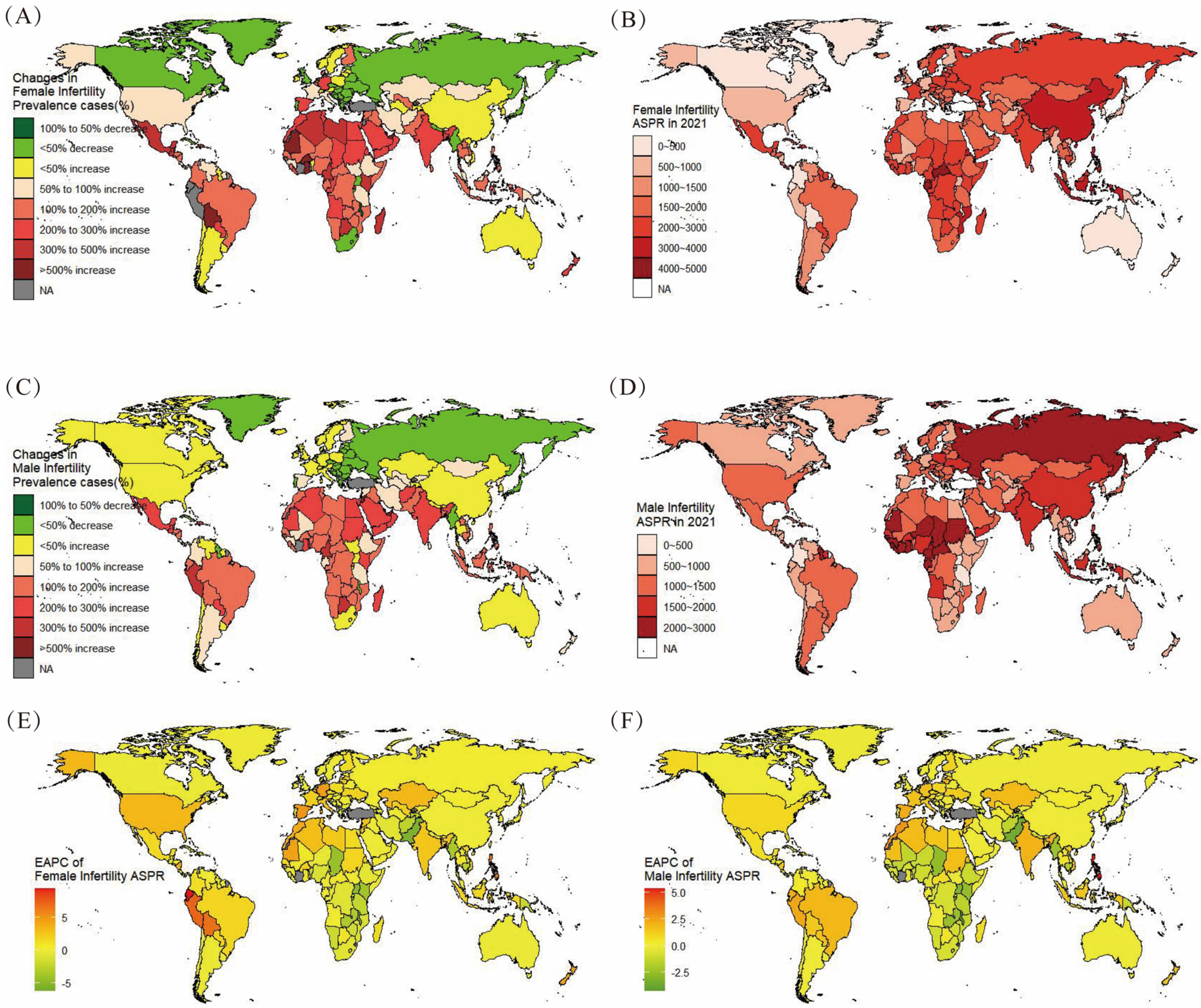

Fig. 3 The ASPR of infertility across 204 countries and territories. **a** Changes in female Infertility Prevalence cases; **b** Female Infertility ASPR in 2021; **c** Changes in male Infertility Prevalence cases; **d** Male Infertility ASPR in 2021; **e** EAPC of female Infertility ASPR; **f** EAPC of male Infertility ASPR. ASPR, age-standardised prevalence rate; EAPC, estimated annual percentage change

Age distribution

In 2021, the number of DALYs increased as individuals aged, starting from 15 years old and reaching a peak within the 35–39 age range, followed by a rapid decline (Fig. 4). This reduction in ASRs after 39 years of age may be associated with lowered fertility expectations (Fig. 4). As individuals get older, the probability of experiencing infertility grows, with a particularly significant rise observed among women (Fig. 4). The ASRs for infertility are notably higher in women than in men, a pattern that is consistent across different countries and regions (Fig. 4). Furthermore, it is essential to note that the highest ASPR for infertility among both genders was found in areas identified as having high-middle and middle SDI scores (Fig. 4).

Association between ASRs and SDI

In 2021, we observed a slight negative correlation between female infertility ASPR and ASDR and the SDI in 204 countries and regions ($r = -0.2$, $P < 0.05$; Fig. 5a, b). In the case of male infertility, inverse relationships were identified between the SDI) and the ASPR ($r = -0.23$, $P < 0.05$) as well as the ASDR ($r = -0.18$, $P < 0.05$; Fig. 5c, d). The ASPR and ASDR rates of female infertility in Eastern Europe, Southeast Asia, and Southern Latin America initially decreased rapidly with rising SDI, experienced a swift decline as SDI increased, reaching a peak before sharply rising again with additional SDI growth (Figure S2a, b). Similarly, the rates of male infertility as measured by ASPR and ASDR in Eastern Europe, Southeast Asia, and Andean Latin America also experienced a swift decline as SDI rose, achieving a peak and

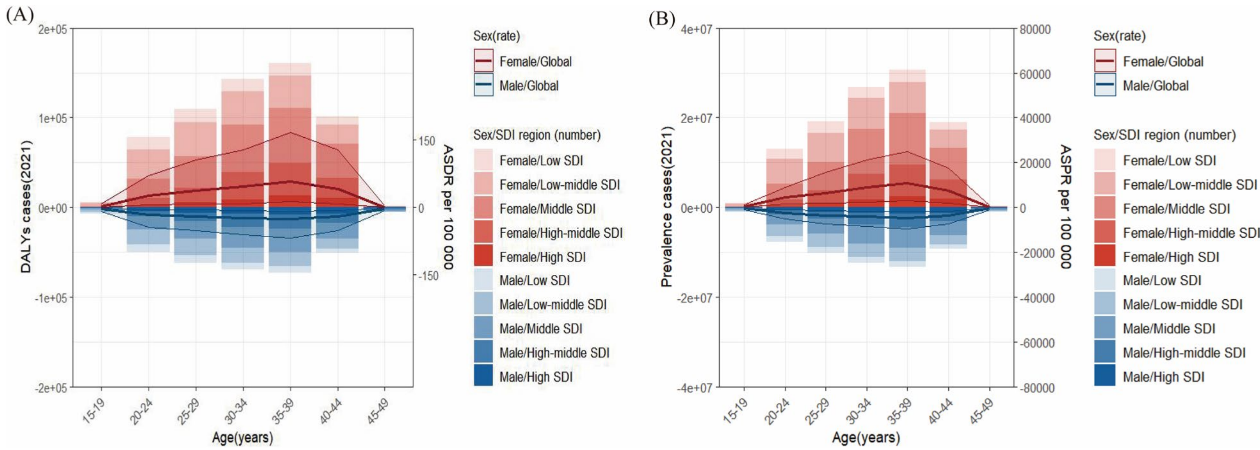

Fig. 4 Burden of infertility by age groups. **a** ASPR by age groups in 2021; **b** ASDR by age groups in 2021. ASPR, age-standardised prevalence rate; ASDR, age-standardised DALYs rate

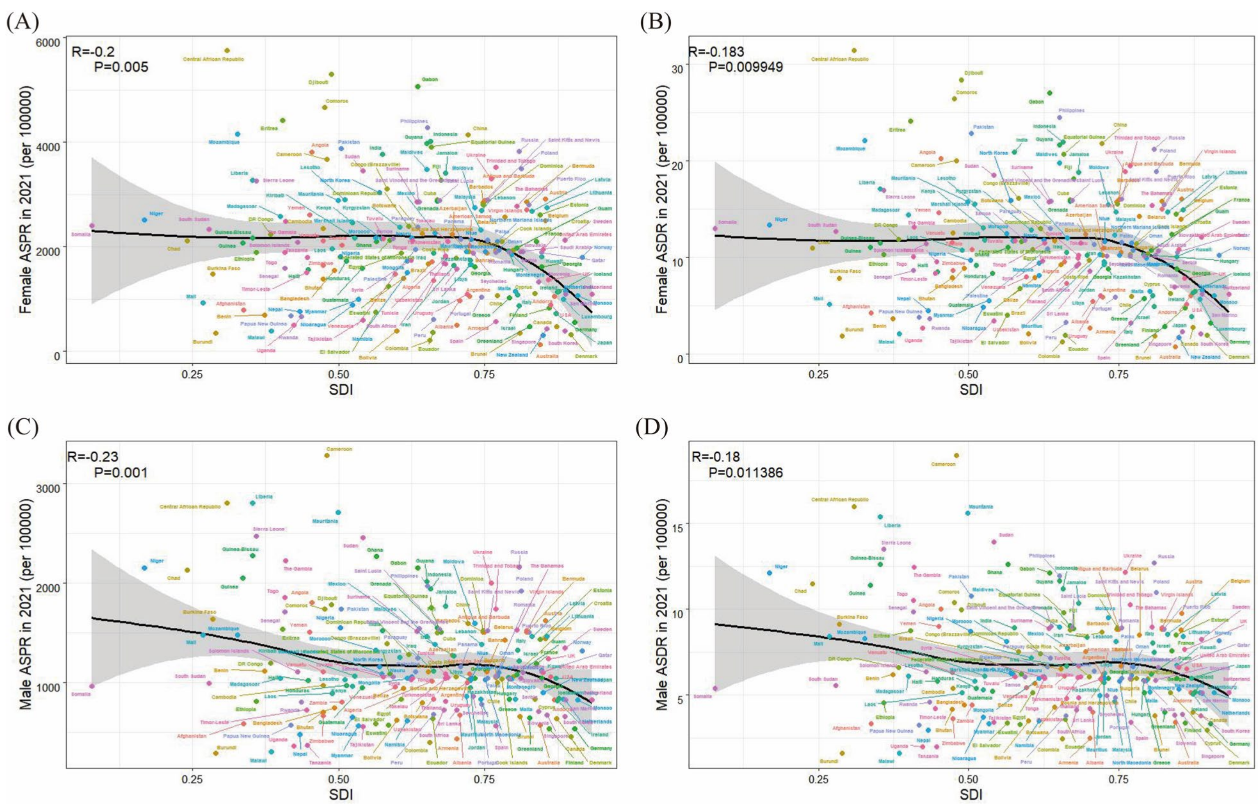

Fig. 5 The interplay between the Socio-demographic Index (SDI) and the standardized prevalence rates as well as Disability-Adjusted Life Years (DALYs) rates of infertility was scrutinized in a global context, encompassing 204 countries and regions for the year 2021 (**a**: ASPR of female infertility. **b**: ASDR of female infertility. **c**: ASPR of male infertility. **d**: ASDR of male infertility. ASPR, age-standardised prevalence rate; ASDR, age-standardised DALYs rate)

then rising again with continued increases in SDI (Figure S2c, d). Conversely, in the East Asia region, both male and female infertility ASPR and ASDR initially showed a gradual increase alongside rising SDI, and then remained relatively stable despite further increases in SDI (Figure S2a–d).

Decomposition analysis

We observed a significant increase in the global burden of infertility (Figures S3a–d; Table S3, S4, S5 and S6), primarily due to population growth, which accounts for about 65% of the increase (Table S3, S4, S5 and S6). Among low-middle SDI countries, the highest prevalence and DALYs burden were observed, and these countries experienced the largest increase in prevalence and DALYs burden from 1990 to 2021 (Figure S3a–d; Table S3, S4, S5 and S6), with population growth contributing approximately 50% (Table S3, S4, S5 and S6). In terms of growth, high-middle SDI and high SDI countries were the last two (Figures S3a–d), with aging populations showing a negative contribution, and the main contribution still being population growth (Table S3, S4, S5 and S6). However, the increase in Prevalence and DALYs burden for female infertility in high SDI regions was mainly due to epidemiological changes (Table S4 and S6). From 1990 to 2021, in terms of GBD regions, South Asia ranked first in both Prevalence and DALYs burden for infertility, primarily due to population growth, which accounted for about 55% (Table S3, S4, S5 and S6). Following closely were North Africa and the Middle East and Southeast Asia, with different contribution ratios (Table S3, S4, S5 and S6). In the North Africa and the Middle East region, aging populations showed a negative contribution, with the main contribution being population growth (Table S3, S4, S5 and S6). The Southeast Asia region was similar to the low-middle SDI region, with population increase contributing about 50% (Table S3, S4, S5 and S6). In the High-income Asia Pacific and Eastern Europe regions, there were a negative growth in Prevalence and DALYs burden for female infertility, with the High-income Asia Pacific region mainly due to contributions from aging populations and epidemiological changes, and the Eastern Europe region mainly due to contributions from aging populations and population growth (Table S4 and S6). Similarly, a negative growth in Prevalence and DALYs burden for male infertility was observed in Central Europe, High-income Asia Pacific, and Eastern Europe regions, with Central Europe and Eastern Europe regions mainly due to contributions from aging populations and population growth, and the High-income Asia Pacific region mainly due to contributions from aging populations and epidemiological changes (Table S3 and S5).

At the national level, the countries with the most significant positive contributions to the increased burden of infertility are India, China, and Indonesia. India and Indonesia are mainly due to population growth and epidemiological changes, with both factors contributing roughly equally (Table S3, S4, S5 and S6). China's primary contribution is due to population growth, with the contribution from population growth far exceeding that from epidemiological changes, while aging populations show a negative contribution (Table S3, S4, S5 and S6). Regarding female infertility, the Russian Federation has the most significant negative contribution, followed by Japan, Ukraine, and Myanmar (Table S4 and S6). The negative growth in the burden of infertility in the Russian Federation and Japan is mainly due to aging populations, with the contribution from aging populations far exceeding that from population growth and epidemiological changes (Table S3, S4, S5 and S6). Ukraine's contribution is mainly due to population growth, while Myanmar's is primarily due to epidemiological changes (Table S3, S4, S5 and S6).

Frontier analysis

As the SDI increases, we observe that the efficiency frontier differences for specific SDI levels decrease (Figure S4a–h). Once the SDI exceeds approximately 0.495, the trends in the frontier ASPR and ASDR for female infertility become stable (Figure S4a–d). The top 5 countries/regions with the highest efficiency frontier differences for female infertility ASDR frontier are the Central African Republic, Djibouti, Comoros, Gabon, and Indonesia (Figure S4b). For female infertility ASPR frontier, the top 5 countries/regions with the highest efficiency frontier differences are the Central African Republic, Djibouti, Comoros, Gabon, and Eritrea (Figure S4d). Once the SDI exceeds approximately 0.46, the trends in the frontier ASPR and ASDR for male infertility become stable (Figure S4e–h). The top 5 countries/regions with the highest efficiency frontier differences for male infertility ASDR and ASPR frontiers are Cameroon, Central African Republic, Mauritania, Liberia, and Sudan (Figure S4f, h). Compared to countries with similar socio-demographic conditions, these countries/regions have significantly higher infertility ASPR and ASDR (Figure S4b–h). Conversely, Austria, Taiwan, and Pakistan have significantly lower female infertility ASPR and ASDR under the same socio-demographic conditions (Figure S4b, d). The Russian Federation, Guinea-Bissau, and Cabo Verde have significantly lower male infertility ASPR and ASDR under similar socio-demographic conditions (Figure S4f, h). In high SDI regions, Sweden, Belgium, Lithuania, Taiwan, and Austria have significantly decreased female infertility ASPR and ASDR (Figure S4B, D). Similarly, in high SDI regions, Sweden, Belgium, Lithuania, Norway, and Austria have significantly decreased male infertility ASPR and ASDR (Figure S4f, h). Countries with increasing ASPR and ASDR for infertility are primarily located in regions/countries with a SDI between 0.6 and 0.8, while countries with decreasing rates are mainly in areas/countries with an SDI between 0.7 and 0.9, indicating that there are different trends among countries with similar SDI levels and a considerable degree of heterogeneity exists (Figure S4b–h).

Projecting disease burden

The study anticipates the ASRs for infertility gender in both males and females from 2022 to 2036. It highlights that the ASPR and ASDR associated with infertility for both genders are expected to show an increase on a global scale (Fig. 6). Notably, the United States, which is the largest developed country, is experiencing a downward trend in both the ASPR and ASDR concerning infertility, particularly in relation to female infertility (Figure S5). Similarly, China, being one of the largest economies in the emerging world, exhibits comparable patterns (Figure S6). This occurrence could be attributed to China's rapid economic growth in recent years, heightened cultural awareness within its population, efficient AIDS prevention measures, and increased public awareness regarding infertility matters.

Discussion

This research offers an in-depth examination of the worldwide epidemiology, enduring trends, and regional variations in the prevalence of infertility, utilizing data derived from the GBD 2021. Our results reveal a significant increase in the global rates of infertility from 1990 to 2021, primarily due to population growth, which accounts for about 65% of the increase. The ASPR and ASDR for infertility were noticeably higher in females than in males. In 2021, the areas with the highest ASPR for both genders experiencing infertility were identified as the high-middle SDI and middle SDI regions, while the lowest ASPR was observed in the high SDI area. Among individual SDI countries, the highest prevalence and DALYs burden were observed in low-middle SDI countries, which experienced the largest expansion in prevalence and DALYs burden from 1990 to 2021. Population growth contributed approximately 50% to this expansion. Regionally, the prevalence of infertility displayed significant variation, with East Asia experiencing the highest rates. Specifically, in 2021, East Asia and Eastern Europe reported the peak ASPR and ASDR for infertility. But, with Eastern Europe region, there was a negative growth in Prevalence and DALYs burden for infertility, mainly due to contributions from aging populations and population growth. From 1990 to 2021, South Asia ranked first in both Prevalence and DALYs burden for infertility, primarily due to population growth, which accounted for about 55%. Following closely were North

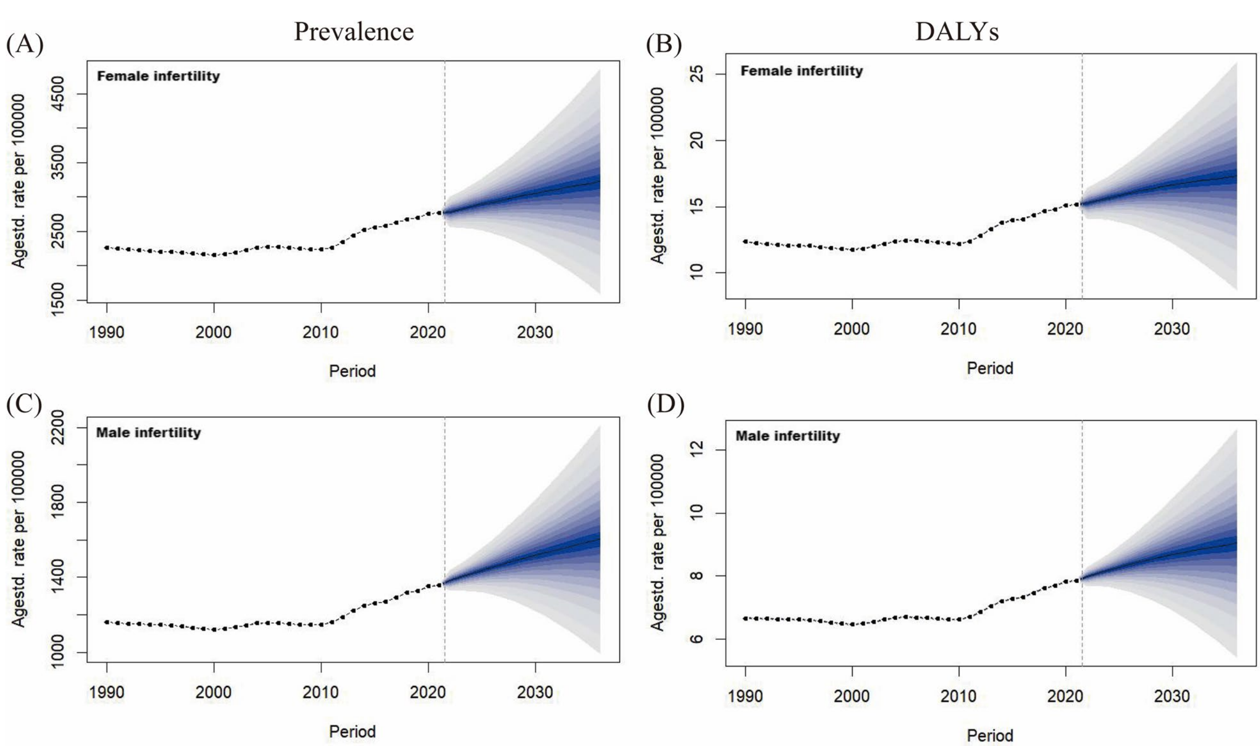

Fig. 6 The global ASR of infertility was assessed from 1990 to 2021, with forecasted ASRs values projected for the period from 2022 to 2036, including the age-standardized prevalence rate and disability-adjusted life years rate. (**a**: ASPR of female infertility. **b**: ASDR of female infertility. **c**: ASPR of male infertility. **d**: ASDR of male infertility. ASPR, age-standardised prevalence rate; ASDR, age-standardised DALYs rate)

Africa and the Middle East and Southeast Asia. In the high-income Asia–Pacific, Central and Eastern Europe regions, the prevalence of infertility and the burden of DALYs are negatively increasing, with population ageing being the common leading cause. Andean Latin America exhibited the highest EAPC of ASPR and ASDR for infertility. In 2021, India held the top position among 204 countries and territories for infertility prevalence cases and DALYs, with China and Indonesia following closely. India and Indonesia are mainly due to population growth and epidemiological changes, with both factors contributing roughly equally. China's primary contribution is due to population growth, with the contribution from population growth far exceeding that from epidemiological changes, while aging populations show a negative contribution. The three countries and regions with the highest infertility ASPR and ASDR are all located in Africa, and these countries have increased the burden of infertility disease to varying degrees, and the increase in their disease burden is mainly due to population growth, although the increase in infertility disease burden in these countries is not the highest. Infertility continues to pose a serious and ongoing challenge in populous countries as well as in economically underdeveloped regions.

In 2021, we observed a slight negative correlation between infertility ASPR and ASDR and the SDI in 204 countries and regions. As the SDI increases, we observe that the efficiency frontier differences for specific SDI levels decrease. Once the SDI exceeds approximately 0.495, the trends in the frontier ASPR and ASDR for female infertility become stable. Once the SDI exceeds approximately 0.46, the trends in the frontier ASPR and ASDR for male infertility become stable. Countries with increasing ASPR and ASDR for infertility are primarily located in regions/countries with a SDI between 0.6 and 0.8, while countries with decreasing rates are mainly in areas/countries with an SDI between 0.7 and 0.9, indicating that there are different trends among countries with similar SDI levels and a considerable degree of heterogeneity exists.

China, as the second most populous country and the largest emerging economy, has seen a decline in fertility rates in recent years, gradually entering an era of aging population. Infertility significantly affects its population growth. Additionally, China's SDI is 0.719, classifying it as a High-middle SDI nation. China has the largest population in the High-middle SDI region, and predicting the trend of infertility in China could be highly representative for the disease burden in this region, playing a certain role in curbing global infertility diseases. The United States, as the world's largest economy and the largest developed country, is a nation of immigrants with cultural and racial diversity, and it ranks third in global population size. Predicting the outcomes of infertility in the United States could be strongly representative for developed countries. Although infertility is also a prominent issue in African countries, the EAPC for infertility ASPR and ASDR in the top three African populous nations—Nigeria, the Democratic Republic of the Congo, and Ethiopia—are all experiencing negative growth. Moreover, the main countries contributing to infertility ASPR and ASDR are in the Middle SDI and High-middle SDI regions, while most African countries are in the Low SDI and Low-middle SDI regions. To ensure the completeness and comprehensiveness of our predictions, we have also included disease forecasts for India. As the world's most populous country, India accounts for approximately 17.99% of the global population and has the highest number of infertility cases globally. With an SDI of 0.578, India is classified as a Low-middle SDI nation, and its prediction results could be representative for the Low and Low-middle regions. Predictions indicate that from 2022 to 2036, a worldwide increase in the ASPR and ASDR related to infertility among both genders is anticipated. This research provides essential data to assist policymakers and health authorities in developing focused approaches for preventing and managing infertility.

The study showed that the probability of experiencing infertility increases with age for both genders. The age of women is an unalterable risk factor, associated with the gradual reduction in the number of oocytes within the ovaries and the continuous decline in their chromosomal and structural integrity [44]. Moreover, factors such as the age at which individuals marry and the age of initial sexual activity may exert a more significant influence on primary infertility than age itself [45]. Furthermore, various studies have suggested that unhealthy lifestyle choices can also lead to infertility. These risk factors linked to lifestyle encompass: being overweight and engaging in excessive physical activity [46, 47]; experiencing physical, social, or psychological stress [48]; tobacco smoking [49]; alcohol intake [50]; use of illicit drugs [51]; and improper timing of sexual intercourse intended for reproduction [52]. There is accumulating evidence concerning the impact of infectious agents on fertility. In women, these agents may cause pelvic inflammatory disease and blockages in the fallopian tubes [53, 54], while in men, they could result in organ damage, create blockages, or provoke cell damage through inflammatory mediators or by attaching to sperm [55]. Sub-Saharan Africa has a high prevalence of HIV and urogenital infections, with prior studies reporting that nearly 30% of infertile women in the region experience tubal factors [56]. The 'Global Health Sector Strategy on sexually transmitted infections, 2016–2021' was created by the WHO, with the objective of eradicating sexually transmitted infection epidemics as a significant public health concern by the year 2030 [57]. Developing nations experience a higher infertility rate, primarily due to sexually transmitted infections and insufficient access to modern medical services [58]. A lack of awareness among participants regarding the natural decline in female fertility with age could potentially heighten infertility risks [27]. There is a necessity for greater dissemination of information about the risk factors associated with secondary infertility and for establishing more diagnostic facilities for infertility at rural health centers [59]. Public health organizations and reproductive health experts must advocate for age-appropriate practices regarding marriage and childbirth, conduct timely medical evaluations for cases of suspected infertility, and promote a healthy lifestyle as the next steps [45].

In addition The availability and quality of infertility services vary widely, often influenced by socioeconomic factors, cultural norms, and healthcare policies [60, 61]. In Iran, the significant geographic disparity in the number of infertility centers, with Tehran having 21 and other provinces having none to two, means that residents in less populated areas may have limited or no access to necessary treatments, potentially leading to delays in seeking care and increased stress for infertile couples [62]. Addition, the absence of a national registry and auditing system for infertility services, coupled with the lack of a structured referral system, hinders effective resource allocation and policy implementation, as it makes it difficult to gather comprehensive data on service success rates and availability, and can lead to an overestimation of service utilization by counting patients multiple times across different centers, thereby masking the true demand for infertility care [62].

Financial barriers significantly contribute to the inequitable distribution of infertility services, as healthcare systems, already burdened by competing priorities like infectious diseases and maternal health, tend to sideline infertility care [63, 64]. This lack of prioritization leads to limited financial resources allocated for infertility treatments, making them prohibitively expensive for many couples [61]. In the United States, infertility is not classified as a disease by the government, which results in inadequate support and coverage for those seeking treatment [65]. Consequently, many individuals face high out-of-pocket costs, which can deter them from pursuing necessary medical interventions [61]. While only 18 US states have enacted mandates requiring insurance coverage for fertility treatments, a significant portion of the population remains uninsured or underinsured, complicating their access to care [62]. Integrating infertility services into primary healthcare can help ensure that individuals receive the support they need without facing overwhelming financial barriers [61, 66].

Several limitations of this research must be recognized. Firstly, the methodological restrictions present in the GBD 2021 investigation could influence the precision and the overall scope of the model's assessments. The absence of infertility data from specific countries and regions has a significant effect on these outcomes. Furthermore, discrepancies in data quality, precision, and comparability may lead to biases [46, 47]. Secondly, rather than relying on actual data from the real world, the GBD 2021 database utilizes model fitting, which may result in either an overestimation or underestimation of the rates. Thirdly, infertility rates in 204 countries and regions were appraised with the aid of a globally consistent population standard to boost comparability; however, these standardized metrics may not accurately depict the actual disease burden of infertility in each nation. Fourthly, the EAPC identifies the typical progression observed in the last 30 years, leaving aside any doubts connected with these rates. Although the EAPC is suitable for detecting linear trends, it could provide incorrect insights when dealing with non-linear rate changes, such as U-shaped, V-shaped, or L-shaped curves. Lastly, an all-encompassing examination of the disease's burden necessitates the inclusion of a broader spectrum of economic, family-centric, and societal impacts. This research did not conduct an in-depth analysis of all potential elements influencing the infertility burden.

Conclusion

This comprehensive study utilizing data from the GBD 2021 provides a detailed overview of the global epidemiological landscape of infertility, highlighting significant increases in prevalence and burden from 1990 to 2021. The findings underscore the critical role of population growth as a primary driver of the observed increases, accounting for approximately 65% of the rise in infertility rates globally. Notably, the ASPR and ASDR for infertility are consistently higher in females compared to males, reflecting the complex interplay of biological and sociodemographic factors influencing reproductive health outcomes. The decomposition analysis highlights the substantial impact of population growth on the global burden of infertility, with epidemiological changes and aging populations also playing significant roles in certain regions and countries. Frontier analysis further elucidates the disparities in infertility burden among countries with similar socio-demographic conditions, emphasizing the need for tailored interventions and policies to address these variations. In conclusion, infertility poses a significant global health challenge, with substantial implications for individuals, families, and societies. Addressing this issue requires a multifaceted approach, encompassing improved access to fertility treatments, enhanced public awareness campaigns, and targeted public health policies. By understanding the complex dynamics influencing infertility prevalence and burden, policymakers and healthcare providers can develop more effective strategies to mitigate this growing health concern and improve reproductive health outcomes worldwide.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12978-025-01966-7.

Additional file 1.

Acknowledgements
We express our deep gratitude to those collaborators who have provided valuable support and made efforts in the Global Burden of Disease Study 2021.

Author contributions
J L F was tasked with the formulation of the manuscript's foundational concepts and its structural design. The thorough literature review and the procurement of data were the domain of Q G W and Y B L. The in-depth analysis and the elucidation of the data were executed by J L F and Y W L, who were also in charge of preparing the manuscript's tables and figures. The initial drafting, thorough proofreading, and comprehensive interpretation of the manuscript were collaboratively managed by J L F, Q G W, and Q B, with Q B identified as the corresponding author. All authors were actively involved in the data analysis, interpretation, discussion, and manuscript writing, and they all reviewed and gave their approval to the final version of the paper.

Funding
Not applicable.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Urology Department, Gui Gang People's Hospital, Eighth Affiliated Hospital of Guangxi Medical University, Guigang 537100, Guangxi Zhuang Autonomous Region, China.

Received: 4 November 2024 Accepted: 7 February 2025
Published online: 19 February 2025

References

1. World Health Organization. Infertility Fact Sheet. 2024; https://www.who.int/news-room/factsheets/detail/infertility#:~:text=Infertility/is/a/disease/of,causes/of/infertility/are/preventable
2. Inhorn MC, Patrizio P. Infertility around the globe: new thinking on gender, reproductive technologies and global movements in the 21st century. Hum Reprod Update. 2015;21(4):411–26. https://doi.org/10.1093/humupd/dmv016.
3. Harris E. Infertility affects 1 in 6 people globally. JAMA. 2023;329(17):1443. https://doi.org/10.1001/jama.2023.6251.
4. Qiao J, Wang Y, Li X, et al. A lancet commission on 70 years of women's reproductive, maternal, newborn, child, and adolescent health in China. Lancet. 2021;397(10293):2497–536. https://doi.org/10.1016/S0140-6736(20)32708-2.
5. Chandra A, Copen CE, 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;67:1–19.
6. GBD 2017 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017 [published correction appears in Lancet. 2019 Jun 22;393(10190):e44. https://doi.org/10.1016/S0140-6736(19)31043-8]. Lancet. 2018;392(10159):1859–1922. https://doi.org/10.1016/S0140-6736(18)32335-3
7. Naab F, Lawali Y, Donkor ES. "My mother in-law forced my husband to divorce me": Experiences of women with infertility in Zamfara State of Ni-geria. PLoS One. 2019;14(12):225149. https://doi.org/10.1371/journal.pone.0225149 Published 2019 Dec 19
8. Bornstein M, Gipson JD, Failing G, Banda V, Norris A. Individual and community-level impact of infertility-related stigma in Malawi. Soc Sci Med. 2020;251: 112910. https://doi.org/10.1016/j.socscimed.2020.112910.
9. Qi J, Sun M, Yue X, Hong X, Dong M, Tan J. The impact of COVID-19 on the mental and sexual health of patients with infertility: a prospective before-and-after study. Reprod Biol Endocrinol. 2024;22(1):1. https://doi.org/10.1186/s12958-023-01174-7. Published 2024 Jan 2.
10. Dong M, Wu S, Tao Y, Zhou F, Tan J. The Impact of Postponed Fertility Treatment on the Sexual Health of Infertile Patients Owing to the COVID-19 Pandemic. Front Med (Lausanne). 2021;8:730994. https://doi.org/10.3389/fmed.2021.730994. Published 2021 Dec 10.
11. Murugappan G, Li S, Alvero RJ, Luke B, Eisenberg ML. Association between infertility and all-cause mortality: analysis of US claims data. Am J Obstet Gynecol. 2021;225(1):57.e1-57.e11. https://doi.org/10.1016/j.ajog.2021.02.010.
12. Kamath MS, Joseph T, Karuppusami R, et al. Knowledge, anxiety levels and attitudes of infertile couples towards COVID-19 and its impact on self-funded fertility treatment: a cross-sectional questionnaire survey. Hum Reprod Open. 2021;2021(4):hoab039. https://doi.org/10.1093/hropen/hoab039. Published 2021 Oct 22.
13. Njagi P, Groot W, Arsenijevic J, Dyer S, Mburu G, Kiarie J. Financial costs of assisted reproductive technology for patients in low- and middle-income countries: a systematic review. Hum Reprod Open. 2023;2023(2):hoad007. https://doi.org/10.1093/hropen/hoad007. Published 2023 Mar 1.
14. Olive E, Bull C, Gordon A, Davies-Tuck M, Wang R, Callander E. Economic evaluations of assisted reproductive technologies in high-income countries: a systematic review. Hum Reprod. 2024;39(5):981–91. https://doi.org/10.1093/humrep/deae039.
15. Aassve A, Cavalli N, Mencarini L, Plach S, Sanders S. Early assessment of the relationship between the COVID-19 pandemic and births in high-income countries. Proc Natl Acad Sci USA. 2021;118(36): e2105709118. https://doi.org/10.1073/pnas.2105709118.
16. Wang Y, Fu Y, Ghazi P, et al. Prevalence of intimate partner violence aga- inst infertile women in low-income and middle-income countries: a syste- matic review and meta-analysis. Lancet Glob Health. 2022;10(6):e820–30. https://doi.org/10.1016/S2214-109X(22)00098-5.
17. Yu J, Fu Y, Zeng L, Xie P, Li L, Zheng Y. Burden of female infertility in China from 1990 to 2019: a temporal trend analysis and forecasting, and comparison with the global level. Sex Health. 2023;20(6):577–84. https://doi.org/10.1071/SH23029.
18. Liu J, Han W, Wang H, Wang Z, Li B, Hong L. Spatiotemporal trends and age-period-cohort analysis for the burden of endometriosis-related infertility: an analysis of the global burden of disease study 2019. J Pers Med. 2023;13(9):1284. https://doi.org/10.3390/jpm13091284. Published 2023 Aug 22.
19. Shen D, Yang S, Qi C, Yang H. Global, regional, and national prevalence and disability-adjusted life-years for female infertility: results from a global burden of disease study, 1990–2019. Gynecol Obstet Invest. https://doi.org/10.1159/000542408. Published online November 21, 2024.
20. Wang Y, Wang W, Li H, Du Q. Trends in the burden of female infertility among adults aged 20–49 years during 1990–2019: an analysis

of data from the Global Burden of Disease Study 2019. BMJ Open. 2024;14(7):e084755. https://doi.org/10.1136/bmjopen-2024-084755. Published 2024 Jul 30.
21. Liu X, Zhang J, Wang S. Global, regional, and national burden of infertile-ty attributable to PCOS, 1990–2019. Hum Reprod. 2024;39(1):108–18. https://doi.org/10.1093/humrep/dead241.
22. Shen D, Wang Y, Hu P, Qi C, Yang H. Analyzing the infertility burden of polycystic ovarian syndrome in China: A comprehensive age-period-cohort analysis with future burden prediction (1990–2030). Gynecol Endocrinol. 2024;40(1):2362251. https://doi.org/10.1080/09513590.2024.2362251.
23. Huang B, Wang Z, Kong Y, Jin M, Ma L. Global, regional and national burden of male infertility in 204 countries and territories between 1990 and 2019: an analysis of global burden of disease study. BMC Public Health. 2023;23(1):2195. https://doi.org/10.1186/s12889-023-16793-3. Published 2023 Nov 8.
24. Sun H, Gong TT, Jiang YT, Zhang S, Zhao YH, Wu QJ. Global, regional, and national prevalence and disability-adjusted life-years for infertility in 195 countries and territories, 1990–2017: results from a global burden of disease study, 2017. Aging (Albany NY). 2019;11(23):10952–10991. https://doi.org/10.18632/aging.102497
25. Borumandnia N, Alavi Majd H, Khadembashi N, Alaii H. Worldwide trend analysis of primary and secondary infertility rates over past decades: a cross-sectional study. Int J Reprod Biomed. 2022;20(1):37–46. https://doi.org/10.18502/ijrm.v20i1.10407. Published 2022 Feb 18.
26. Shu J, Jin W. Prioritizing non-communicable diseases in the post-pandemic era based on a comprehensive analysis of the GBD 2019 from 1990 to 2019. Sci Rep. 2023;13(1):13325. https://doi.org/10.1038/s41598-023-40595-7. Published 2023 Aug 16.
27. Xi JY, Lin X, Hao YT. Measurement and projection of the burden of dise-ase attributable to population aging in 188 countries, 1990–2050: A populat-ion-based study. J Glob Health. 2022;12:04093. https://doi.org/10.7189/jogh.12.04093. Published 2022 Oct 30.
28. Wang C, Yang X, Zhang H, et al. Temporal trends in mortality of tuberculosis attributable to high fasting plasma glucose in China from 1990 to 2019: a joinpoint regression and age-period-cohort analysis. Front Public Health. 2023;11:1225931. https://doi.org/10.3389/fpubh.2023.1225931. Published 2023 Jul 27.
29. Bazargan-Hejazi S, Dehghan K, Edwards C, et al. The health burden of n-on-communicable neurological disorders in the USA between 1990 and 2017. Brain Commun. 2020;2(2):fcaa097. https://doi.org/10.1093/braincomms/fcaa097. Published 2020 Jul 9.
30. Khan MAB, Hashim MJ, King JK, Govender RD, Mustafa H, Al KJ. Epidemiology of type 2 diabetes—global burden of disease and Forecas- ted Trends. J Epidemiol Glob Health. 2020;10(1):107–11. https://doi.org/10.2991/jegh.k.191028.001.
31. Yang R, Zhang X, Bai J, Wang L, Wang W, Cai J. Global, regional, and national burden of hypertensive heart disease among older adults in 204 countries and territories between 1990 and 2019: a trend analysis. Chin Med J (Engl). 2023;136(20):2421–30. https://doi.org/10.1097/CM9.0000000000002863.
32. Dupont C, Aegerter P, Foucaut AM, et al. Effectiveness of a therapeutic multiple-lifestyle intervention taking into account the periconceptional environment in the management of infertile couples: study design of a randomized controlled trial - the PEPCI study. BMC Pregnancy Childbirth. 2020;20(1):322. https://doi.org/10.1186/s12884-020-2855-9. Published 2020 May 26.
33. Global burden and strength of evidence for 88 risk factors in 204 countries and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. The Lancet. 2024;403(10440):2162–2203. https://doi.org/10.1016/s0140-6736(24)00933-4
34. GBD 2021 Diseases and Injuries Collaborators. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2024;403(10440):2133–2161. https://doi.org/10.1016/S0140-6736(24)00757-8
35. Kundu S, Ali B, Dhillon P. Surging trends of infertility and its behavioural determinants in India. PLoS One. 2023;18(7):e0289096. https://doi.org/10.1371/journal.pone.0289096. Published 2023 Jul 25.
36. Hoy DG, Smith E, Cross M, et al. Reflecting on the global burden of musculoskeletal conditions: lessons learnt from the global burden of disease 2010 study and the next steps forward. Ann Rheum Dis. 2015;74(1):4–7. https://doi.org/10.1136/annrheumdis-2014-205393.
37. Zegers-Hochschild F, Adamson GD, Dyer S, 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.
38. Murugappan G, Leonard SA, Farland LV, et al. Association of infertility w-ith atherosclerotic cardiovascular disease among postmenopausal participants in the Women's Health Initiative. Fertil Steril. 2022;117(5):1038–46. https://doi.org/10.1016/j.fertnstert.2022.02.005.
39. GBD 2021 Rheumatoid Arthritis Collaborators. Global, regional, and nation-al burden of rheumatoid arthritis, 1990–2020, and projections to 2050: a sy-stematic analysis of the Global Burden of Disease Study 2021. Lancet Rh Eumatol. 2023;5(10):e594-e610. https://doi.org/10.1016/S2665-9913(23)00211-4. Published 2023 Sep 25
40. Wang Y, Jing W, Liu J, Liu M. Global trends, regional differences and age distribution for the incidence of HIV and tuberculosis co-infection from 1990 to 2019: results from the global burden of disease study 2019. Infect Dis (Lond). 2022;54(11):773–83. https://doi.org/10.1080/23744235.2022.2092647.
41. Xie Y, Bowe B, Mokdad AH, et al. Analysis of the Global Burden of Di- sease study highlights the global, regional, and national trends of chronic kidney disease epidemiology from 1990 to 2016. Kidney Int. 2018;94(3):567–81. https://doi.org/10.1016/j.kint.2018.04.011.
42. Zhang T, Sun L, Yin X, Chen H, Yang L, Yang X. Burden of drug use disorders in the United States from 1990 to 2021 and its projection until 2035: results from the GBD study. BMC Public Health. 2024;24(1):1639. https://doi.org/10.1186/s12889-024-19142-0. Published 2024 Jun 19.
43. Wang W, Wang Y, Wang F, et al. Notable dysthymia: evolving trends of major depressive disorders and dysthymia in China from 1990 to 2019, and projections until 2030. BMC Public Health. 2024;24(1):1585. https://doi.org/10.1186/s12889-024-18943-7. Published 2024 Jun 13.
44. Leridon H. Can assisted reproduction technology compensate for the natura-l decline in fertility with age? A model assessment. Hum Reprod. 2004;19(7):1548–53. https://doi.org/10.1093/humrep/deh304.
45. Liang S, Chen Y, Wang Q, et al. Prevalence and associated factors of infertility among 20–49 year old women in Henan Province, China. Reprod Health. 2021;18(1):254. https://doi.org/10.1186/s12978-021-01298-2. Published 2021 Dec 20.
46. Tang J, Xu Y, Wang Z, et al. Association between metabolic healthy obesity and female infertility: the national health and nutrition examination surv-ey, 2013–2020. BMC Public Health. 2023;23(1):1524. https://doi.org/10.1186/s12889-023-16397-x. Published 2023 Aug 10.
47. Zhang H, Hua L, Liu D, Su X, Chen J, Chen J. Effects of physical activity on infertility in reproductive females. Reprod Biol Endocrinol. 2024;22(1):62. https://doi.org/10.1186/s12958-024-01234-6. Published 2024 May 29.
48. Jesse E, Tay K, Sellke N, et al. (200) The fertility and childbearing experiences of US male physicians. J Sex Med. 2024;21(Supplement_1):0–0. https://doi.org/10.1093/jsxmed/qdae001.190
49. He S, Wan L. Associations between smoking status and infertility: a cross- sectional analysis among USA women aged 18–45 years. Front Endocrinol (Lausanne). 2023;14:1140739. https://doi.org/10.3389/fendo.2023.1140739. Published 2023 Apr 19.
50. Xu W, You Y, Yu T, Li J. Insights into modifiable risk factors of infertility: a mendelian randomization study. Nutrients. 2022;14(19):4042. https://doi.org/10.3390/nu14194042. Published 2022 Sep 28.
51. Mueller BA, Daling JR, Weiss NS, Moore DE. Recreational drug use and the risk of primary infertility. Epidemiology. 1990;1(3):195–200. https://doi.org/10.1097/00001648-199005000-00003.
52. Wilcox AJ, Weinberg CR, Baird DD. Timing of sexual intercourse in relation to ovulation. Effects on the probability of conception, survival of the pregnancy, and sex of the baby. N Engl J Med. 1995;333(23):1517–1521. https://doi.org/10.1056/NEJM199512073332301
53. Ravel J, Moreno I, Simón C. Bacterial vaginosis and its association with infertility, endometritis, and pelvic inflammatory disease. Am J Obstet Gynecol. 2021;224(3):251–7. https://doi.org/10.1016/j.ajog.2020.10.019.
54. Duan G, Wei Z, Zhang J, et al. NIR-II fluorescence nanoprobe based on Erbium for fallopian tube diseases diagnosis. Mater Des. 2023;227:111726–111726. https://doi.org/10.1016/j.matdes.2023.111726.

55. Ochsendorf FR. Sexually transmitted infections: impact on male fertility. Andrologia. 2008;40(2):72–5. https://doi.org/10.1111/j.1439-0272.2007.00825.x.
56. Farquhar CM, Bhattacharya S, Repping S, et al. Female subfertility. Nat Rev Dis Primers. 2019;5(1):7. https://doi.org/10.1038/s41572-018-0058-8. Published 2019 Jan 24.
57. World Health Organization. Global health sector strategy on sexually transmitted infections, 2016–2021. Available:http://apps.who.int/iris/bitstream/handle/10665/246296/WHO-RHR-16.09-eng.pdf;jsessionid=51BFC17A28B76FCF246AACEBF08826DD?s-equence=1
58. Vayena E, Rowe PJ, Peterson HB. Assisted reproductive technology in dev-eloping countries: Why should we care? Fertil Steril. 2002;78(1):13–5. https://doi.org/10.1016/s0015-0282(02)03177-1.
59. Patra S, Unisa S. Addressing reproductive health knowledge, infertility and coping strategies among rural women in India. J Biosoc Sci. 2021;53(4):557–65. https://doi.org/10.1017/S0021932020000371.
60. Blakemore JK, Maxwell SM, Hodes-Wertz B, Goldman KN. Access to infertility care in a low-resource setting: bridging the gap through resident and fellow education in a New York City public hospital. J Assist Reprod Genet. 2020;37(7):1545–52. https://doi.org/10.1007/s10815-020-01781-y.
61. Morshed-Behbahani B, Lamyian M, Joulaei H, Rashidi BH, Montazeri A. Infertility policy analysis: a comparative study of selected lower middle- middle- and high-income countries. Global Health. 2020;16(1):104. https://doi.org/10.1186/s12992-020-00617-9. Published 2020 Oct 23.
62. Abedini M, Ghaheri A, Omani Samani R. Assisted reproductive technology in Iran: the first national report on centers, 2011. Int J Fertil Steril. 2016;10(3):283–289. https://doi.org/10.22074/ijfs.2016.5044
63. Mackenbach JP, McKee M. A comparative analysis of health policy performance in 43 European countries. Eur J Public Health. 2013;23(2):195–201. https://doi.org/10.1093/eurpub/cks192.
64. Ogura S, Jakovljevic MM. Editorial: global population aging-health care, social and economic consequences. Front Public Health. 2018;6:335. https://doi.org/10.3389/fpubh.2018.00335. Published 2018 Nov 20.
65. Kissin DM, Boulet SL, Jamieson DJ. Assisted reproductive technology surveillance and research team. Fertility treatments in the united states: improving access and outcomes. Obstet Gynecol. 2016;128(2):387–390. https://doi.org/10.1097/AOG.0000000000001419
66. Oppenheimer D, Rego F, Nunes R. The search for the principle of justice for infertile couples: characterization of the brazilian population and bioethical discussion. BMC Med Ethics. 2023;24(1):69. https://doi.org/10.1186/s12910-023-00947-4. Published 2023 Sep 4.

Publisher's Note