# Epidemiological trends, disparities, and developmental correlates of infertility in women of advanced maternal age, 1990–2023: a comprehensive analysis within the GBD framework

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## Summary

**Background** With the acceleration of global population ageing, female infertility among women of advanced reproductive age of 35–49 years has become a severe public health issue, carrying significant economic implications for women, families, and health-care systems, as rising treatment costs and productivity losses highlight the urgency of integrated health and economic policy responses. This study aims to investigate the epidemiological trends, regional and national disparities, and the development potential related to advanced-age female infertility, as well as to project the future burden up to 2036.

**Methods** We used data from the Global Burden of Disease 2023 study, which covered 204 countries and regions from 1990 to 2023. Core indicators included age-standardised prevalence rate (ASPR) and disability-adjusted life-years (DALYs) specific to women of advanced reproductive age. First, we conducted multilevel trend analyses (eg, global, regional, and national) and applied health equity indicators to quantify transnational disparities. Subsequently, frontier analysis determined the minimum achievable disease burden according to the Socio-demographic Index (SDI). Finally, a Bayesian age-period-cohort model was used to project trends up to 2036.

**Findings** Data from 2023 indicated that approximately 53·60 million women aged 35–49 years worldwide suffered from infertility, with an ASPR of 6907·12 (95% uncertainty interval (UI) 1883·5–16396·17) in 2023. Analyses from 1990 to 2023 showed a continuous increase in disease burden across all regions. Although the burden gap between low-SDI and high-SDI regions narrowed by 23·10%, the burden has progressively shifted from low-SDI to high-SDI countries, reflecting rising infertility in more developed settings. Furthermore, frontier analysis identified Central African Republic, Gabon, and Djibouti as countries with the greatest potential for burden reduction. It is projected that, compared with 2023, the number of infertility cases in this age group will increase by approximately 48·58% and DALYs by nearly 50% by 2036.

**Interpretation** Advanced-age female infertility represents a growing global health challenge. Despite improved regional equity, low-SDI countries continue to face significant burdens. This necessitates implementing tailored public health strategies and prioritising resource allocation to mitigate future burdens.

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## Introduction

Infertility is a major reproductive health condition, defined by WHO as failure to achieve a clinical pregnancy after 12 months of regular unprotected intercourse.[1,2] Approximately 8–12% of reproductive-aged couples worldwide experience infertility, with the burden disproportionately concentrated among women aged 35–49 years.[3] This heightened risk is largely biological, driven by age-related declines in ovarian reserve and oocyte quality, which reduce natural fecundity, increase miscarriage risk, and lower the success rates of assisted reproductive technologies (ART).[3–5] As population ageing and socioeconomic transitions accelerate, the number of women exposed to advanced-age infertility risk is rising, expanding its public health relevance.

Beyond clinical consequences, infertility carries substantial psychological distress, financial strain, and social stigma, which can undermine marital stability and family wellbeing.[6–9] At the societal level, persistently low fertility rates and unequal access to reproductive health care might intensify population ageing, constrain

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## Research in context

### Evidence before this study

Infertility is an escalating global public health concern, particularly among women of advanced reproductive age of 35–49 years. We conducted a literature search in PubMed, Embase, and Web of Science from database inception to Jan 31, 2026, using the search terms "infertility", "subfertility" separated with "AND" from the terms "advanced maternal age", "advanced age", "35–49 years", and "older women", further separated with "AND" from the terms "global burden of disease", "GBD", "prevalence", "disability-adjusted life years", "DALY", "epidemiology", "trend", "frontier analysis", and "health inequality", with no language restrictions. Existing evidence, largely derived from the Global Burden of Disease (GBD) framework, has assessed infertility at the population level but with notable knowledge gaps. First, there has been limited focus on women aged 35–49 years, who bear the highest burden of female infertility. Second, few studies have examined regional health inequalities or evaluated countries' developmental capacities to improve infertility outcomes. Third, while prevalence and disability-adjusted life-years (DALYs) have been reported, analyses of the specific burden and temporal trends among women of advanced reproductive age remain scarce. This absence of focused evidence prevents meaningful interpretation and leaves the public health strategy without a solid empirical foundation.

### Added value of this study

Our analysis of the GBD 2023 dataset provides the first comprehensive assessment of infertility burden among women aged 35–49 years across 204 countries and territories. Since 1990, both the age-standardised prevalence rate and DALYs attributable to infertility have risen steadily, by 0·45% and 0·47% per year, respectively. In 2023, an estimated 53·60 million women in this age group were affected by infertility, with projections indicating that this burden will continue to rise in the future. In the absence of targeted intervention, a continued escalation in new infertility cases is likely. Inequality analyses showed a 23·10% reduction in the relative disparity in infertility-related DALYs between low-Socio-demographic Index (SDI) and high- SDI regions since 1990—suggesting some progress in equity yet exposing persistent structural gaps. These findings highlight an urgent need for more inclusive, accessible, and context-specific reproductive health strategies to address the growing burden of infertility and reduce inequities in care and outcomes globally.

### Implications of all the available evidence

Our study provides up-to-date evidence to inform optimal allocation of health resources and to help narrow health inequalities across countries and regions. The evidence highlights an urgent and growing public health challenge, with the number of women aged 35–49 years affected increasing rapidly. Our study provides timely evidence to guide the optimal allocation of health resources and reduce global reproductive health inequalities. The projected increase of nearly 50% in infertility cases among women aged 35–49 years by 2036, alongside the steady rise in age-standardised prevalence rates and DALYs since 1990, underscores the urgent need for early detection, expanded access to fertility care, and integration of infertility into national and global health agendas. While disparities between high-SDI and low-SDI regions have narrowed, access gaps remain, especially in low-resource settings. By identifying exemplar countries with low infertility burdens at similar development levels, we highlight actionable models for policy transfer. These insights support the design of equitable, context-specific, and sustainable interventions that address both clinical and social dimensions of infertility, with far-reaching implications for women's health, mental wellbeing, family planning, and workforce participation.

female labour force participation, and adversely affect long-term economic development.[10–12] Demand for fertility services is also increasing, placing added pressure on health systems, particularly in settings where access to fertility evaluation and treatment remains scarce.[13,14]

The Global Burden of Disease (GBD) framework offers a useful tool for analysing the epidemiological trends and health inequalities associated with infertility. By capturing both absolute and relative disparities, GBD analyses provide valuable insights into how socioeconomic development shapes disease burden over time.[15,16] WHO has emphasised the importance of health equity monitoring in identifying vulnerable populations and guiding the formulation of fairer, more effective health policies.[17] Despite these strengths, most GBD-based infertility studies have focused on aggregate reproductive age groups, with limited attention to women aged 35–49 years—those who face the highest burden of infertility.[18,19] Moreover, few studies have systematically assessed regional health inequalities or examined countries' capacities to improve infertility outcomes in relation to their level of social and economic development.

To address these gaps, this study provides a comprehensive analysis of the global, regional, and national burden of advanced-age female infertility (age 35–49 years) from 1990 to 2023 using GBD 2023 data. It examines temporal trends, quantifies inequality, evaluates key contributing factors, and identifies countries with the greatest potential for improvement. Future projections to 2036 aimed to offer forward-looking evidence to guide context-specific health interventions and equitable resource allocation. By spotlighting this underexamined yet high-burden population, the objective of this study was to inform targeted, data-driven strategies for improving reproductive health outcomes and to advance global health equity.

| | Prevalence | | | Disability-adjusted life-years | | |
|---|---|---|---|---|---|---|
| | Age-standardised rates per 100 000 population, 1990 (95% UI) | Age-standardised rates per 100 000 population, 2023 (95% UI) | Estimated annual percentage change (95% CI) | Age-standardised rates per 100 000 population, 1990 (95% UI) | Age-standardised rates per 100 000 population, 2023 (95% UI) | Estimated annual percentage change (95% CI) |
| Overall | 6001·02 (1709·28–13970·96) | 6907·12 (1883·5–16396·17) | 0·45 (0·34 to 0·55) | 31·31 (6·56–93·29) | 36·29 (6·91–107·24) | 0·47 (0·36 to 0·58) |
| SDI regions (n=4) | | | | | | |
| High-middle SDI | 7786·06 (2282·2–17607·77) | 7983·04 (2246·55–18736·44) | 0 (–0·06 to 0·07) | 40·39 (8·38–121·75) | 41·86 (8·36–120·85) | 0·03 (–0·03 to 0·1) |
| Middle SDI | 6323·2 (2017·86–13899·12) | 7391·84 (2109·19–16979·4) | 1·12 (0·87 to 1·38) | 33·4 (7·5–98·03) | 39·22 (8·03–116·09) | 1·14 (0·88 to 1·4) |
| Low-middle SDI | 5509·02 (1269·17–13822·51) | 6657·35 (1591·83–16591·12) | 0·89 (0·43 to 1·35) | 28·78 (5·24–81·8) | 35·37 (6·43–106·04) | 0·94 (0·48 to 1·41) |
| Low SDI | 5225·79 (1596·82–11675·98) | 5778·6 (1427·56–13523·83) | 0·06 (–0·43 to 0·55) | 27·08 (6·26–75·28) | 30·29 (5·79–90·03) | 0·11 (–0·38 to 0·6) |
| GBD regions (n=21) | | | | | | |
| Andean Latin America | 254·32 (109·52–647·74) | 1431·39 (88·96–6179·55) | 7·62 (6 to 9·28) | 1·36 (0·35–4·16) | 7·44 (0·31–35·82) | 7·52 (5·92 to 9·15) |
| Australasia | 402·46 (62·86–2722·54) | 522·96 (72·35–3475·47) | 1·08 (0·91 to 1·24) | 2·19 (0·22–14·53) | 2·82 (0·26–18·42) | 1·01 (0·86 to 1·16) |
| Caribbean | 6160·67 (2412·21–12664·59) | 6008·54 (2058·26–12835·88) | –0·23 (–0·47 to 0) | 32·61 (9·15–89·65) | 31·68 (7·9–88·16) | –0·24 (–0·46 to –0·01) |
| Central Asia | 2751·23 (397·7–7426·53) | 3118·91 (242·12–9469·94) | 1·25 (0·91 to 1·59) | 14·4 (1·56–47·35) | 16·27 (1·12–56·11) | 1·22 (0·89 to 1·55) |
| Central Europe | 3937·32 (602·82–10643·82) | 5008·91 (947·32–13037·32) | 0·79 (0·64 to 0·93) | 20·58 (2·33–67·95) | 26·04 (3·5–82·86) | 0·77 (0·63 to 0·91) |
| Central Latin America | 2869·26 (398·86–7608·03) | 5203·29 (742·59–13273·25) | 0·89 (0·64 to 1·13) | 14·91 (1·63–55·27) | 26·65 (2·71–91·34) | 0·86 (0·62 to 1·1) |
| Central Sub-Saharan Africa | 8132·51 (2050·46–18420·27) | 8734·25 (2062·97–20194·91) | 0·06 (–0·53 to 0·66) | 41·47 (7·96–122·56) | 44·68 (8·15–134·58) | 0·1 (–0·48 to 0·69) |
| East Asia | 11444·66 (3472·24–25165·43) | 12030·89 (3799·54–26629·75) | 0·01 (–0·03 to 0·05) | 58·91 (12·62–178·88) | 62·21 (13·25–177·54) | 0·02 (–0·02 to 0·06) |
| Eastern Europe | 5568·6 (1249·46–13509·25) | 6214·39 (1574·91–15206·57) | 0·8 (0·66 to 0·93) | 29·63 (5·87–85·97) | 32·94 (6·74–94·15) | 0·78 (0·65 to 0·92) |
| Eastern Sub-Saharan Africa | 6761·49 (3157·36–12603·32) | 7221·22 (1737·74–16505·74) | –1·25 (–1·87 to –0·63) | 34·83 (10·61–90·03) | 37·2 (7·18–109·3) | –1·24 (–1·84 to –0·63) |
| High-income Asia Pacific | 3026·6 (127·33–11110) | 2866·84 (126·71–10700·09) | –0·19 (–0·49 to 0·11) | 15·79 (0·51–67·7) | 14·85 (0·52–63·55) | –0·21 (–0·51 to 0·1) |
| High-income North America | 960·91 (67·97–4292·53) | 2013·03 (93·07–7057·77) | 3·88 (2·4 to 5·38) | 5·33 (0·28–24·58) | 10·89 (0·42–44·25) | 3·78 (2·32 to 5·27) |
| North Africa and Middle East | 3220·39 (1646·41–5695·83) | 5029·41 (1144·63–11782·77) | 1·07 (0·67 to 1·47) | 17·49 (6·13–45·08) | 26·83 (5·32–79·99) | 1·02 (0·62 to 1·43) |
| Oceania | 4668·96 (784·63–12229·84) | 2373·42 (648·7–5070·73) | –2·59 (–3·1 to –2·08) | 24·55 (3·15–81·86) | 12·63 (2·79–37·03) | –2·56 (–3·05 to –2·06) |
| South Asia | 5255·1 (750·01–13331·65) | 6322·28 (1567·44–15365·58) | 1·53 (0·84 to 2·22) | 27·48 (3·54–82·16) | 33·99 (6·72–99·58) | 1·59 (0·9 to 2·29) |
| Southeast Asia | 5651·23 (1629·74–12577·98) | 7904·07 (2345·19–18056·13) | 1·35 (1·06 to 1·63) | 30·22 (6·77–90·63) | 42·1 (9·1–123·49) | 1·35 (1·07 to 1·63) |
| Southern Latin America | 3575·29 (118·65–10648·54) | 3313·44 (112·59–10088·19) | –0·1 (–0·23 to 0·02) | 18·64 (0·52–63·8) | 17·32 (0·5–61·45) | –0·09 (–0·21 to 0·03) |
| Southern Sub-Saharan Africa | 6337·16 (1291·6–15136·47) | 7139·19 (1166·16–17822·42) | –0·48 (–1·17 to 0·21) | 32·93 (5·82–98·34) | 36·81 (5·16–114) | –0·53 (–1·22 to 0·17) |
| Tropical Latin America | 3698·48 (1129·65–8327·41) | 5217·57 (840·42–13246·88) | 1·62 (1·21 to 2·02) | 20·07 (4·97–61·23) | 27·52 (3·61–91·47) | 1·56 (1·15 to 1·96) |
| Western Europe | 2807·72 (728·53–6410·59) | 4174·61 (681·06–11168·5) | 1·39 (1·13 to 1·65) | 15·32 (3·22–41·84) | 22·43 (3·16–66·66) | 1·34 (1·09 to 1·6) |
| Western Sub-Saharan Africa | 4612·8 (1270·78–10871·47) | 5470·79 (666·51–13749·1) | –0·51 (–0·88 to –0·13) | 23·58 (5·06–72·94) | 28·1 (2·68–93·01) | –0·47 (–0·84 to –0·09) |

SDI=Socio-demographic Index. UI=uncertainty interval.

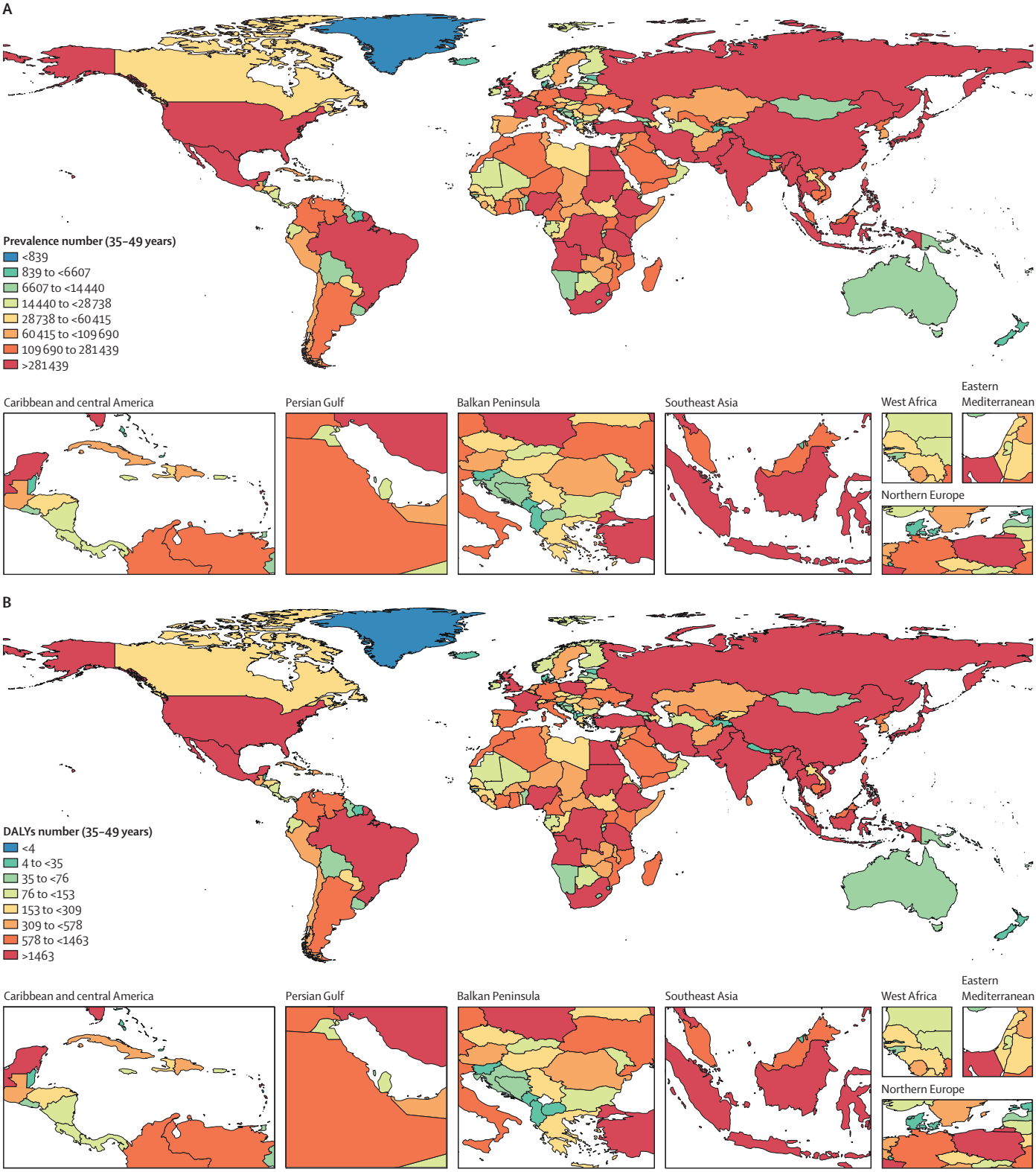
***Table:*** **Age-standardised burden of disease outcomes for infertility in women aged 35–49 years in the global population, across all SDI and Global Burden of Disease regions**

## Methods

### Data sources

This research was conducted using data from the GBD 2023 database. The GBD age-weight structure reflected long-term average global age proportions, which were relatively stable over short intervals, assuming no drastic shifts in global age structure between 2021 and 2023. Therefore, our study applied the GBD 2021 age weights to GBD 2023 populations to achieve a negligible effect on the calculation of age-standardised prevalence rates (ASPRs), as GBD 2023 age weights are not yet available. Relevant methodological details, including the calculation of age-standardised rates for the specific age group (35–49 years) and corresponding explanations, are provided in the appendix (pp 28–29). To ensure comparability across populations and over time, the GBD study applies standardised case definitions and modelling approaches to harmonise data from diverse sources, including vital registration systems, household surveys, disease registries, and published scientific literature.[20] The data source and relevant methodological details are provided in the appendix (pp 28–29). Data collection and metric evaluation were performed using consistent and standardised methods.[15] The analysis focused on infertility in women aged 35–49 years from 1990 to 2023 to assess temporal trends and disease burdens. For

See Online for appendix

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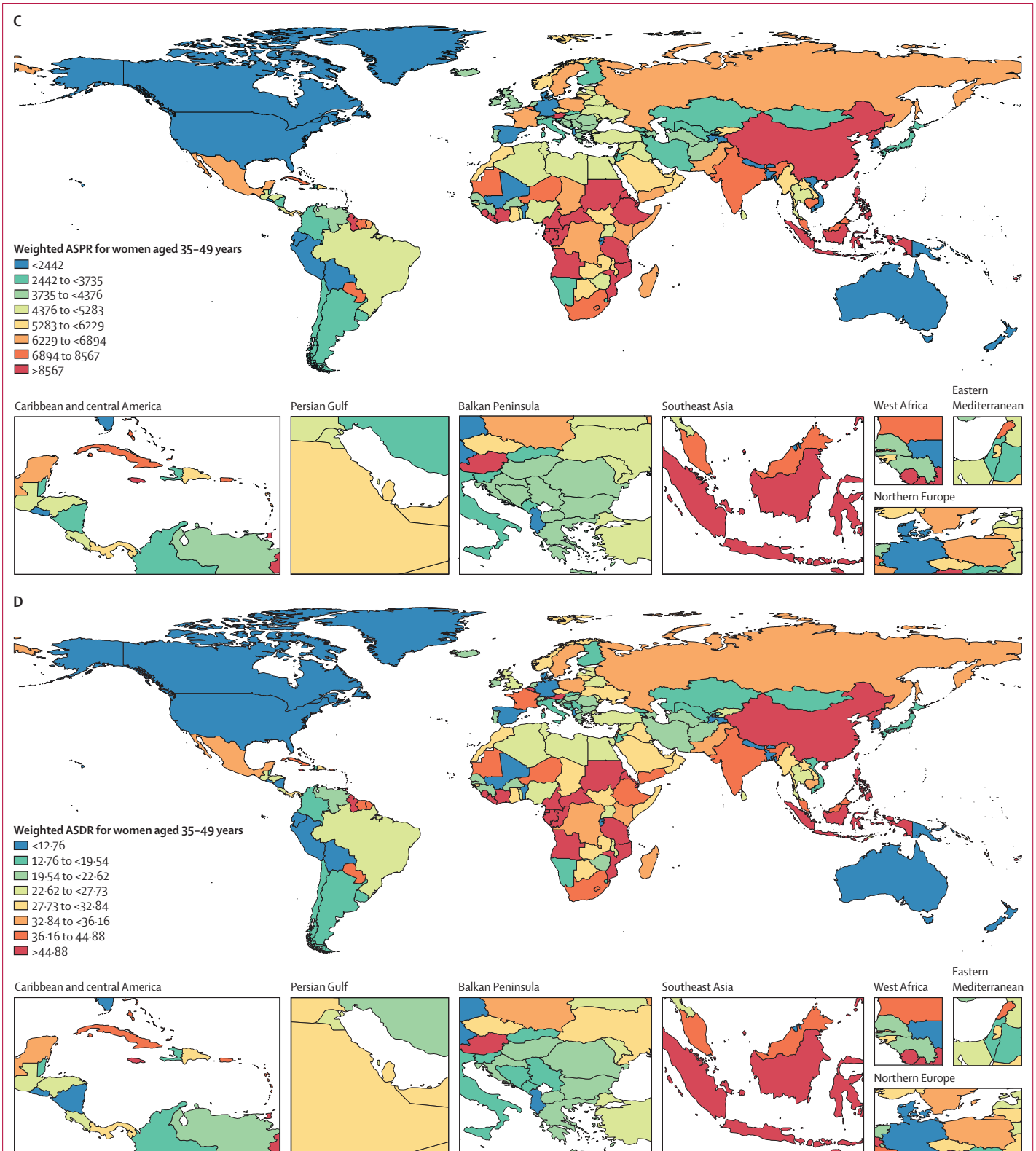


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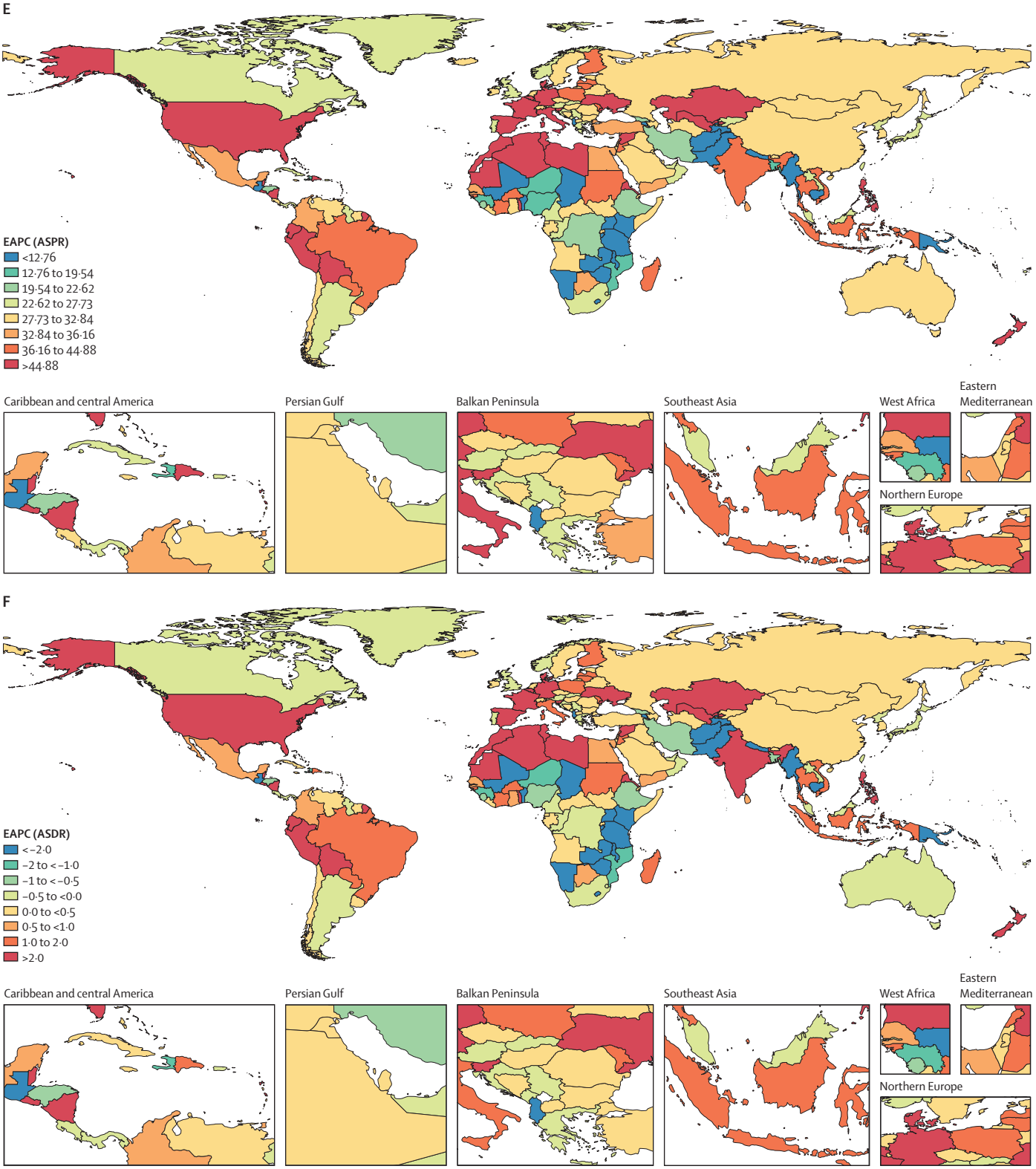

E
EAPC (ASPR)
<12·76
12·76 to 19·54
19·54 to 22·62
22·62 to 27·73
27·73 to 32·84
32·84 to 36·16
36·16 to 44·88
>44·88
Caribbean and central America
Persian Gulf
Balkan Peninsula
Southeast Asia
West Africa
Eastern Mediterranean
Northern Europe
F
EAPC (ASDR)
< −2·0
−2 to < −1·0
−1 to < −0·5
−0·5 to <0·0
0·0 to <0·5
0·5 to <1·0
1·0 to 2·0
>2·0
Caribbean and central America
Persian Gulf
Balkan Peninsula
Southeast Asia
West Africa
Eastern Mediterranean
Northern Europe

age-specific analysis, this population was further stratified into four subgroups: 35–39, 40–44, and 45–49 years. The extracted data encompassed multiple dimensions, including demographic characteristics, time period (1990–2023), and geographical distribution across 204 countries and territories. These included all WHO member states, four Socio-demographic Index (SDI) regions,[21,22] and 21 GBD regions grouped by epidemiological similarity and geographical proximity.[23] The SDI is a composite measure capturing key socioeconomic determinants of health (appendix p 28). As the GBD dataset is publicly accessible and de-identified, its use does not require previous ethical approval. Ethical approval for the use of de-identified data in the GBD study was obtained from the University of Washington Institutional Review Board, which authorised a waiver of informed consent.

### Analytical metrics

To ensure consistency and comparability, ASPR and age-standardised disability-adjusted life-years (DALYs) were calculated according to the age distribution of the GBD world standard population. Even though infertility is not a direct cause of death, it could coexist with underlying systemic conditions that are associated with increased long-term health risks and mortality.[24,25] Those mortality risks should be attributed to the comorbid conditions rather than to infertility itself. From a GBD methodological perspective, infertility is classified as a non-fatal condition; consequently, the DALYs reported in this study are entirely driven by years lived with disability (YLDs), with years of life loss (YLLs) equal to zero, since DALYs are calculated by YLLs plus YLDs. This followed the standard GBD approach for non-fatal causes and using DALYs as a summary measure ensured comparability across diseases, regions, and time periods within the GBD framework. Furthermore, the GBD systematically adjusts epidemiological data using advanced statistical models, including MR-BRT and DisMod-MR version 2·1, to account for biases arising from differences in data sources, definitions, and measurement methods. Building on these standardised adjustments, the present study analyses epidemiological estimates obtained directly from the publicly available GBD database.[20] These adjustments ensure internal consistency in estimates across different regions, ages, and years, and aim to minimise the effect of heterogeneity on study results through standardisation and calibration steps.[26,27]

### Statistical analysis

We applied the Spearman correlation analysis method, aiming to initially explore and describe the relationship between SDI and age-standardised infertility rate among the female population aged 35–49 years.

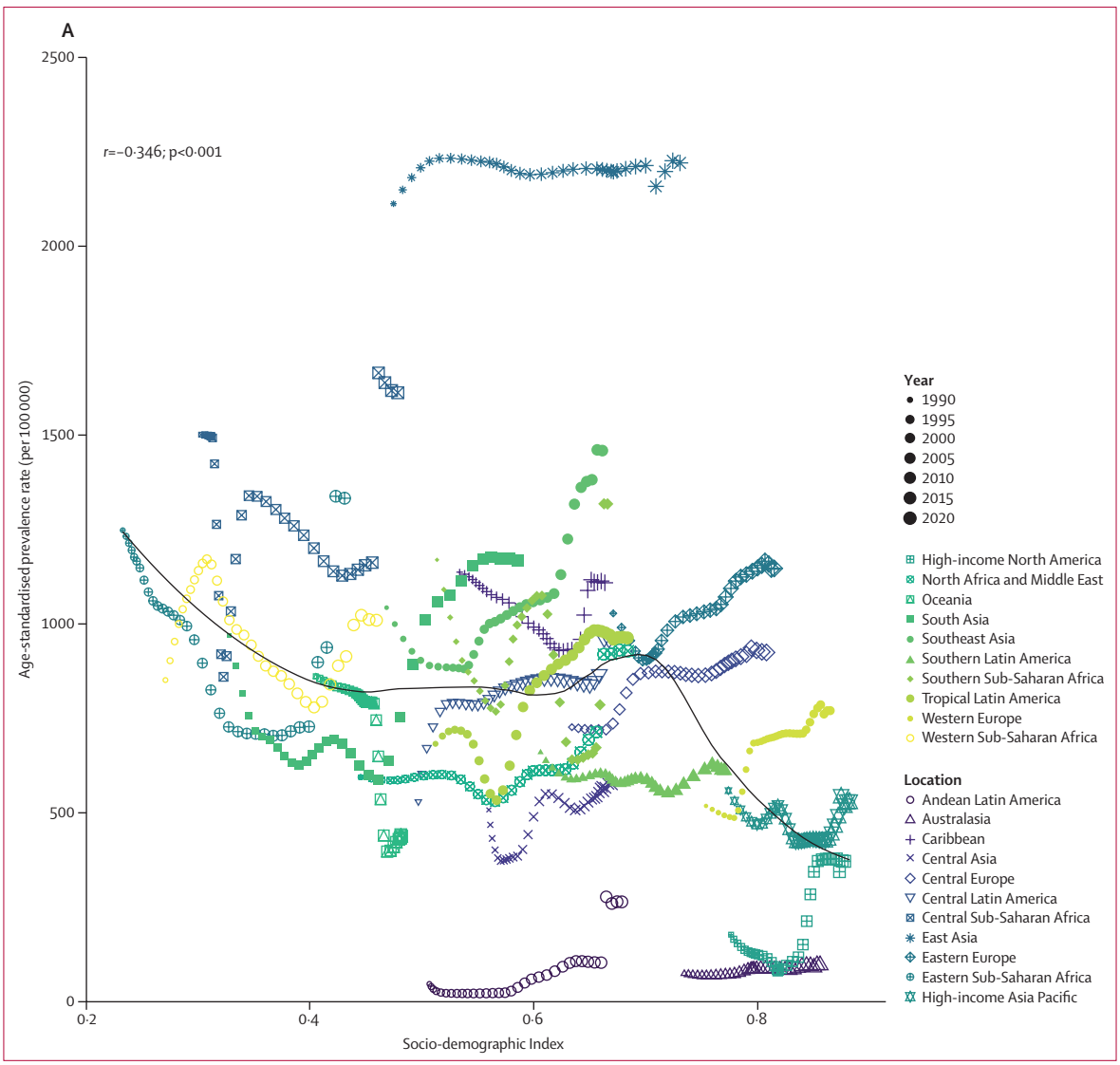
To assess the patterns in age-standardised rates across time, we employed the estimated annual percentage change (EAPC), which was derived using a regression model fitting the natural logarithm of the rate to the calendar year. Detailed definitions and methodological procedures for EAPC are provided in the appendix (p 29).[28] A joinpoint regression model was used to assess long-term trends from 1990 to 2023, allowing for the calculation of the average annual percentage change (AAPC) and the annual percentage change (APC) across specific time intervals.[27,29] To address the collinearity inherent among age, period, and cohort variables, a Bayesian Markov Chain Monte Carlo approach was adopted to construct a Bayesian age-period-cohort (BAPC) model. This model was then applied to project the infertility-related disease burden among women aged 35–49 years from 2024 to 2036.[30] Also, we employed the Autoregressive Integrated Moving Average (ARIMA) model to forecast time-series trends for both the overall group and specific age subgroups (35–39, 40–44, and 45–49 years), assessing disease burden changes and future trajectories.[31]

Using the slope of inequality index and the concentration index as defined by WHO, the study evaluated both absolute and relative inequalities in the burden of infertility among women of advanced reproductive age of 35–49 years.[17] The slope of inequality index, derived from regression of health outcomes against SDI-ranked population data, reflects absolute disparities across socioeconomic strata. The concentration index measures relative inequality by comparing cumulative distributions of infertility cases and population ranked by SDI. We analysed data for 204 countries and territories from 1990 to 2023 to examine trends in health inequalities.

We also employed a frontier model to analyse the association between SDI and the burden of infertility among women aged 35–49 years.[32] This model incorporates ASPR along with age-standardised DALYs. The main goal of frontier analysis is to determine the theoretically lowest possible ASPR and age-standardised DALY values achievable for each region or country, considering their current level of socioeconomic development. These minimums provide benchmarks for optimal performance. By measuring the difference between actual loads and theoretical minimums, this methodology identifies areas for improvement and prioritises targeted interventions. In addition, absolute

***Figure 1:*** **Global burden of disease for infertility among women of advanced reproductive age (35–49 years) in 204 countries and territories in 2023, including total prevalence, ASPR, absolute number of DALYs, age-standardised DALY rate, and EAPC**

(A) Total prevalence in 2023. (B) Absolute DALYs in 2023. (C) Age-standardised prevalence rate in 2023. (D) Age-standardised DALYs rate in 2023. (E) Estimated annual percentage change in age-standardised prevalence from 1990 to 2023. (F) Estimated annual percentage change in age-standardised DALYs from 1990 to 2023. ASPR=age-standardised prevalence rate. ASDR=age-standardised DALY rate. DALYs=disability-adjusted life-years. EAPC=estimated annual percentage change.

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distances between the 2023 ASPR and AS-DALY values and the front line were calculated for each country or area to assess the potential for improvement.

All the metrics and formulas introduced above are explained in detail in the appendix (pp 28–29). Most data analyses were conducted using Excel 2021 and R (version 4.3.3). All estimates are reported with corresponding 95% CIs, and statistical significance was defined as a two-tailed p value of <0·05. Model fitting and calculations of AAPC and APC were performed using Joinpoint software (version 5.4.0), which was downloaded from the official Joinpoint Regression Program website.

For the **Joinpoint Regression Program** see https://www.cancer.gov

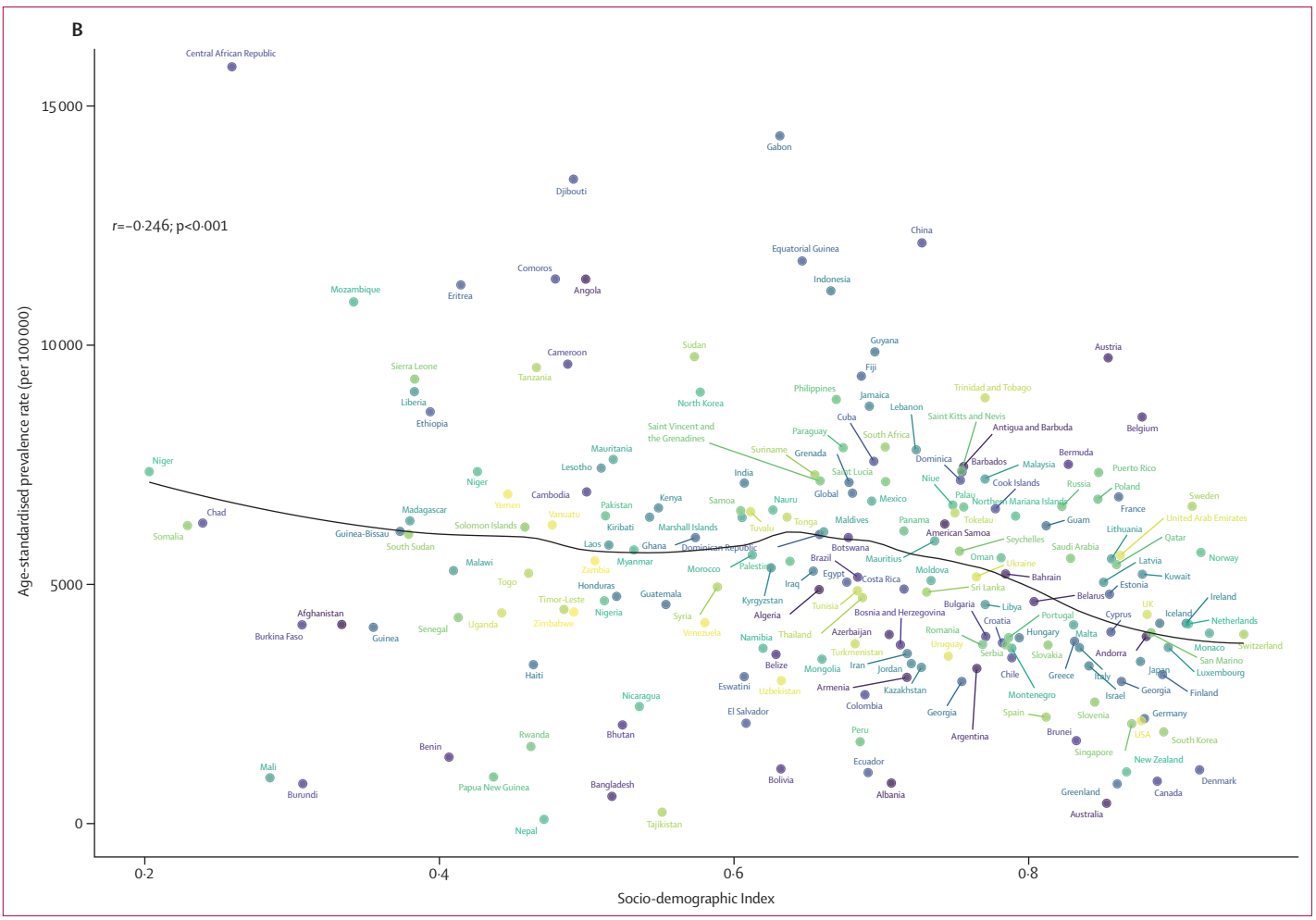
### Role of the funding source

The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

## Results

Between 1990 and 2023, the ASPR per 100 000 population for women aged 35–49 years increased from 6001·02 (95% uncertainty interval [UI] 1709·28–13 970·96) in 1990 to 6907·12 (1883·5–16 396·17) in 2023, with an EAPC of 0·45 (0·34–0·55). The health burden was further reflected in age-standardised DALY rate per 100 000 population, which increased from 31·31 (6·56–93·29) in 1990 to 36·29 (6·91–107·24) in 2023, and a significant EAPC of 0·47 (0·36–0·58). Overall, all burden indexes showed positive EAPC values, indicating a global burden of infertility among women aged 35–49 years over the three-decade period (table).

Regional patterns for infertility burden among women aged 35–49 years varied. Among SDI regions, the high-middle SDI region had the highest infertility prevalence and DALYs in 2023, whereas the low SDI region reported

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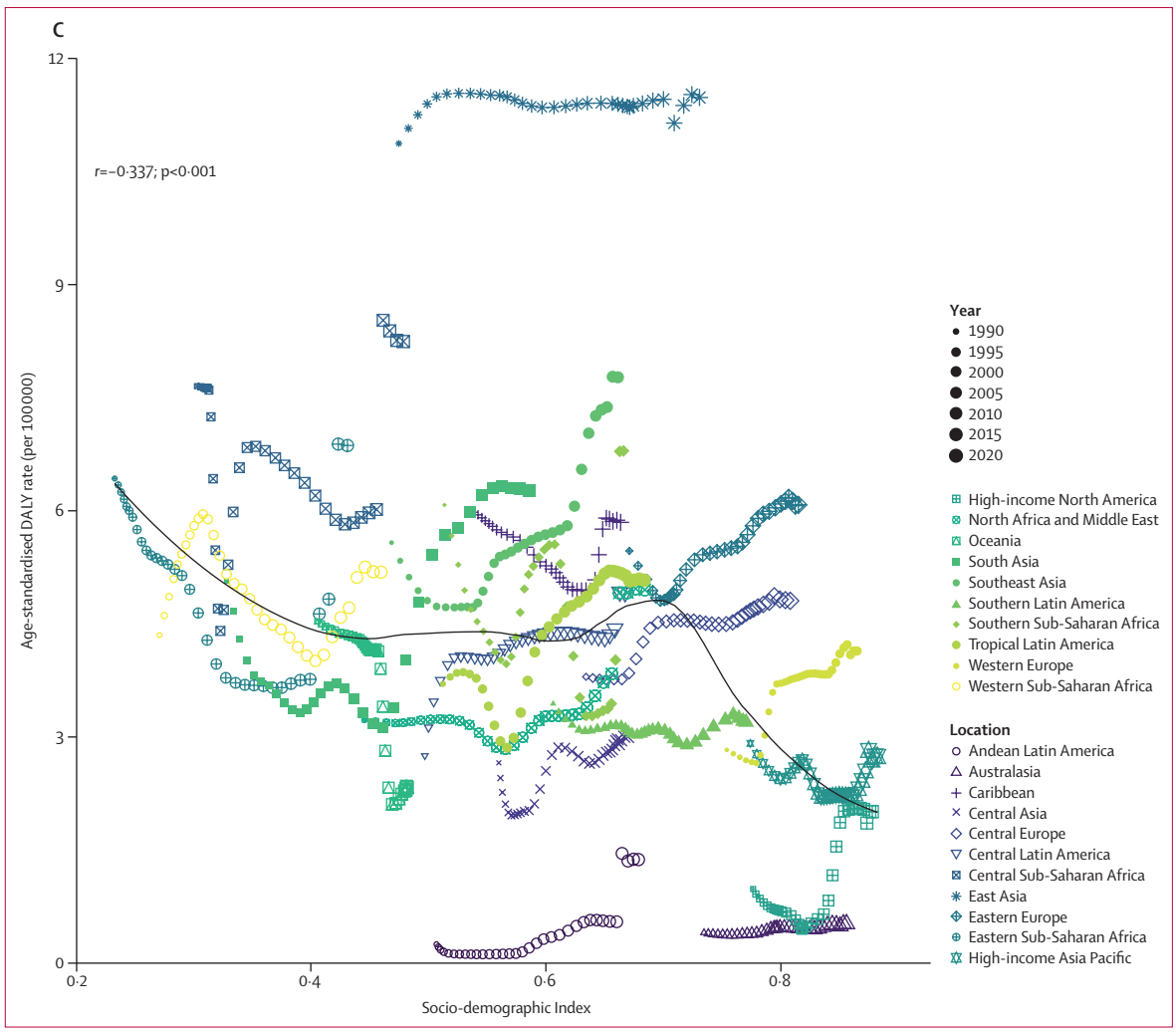
the lowest. Notably, the largest increase in infertility rate over time occurred in middle SDI regions (table). Among the 21 GBD regions, East Asia had recorded the highest infertility burden, with an ASPR of 12 030·89 (95% UI 3799·54–26 629·75) and age-standardised DALYs of 62·21 (13·25–177·54) per 100 000 population. In contrast, Australasia had the lowest ASPR at 522·96 (72·35–3475·47) and DALYs at 2·82 (0·26–18·42) per 100 000 population. The Andean Latin America showed the steepest increases (EAPC for prevalence 7·62 [95% CI 6·00–9·28]; DALYs 7·52 [5·92–9·15]), whereas the greatest declines in infertility were observed in Oceania (EAPC for prevalence –2·59 [–3·1 to –2·08]; DALYs –2·56 [–3·05 to –2·06]; table).

In 2023, among 204 countries and territories, the Central African Republic reported the highest infertility burden in women aged 35–49 years, with an ASPR of 15 818·82 (95% UI 5804·93–32 093·08) and DALYs of 82·07 (24·05–221·58) per 100 000 population. Nepal had the lowest ASPR at 88·51 (59·64–130·06) and DALYs of 0·51 (0·17–1·29) per 100 000 population (figure 1). More than 100 countries showed increasing infertility burdens, with Ecuador showing the most rapid rise (EAPC in ASPR and DALYs: 9·06 [7·29–10·86] and 8·98 [7·24–10·75], respectively). In contrast, Malawi showed the sharpest decline (ASPR EAPC: –9·78 [–12·38 to –7·1]; DALYs EAPC: –9·76 [–12·34 to –7·1]). Nearly half of all countries showed decreasing trends, whereas several countries such as Japan, North Korea, and Singapore showed relatively stable infertility burdens over time. Detailed figures and data on country-level infertility burden in women aged 35–49 years are provided in figure 1 and the appendix (pp 2–18).

Globally and across 21 GBD regions, a non-linear relationship was observed between SDI and both ASPR and age-standardised DALYs in women aged 35–49 years (figure 2). Overall, the burden of infertility declined with increasing SDI, with a relatively stable trend observed at an SDI of 0·40 to 0·60 and a modest increase noted at an SDI of 0·60 to 0·70. Notably, East Asia consistently showed the highest burden in

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infertility, despite rising SDI values (figure 2A, C). In the cross-sectional analysis of 204 countries in 2023, countries with higher SDI generally had a lower burden than those with lower SDI, whereas a slight non-linear fluctuation was observed in the mid-SDI range (figure 2B, D). The EAPC of ASPR and DALYs initially showed a slight decrease and then plateaued, whereas EAPC values first increased and then rose more moderately with rising SDI levels (appendix p 24).

Using Joinpoint regression models, we analysed temporal trends in the global infertility burden among women aged 35–49 years from 1990 to 2023. The general upward trend was observed in both ASPR and age-standardised DALYs among women aged 35–49 years, characterised by a distinct W-shaped fluctuation pattern; trends in ASPR and DALYs were closely aligned (figure 3A; appendix p 25). Joinpoint analysis across the four SDI regions revealed broadly similar patterns to the global trend, with notable regional differences. For instance, the high-middle SDI region showed an early rise in the 1990s diverging from the global pattern (figure 3B); and the middle SDI region had a sustained increase since 1997 (figure 3C). The overall data and detailed annual percentage changes in DALYs are in the appendix (pp 20, 25),

We applied a BAPC model to project the global infertility burden among women of advanced reproductive age (35–49 years) from 2024 to 2036 (figure 4). The projections indicate a sustained upward trend, with both the ASPR and age-standardised DALYs expected to rise substantially. Compared with 2023, the number of infertility cases in this age group could increase by approximately 48·58% by 2036 (from 53·60 million [95% UI 14·63–127·27] in 2023 to 79·64 million [19·71–139·56] in 2036), and DALYs are also projected to increase by nearly 50% over the same period. All age subgroups show significant increases, with ARIMA indicating that women aged 35–39 years could experience the steepest rise, indicating growing challenges in this demographic (appendix p 26).

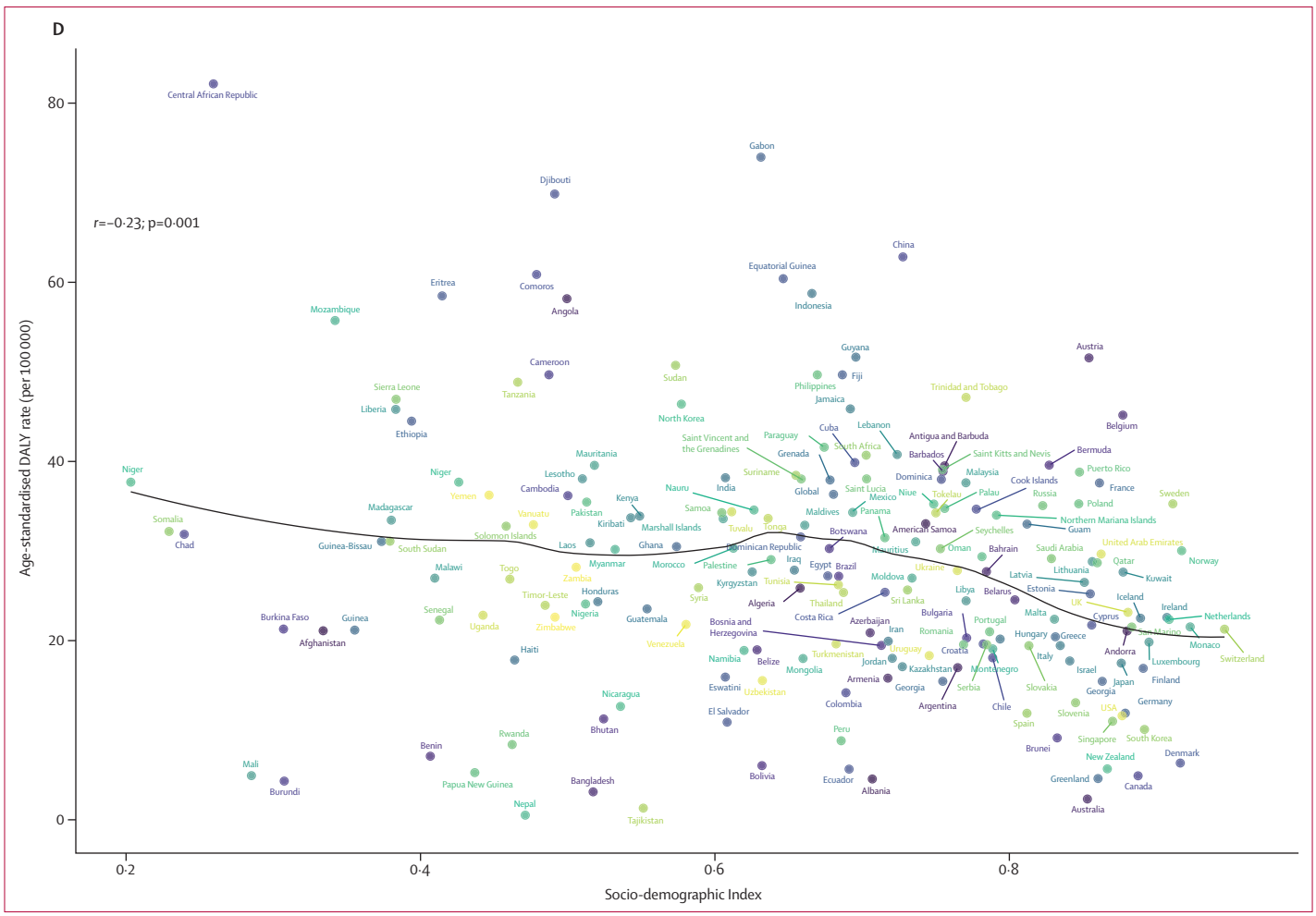



***Figure 2:*** **Results of the global burden of disease for infertility in women of advanced reproductive age (35–49 years), including SDI analysis at the global level, across 21 regions, and in 204 countries**

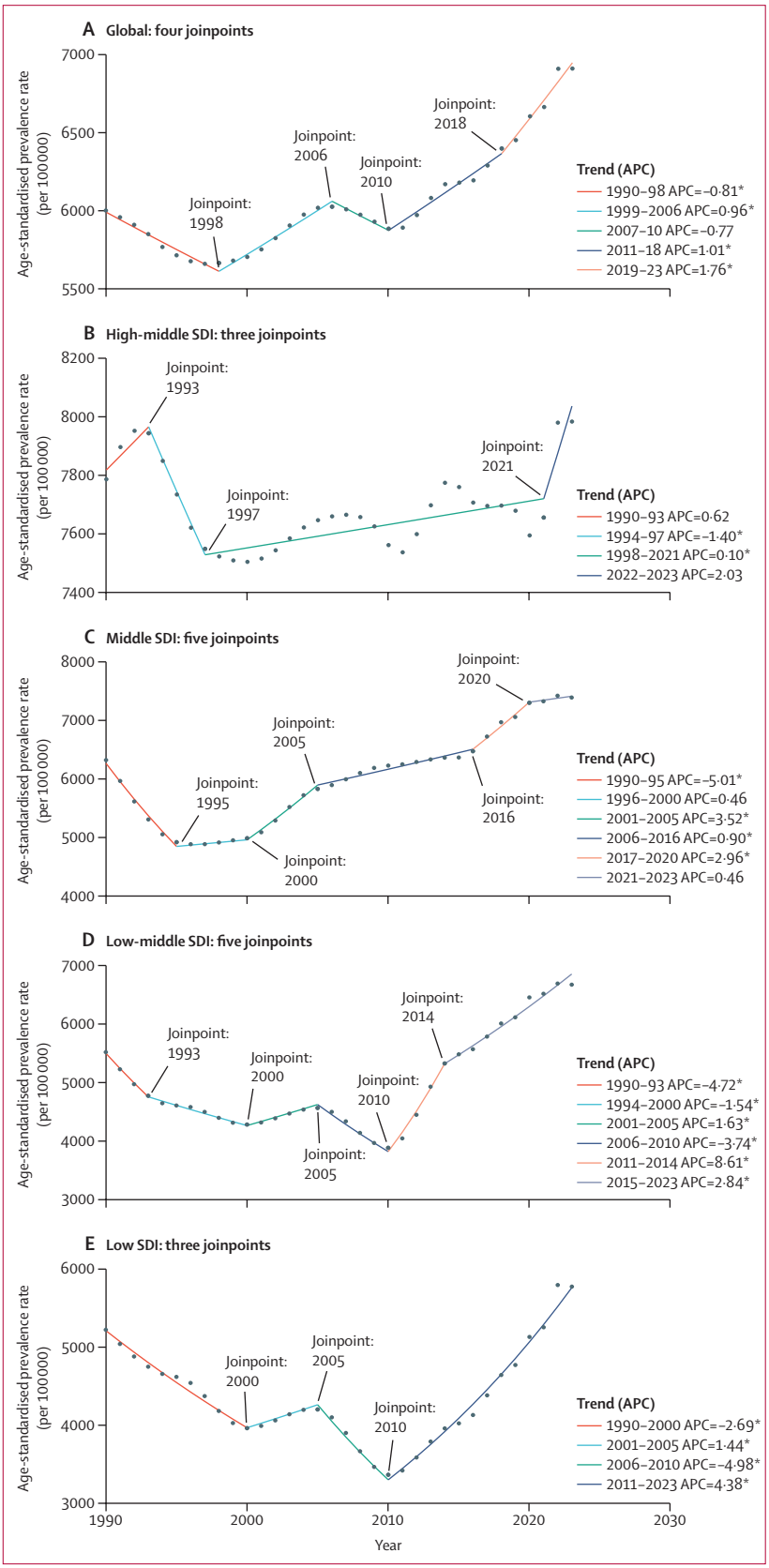
(A) Association and temporal trends between SDI and ASPR across 21 regions from 1990 to 2023. (B) Distribution of ASPR across 204 countries by SDI in 2023. (C) Association and temporal trends between SDI and ASDR across 21 regions from 1990 to 2023. (D) Distribution of ASDR across 204 countries by SDI in 2023. ASDR=age-standardised DALY rate. ASPR=age-standardised prevalence rate. SDI=Socio-demographic Index.

Our study observed both absolute and relative inequalities in the infertility burden among women of advanced reproductive age, particularly across SDI levels, with disparities narrowing over time. In 1990, the slope index of inequality indicated a gap of –5444·5 cases per 100 000 population between the lowest and highest SDI countries, and this gap narrowed by approximately 23·10% to –4187·1 per 100 000 population in 2023. Such change was mirrored by the age-standardised DALYs gap that declined from 25·9 to 19·9 per 100 000 population from 1990 to 2023 (appendix p 27). Additionally, the concentration index for infertility burden improved from –0·24 (95% CI –0·51 to 0·02) to 0·24 (0·05 to 0·43), suggesting a shift in burden towards higher-SDI countries from 1990 to 2023 (appendix p 27).

We evaluated ASPR, DALYs, and SDI to assess potential for improvement across development levels (appendix p 27). 15 countries and territories showed the largest gaps to optimal ASPR performance, including Cameroon, Congo (Brazzaville), Austria, Guyana, Sudan, Mozambique, Indonesia, Eritrea, Comoros, Angola, Equatorial Guinea, China, Djibouti, Gabon, and Central African Republic. For DALYs, all countries remained the same except Congo (Brazzaville), which was replaced by Fiji. Among low-SDI countries (SDI <0·50), Nepal, Burundi, Mali, Papua New Guinea, and Papua Benin had the smallest gaps to the performance frontier, indicating performance close to the best achievable level with minimal room for improvement. In contrast, high-SDI countries (SDI >0·85) such as Norway, Sweden, France, Belgium, and Austria were furthest from the frontier, reflecting worse-than-expected performance and greater potential for improvement.

## Discussion

This study assessed the burden, trends, and inequalities of infertility among women aged 35–49 years globally




from 1990 to 2023. The burden is highest in high-middle and middle-SDI settings, driven by a combination of sociodemographic transitions, including delayed marriage and childbearing, and the growing population of older women of reproductive age, as well as rising demand for fertility care alongside persistent gaps in access to affordable evaluation and treatment. At the same time, inequality reoriented over time, with the relative burden becoming more concentrated in higher-SDI contexts, showing that development alone does not eliminate risk or access gaps.

International and regional burden of infertility among women of advanced reproductive age is heterogeneous. In general, higher-SDI regions showed the fastest increases in ASPR and DALYs, whereas low-SDI regions generally remained stable or even declined. Such patterns reflect a complex interplay of socioeconomic, cultural, and policy influences. For instance, East Asia—a higher-SDI region—has consistently maintained the highest burden, likely due to its large population and robust surveillance system, although rates have plateaued in recent years.[19] Contributing factors include delayed childbearing, evolving social norms, economic conditions, expanded women's rights, and uneven access to ART.[19,33,34] Policy reforms in Japan, South Korea, and several Chinese tier-1 cities have improved ART affordability, yet coverage remains scarce, especially for low-income women within these societies.[35,36] In contrast, Australasia reported the lowest burdens, associated with advanced health care and healthier lifestyles,[37] whereas eastern sub-Saharan Africa displayed low and declining rates, driven by early marriage, high natural fertility, and strong pronatalist norms rooted in cultural and religious expectations.[38,39] Persistent national-level inequalities, as seen in the Central African Republic and Malawi, along with variability in data quality—particularly in low-income and middle-income countries (LMICs)—further contribute to the observed variations.

The shifting burden of infertility among women of advanced maternal age from 1990 to 2023 provides a critical lens through which to examine societal change during the late demographic transition. An initial decline in the early 1990s corresponded to a period of global economic growth and strengthened basic health care, notably in parts of Europe and East Asia, where expanded reproductive health education likely contributed.[40] The subsequent increase from the late 1990s onward coincided with rising female participation in education

***Figure 3:*** **Joinpoint regression analysis of age-standardised prevalence rate (per 100 000) of advanced-age female infertility from 1990 to 2023, globally and by SDI region**
(A) Global. (B) High-middle SDI region. (C) Middle SDI region. (D) Low-middle SDI region. (E) Low SDI region. The APC and corresponding intervals are shown within each panel. APC=annual percentage change. SDI=Socio-demographic Index. *p<0·05, and indicates that the APC is significantly different from zero at the α=0·05 level.

and the labour force, leading to widespread delays in childbearing and a consequent rise in age-related infertility.[41,42] A transient dip in observed infertility between 2006 and 2010 coincided with the global financial crisis, suggesting macroeconomic instability can alter reproductive timing. However, this modest decline might reflect underdiagnosis due to economic barriers rather than a true reduction in prevalence. The sustained rise in infertility since 2010 reflects delayed childbearing intersecting with obesity, stress, and expanded ART access, which has improved case detection and extended reproductive windows.[43–45] Bayesian projections estimate female infertility prevalence will approach 80 million cases by 2036, with the sharpest increase among women aged 35–39 years. Future biomedical advances and policy reforms may help mitigate this trend, underscoring the need for continued data monitoring and targeted prevention strategies.

Crucially, our results indicate not only a reduction in inequality but a reorientation of it. The relative burden shifted from being disproportionately borne by low-SDI settings in 1990 to being more prominent in higher-SDI settings by 2023. Economic barriers appear central: high out-of-pocket costs for diagnostic evaluation and ART restrict access and sustain disparities.[46,47] In higher-SDI settings, affordability constraints often intersect with delayed childbearing and work-family trade-offs; in lower-SDI settings, limited-service availability, under-resourced health systems, and gender inequities further constrain access.[48–50]

Beyond clinical implications, infertility among women of advanced reproductive age carries significant economic consequences at individual, household, and societal levels. In addition to the cross-national inequalities in ART access that exacerbate health disparities.[47,51] Economic analyses show that infertility constraints undermine women's labour market participation, career trajectories, and lifetime earnings potential, ultimately diminishing overall economic productivity.[10,52] At a macroeconomic level, persistently low fertility accelerates population ageing, strains social security systems, and impedes long-term economic growth, underscoring the importance of policy measures that ensure affordable, equitable access to fertility care.[11,53]

Interestingly, the greatest potential to reduce infertility ASPR was observed in low-SDI and middle-SDI African nations such as Cameroon, Congo (Brazzaville), and

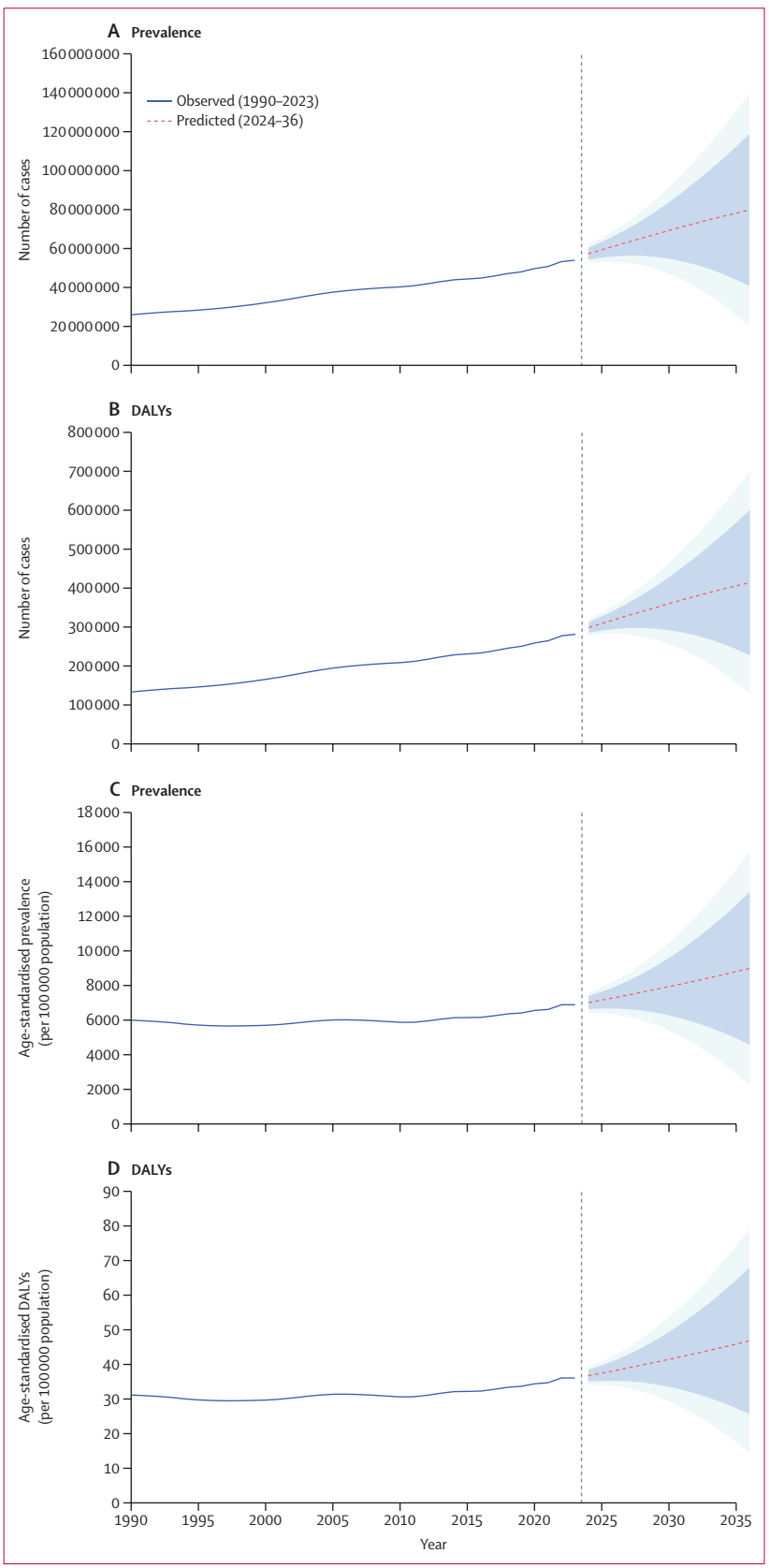



***Figure 4:*** **Time trends and predictions (1990–2036) for age-standardised prevalence and DALYs of infertility in women aged 35–49 years**
(A) Actual prevalence numbers for women aged 35–49 years from 1990 to 2036. (B) Actual DALYs numbers for women aged 35–49 years from 1990 to 2036. (C) Age-standardised prevalence rate for women aged 35–49 years from 1990 to 2036. (D) Age-standardised DALYs rate for women aged 35–49 years from 1990 to 2036. The light blue radiating shaded band represents the 95% prediction interval, and the dark blue radiating shaded band represents the 80% prediction interval.

Sudan, but also in some middle-SDI and high-SDI countries such as China and Austria. Notably, low-SDI countries such as Benin and Nepal perform near the frontier, likely due to effective local strategies and sociodemographic factors such as earlier childbearing.[54] Nevertheless, the high-welfare countries such as Norway and Sweden perform below expected levels, highlighting the enduring influence of structural barriers and policy shortcomings.[55,56]

With the global infertility burden rising among women of advanced reproductive age, equitable action is urgent: despite advances in ART,[57–59] high costs continue to restrict access in LMIC settings, worsening disparities.[60,61] To address this, policy makers should prioritise scalable, evidence-based interventions, including expanding public ART coverage, integrating infertility care into primary health services, and ensuring affordability through national insurance schemes or targeted subsidies.[62] Additionally, investments in mobile health platforms, task-shifting to trained community health workers, and localised public awareness campaigns can enhance reach in resource-limited settings. Prioritising research, artificial intelligence integration, and international collaboration remains crucial to reducing inequalities and improving global reproductive health outcomes.[63,64]

The study's strengths include the use of GBD 2023 data and an analytical framework that combined stratified assessments (by age, SDI, and region), inequality metrics, frontier benchmarking, and forecasting to 2036. Key limitations should be acknowledged. Disparities in data availability, health-care infrastructure, and care-seeking behaviour across regions might introduce bias into infertility estimates. Unlike many conditions with objective diagnostic criteria, infertility prevalence is strongly influenced by whether individuals seek medical evaluation and by the availability of reproductive health services. Consequently, the higher burden observed in high SDI regions might partly reflect greater disease awareness, higher health-care use, more complete data registration, and the broader availability of diagnostic services and treatments such as ART. In contrast, infertility burden in low SDI regions might be underestimated due to underdiagnosis associated with limited health-care access, resource constraints, geopolitical instability, and differences in reproductive intentions and care-seeking patterns. These structural and behavioural factors should therefore be considered when interpreting cross-regional differences in infertility burden. The absence of granular service delivery and aetiological data (eg, ART availability, provider density, and endometriosis prevalence) limits mechanistic inference. Our study captured only early phases of major coronavirus outbreaks, and longer-term effects from health-care disruptions and widening inequities might not be fully reflected.[65] Finally, infertility among women aged 50–54 years is not covered in GBD 2023, likely leading to an underestimation of the total burden.

In summary, this study highlighted the rising burden of infertility among women of advanced reproductive age, particularly in higher-income countries but also increasingly in low-income and middle-income settings, driven by ageing populations, delayed childbearing, socioeconomic pressures, and persistent health disparities. Addressing this challenge is multifactorial and requires coordinated efforts across stakeholders, including investment in ART, promotion of earlier family planning, strengthening of health-care systems, and enhanced global collaboration to ensure equitable access to reproductive care.

#### Contributors

YD, FW, and WZ: conceptualisation, data curation, formal analysis, methodology, visualisation, writing of the original draft, and software. HD, YP, and LZ: data curation, formal analysis, methodology, visualisation, and writing of the original draft. RL: data curation, validation, and software. OG, LNM, and ZP: interpreting data, review and editing. WZ and NZ: project administration, resources, project administration, and funding acquisition. L-JL: resource, conceptualisation, software, methodology, statistical analysis supervision, review and editing, and finalising. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

#### Declaration of interests

We declare no competing interests.

#### Data sharing

Data from the GBD study are publicly available at https://vizhub.healthdata.org/gbd-results/.

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