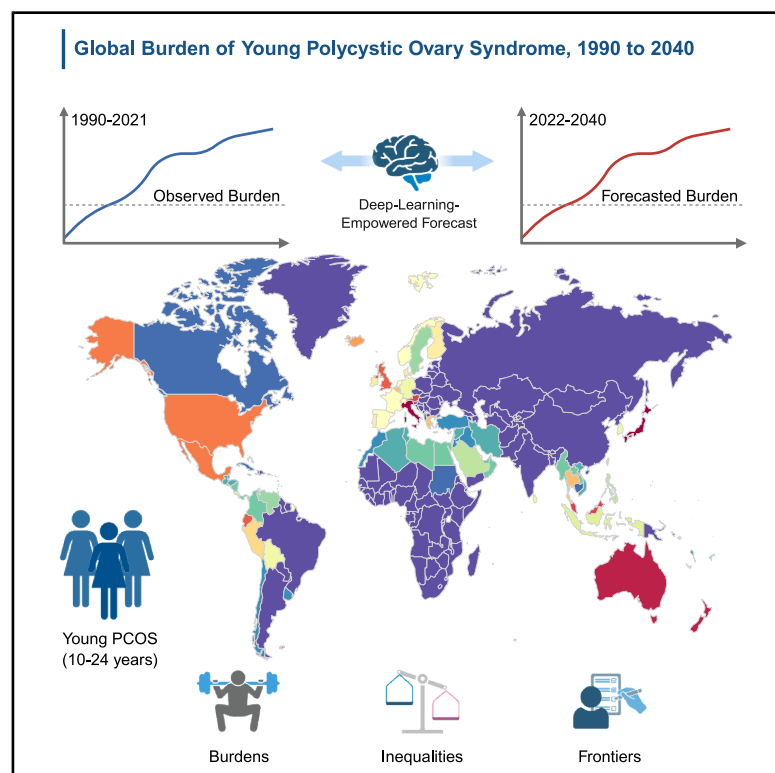


# Mapping burdens and inequalities of polycystic ovary syndrome in young females across 953 locations 1990–2040 with deep learning forecasts

## Graphical abstract



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## In brief

Health sciences; Medicine; Public health;  
Reproductive medicine

## Highlights

- Global PCOS burden in ages 10–24 increased substantially from 1990 to 2021
- Significant geographic and socio-economic inequalities in PCOS burden persist
- Deep-learning models forecast a continued rise in PCOS burden through 2040
- Targeted interventions are needed in regions with rising PCOS trends



## Article

# Mapping burdens and inequalities of polycystic ovary syndrome in young females across 953 locations 1990–2040 with deep learning forecasts

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## SUMMARY

Polycystic ovary syndrome (PCOS) is the most common reproductive endocrine disorder impacting the health of young female populations. Using harmonized estimates from 953 locations, we assessed temporal trends, geographic inequalities, and forecasts of PCOS among individuals aged 10–24 years from 1990 to 2040. Between 1990 and 2021, global prevalence and disability burden increased by more than 30%, with the highest burden observed among those aged 20–24 years. Substantial geographic heterogeneity was identified, with particularly high prevalence in Europe and East Asia. While high-income regions carried the greatest absolute burden, low- and middle-income regions showed the fastest growth, accompanied by widening socio-economic inequalities. Forecasting analyses suggest that PCOS burden in young populations will continue to rise through 2040. These findings characterize the evolving global landscape of PCOS, providing evidence to support targeted public health surveillance and prevention strategies for adolescent and young adult populations.

## INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most prevalent endocrine disorder affecting women of reproductive age and is characterized by a broad range of reproductive, metabolic, derma-

tological, and psychological manifestations.<sup>1</sup> Owing to its chronic and multisystem nature, PCOS requires long-term, multidisciplinary management across diverse healthcare settings. Globally, PCOS affects an estimated 10%–13% of females,<sup>2</sup> imposing substantial and sustained health and



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economic burdens. The condition typically emerges during adolescence and persists across the life course, with diagnosis based on menstrual irregularity, hyperandrogenism, and, in young adults, polycystic ovarian morphology or elevated anti-Müllerian hormone levels. The rapidly increasing prevalence of overweight and obesity among adolescents, a major risk factor for PCOS, represents an emerging public health concern.<sup>3</sup> In economic terms, PCOS imposed an annual cost exceeding USD 15 billion in the United States (US) alone in 2021<sup>4</sup> and accounted for approximately 80% of anovulatory infertility cases worldwide in 2014,<sup>5</sup> underscoring its long-term implications for population health and workforce participation. Early identification and timely intervention are, therefore, essential to mitigate fertility impairment and pregnancy-related complications,<sup>6,7</sup> reduce long-term metabolic and cardiovascular risks,<sup>8,9</sup> and improve overall quality of life.<sup>10</sup> A clear understanding of the burden of PCOS among young women is, thus, critical for informing long-term health system planning and prevention strategies.

Marked geographic variation in PCOS prevalence has been reported, with estimates ranging from 2.2% in China to 26.0% in Australia,<sup>11</sup> reflecting differences in healthcare access, diagnostic practices, genetic susceptibility, and environmental exposures.<sup>12</sup> Subnationally, the overall prevalence of PCOS in the US was 5.2% in 2019,<sup>13</sup> with substantially higher prevalence observed in southern states.<sup>11</sup> However, subnational data remain largely unavailable in many countries due to the absence of systematic screening program and disease registries. Moreover, existing studies have largely focused on single populations or relied on single-source data,<sup>13,14</sup> limiting a coherent understanding of the global to local burden of young PCOS. As a result, systematic and comparable estimates of young PCOS burden remain scarce. Although recent studies based on the Global Burden of Disease (GBD) 2021 framework have quantified the overall burden of PCOS at global and national levels, they have not comprehensively examined subnational heterogeneity, socio-demographic inequalities, or age-specific patterns, especially among adolescents and young women.<sup>15,16</sup> In addition, the socio-demographic determinants of young PCOS burden remain insufficiently characterized. Few studies have assessed disparities in the distribution of observed young PCOS burden, evaluated achievable levels of disease control across socio-demographic contexts, or generated long-term forecasts. These gaps constrain effective healthcare planning in the context of evolving demographic and epidemiological transitions. Furthermore, conventional forecasting approaches, such as autoregressive integrated moving average (ARIMA) or Bayesian age-period-cohort model (BAPC) models, are limited in their ability to capture the non-linear and multifactorial dynamics of disease burden.<sup>17–19</sup> Consequently, evidence on the future trajectory of PCOS burden among young females remains limited.

To address these gaps, we systematically quantified the prevalence, incidence, and disability-adjusted life years (DALYs) of PCOS among females aged 10–24 years. We characterized their distribution across socio-demographic contexts and estimated achievable burden frontiers across 953 global to subnational locations. We further forecasted trends in PCOS burden through 2040 by using a tailored attention-based deep learning framework.

## RESULTS

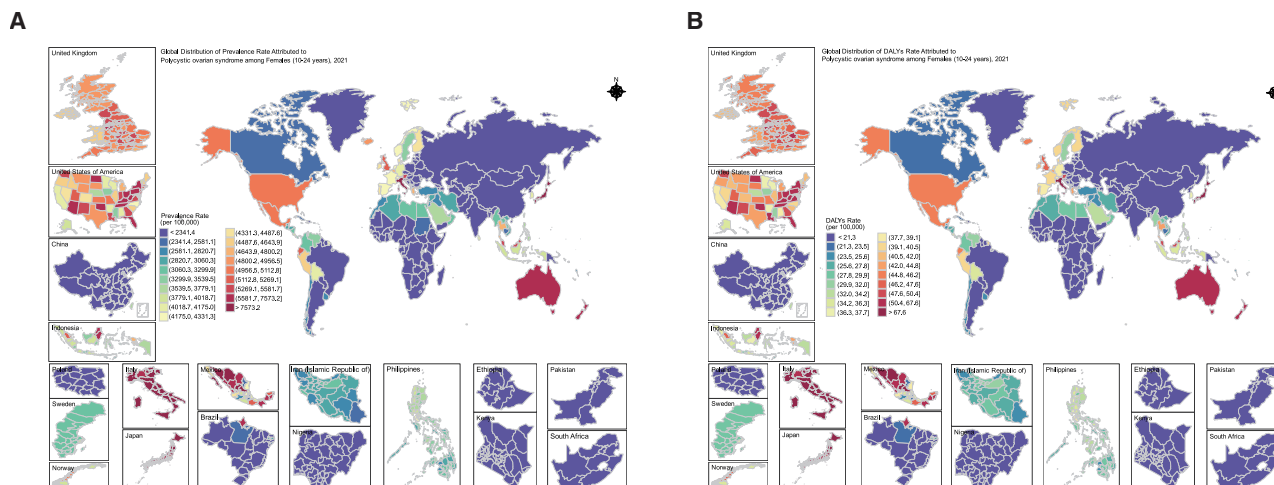
### Global trends in PCOS burden among young females

Between 1990 and 2021, global prevalence, incidence, and DALY rates of PCOS among females aged 10–24 years increased notably by 31.1% (95% UI: -21.7–119.4), 29.0% (-38.2–168.9), and 30.6% (-56.3–290.7), respectively (Figures 1C and 1D). By 2021, the global prevalence rate reached 2,141.6 (1,467.0–3,042.8) per 100,000 females, corresponding to 19,709,918.0 (13,501,452.0–28,003,744.0) prevalent cases worldwide. The incidence rate was 242.5 (138.8–390.8), corresponding to 2,232,036.0 (1,277,767.0–3,596,834.0) new cases. The DALY rate increased to 19.4 (8.6–40.9), corresponding to 178,473.0 (78,756.0–376,210.0) total DALYs (Figures 1A and 1B). Age stratification revealed that the highest prevalence rate was observed in the 20- to 24-year age group, at 3,454.0 (2,489.1–4,742.6), compared with 2,523.8 (1,707.0–3,613.4) in those aged 15–19 years and 588.5 (311.6–960.1) in those aged 10–14 years.

In 2021, the high-socio-demographic index (SDI) region experienced the highest burden of PCOS among the five SDI regions, with prevalence and incidence rates of 4,695.8 (3,333.7–6,530.2) and 543.6 (304.0–872.4), respectively. Within this region, the 20- to 24-year age group exhibited the highest prevalence rate, at 7,520.0 (5,583.8–10,152.7). Corresponding prevalence rates were 5,160.1 (3,644.0–7,206.4) for those aged 15–19 years and 1,180.7 (592.8–1,941.2) for those aged 10–14 years. From 1990 to 2021, all SDI regions exhibited increasing trends in young PCOS burden. The middle-SDI region experienced the largest increases in both prevalence (68.9% [0.1–184.9]) and incidence (63.0% [-20.3–233.0]) rates, reaching 2,648.3 (1,790.1–3,758.0) and 295.0 (171.8–473.3) in 2021, respectively. The middle-SDI region also showed the sharpest increase in DALY rates, whereas the high-SDI region recorded the smallest increase across these burden metrics (Tables 1 and S1; Data S1).

### Regional and national disparities in young PCOS burden

Analysis of 204 countries and territories across 21 GBD regions revealed substantial regional variations (Figures 1C and 1D). Between 1990 and 2021, the prevalence, incidence, and DALY rates increased markedly across all 21 GBD regions. In 2021, the majority of the top 100 countries and territories with the



**Figure 1. Geographic distribution of prevalence and DALY rates of young PCOS in 2021**

(A) Geographic distribution of the prevalence rate of young PCOS in 2021.

(B) Geographic distribution of the DALY rate of young PCOS in 2021. Rates are expressed per 100,000 females aged 10–24 years. Color gradients indicate increasing burden across locations. Estimates are derived from the GBD 2021 framework and represent population-level modeled estimates, with UIs shown where applicable. Interval labels in the map legends use the notation “(a, b]” to denote left-open, right-closed UIs, indicating values greater than “a” and up to and including “b.”

PCOS, polycystic ovary syndrome; DALY, disability-adjusted life years; UIs, uncertainty intervals; SDI, socio-demographic index.

highest prevalence rates were concentrated in Western Europe (23%), North Africa and Middle East (19%), and Oceania (16%). Similar age-related trends persisted regionally. In the high-income Asia Pacific, prevalence rates were 1,363.5 (570.7–2,488.9) among those aged 10–14 years, 7,343.3 (5,094.3–10,196.5) among those aged 15–19 years, and 10,769.9 (7,668.7–14,877.5) among those aged 20–24 years. The highest incidence and DALY rates were also observed in these three high-SDI regions (Figures 3E and 3F). With respect to temporal trends, the largest proportional increases in prevalence between 1990 and 2021 were observed in Western Sub-Saharan Africa (15% of the top 100 countries), followed by Southeast Asia (12%) and Oceania (11%). Similar trends were observed for incidence and DALY rates. Among the 56 international regions, the highest prevalence rates in 2021 were recorded in high-income region (5,076.8 [3,582.8–7,060.6]), World Bank high-income region (4,863.9 [3,447.6–6,760.0]), and North America (4,781.2 [3,417.4–6,556.2]). Regarding percentage change in prevalence from 1990 to 2021, the largest increases were observed in Southeast Asia, East Asia, and Oceania (102.7% [17.7–248.7]), the Association of Southeast Asian Nations (98.6% [16.1–239.5]), and the South Asia region as defined by the World Bank (83.8% [7.4–214.6]). Similar regional patterns were observed for DALY rates and their percentage changes (Table 1, Data S1, and Figures S1 and S2).

At the national level, prevalence rates increased in 99.0% of the 204 countries and territories between 1990 and 2021, with the largest increases observed in Equatorial Guinea (156.0% [40.3–368.7]), the Maldives (145.4% [39.5–332.4]), and Myanmar (117.5% [26.0–275.3]) (Figures 1A and 1B). Incidence rates increased in 97.5% of countries and territories over the same period, with these same countries exhibiting the most pro-

nounced growth. Among the top 100 countries and territories with the largest increases in prevalence and incidence rates, 75% and 68%, respectively, were located in low- and middle-SDI regions. In 2021, 113 of 204 countries (55.4%) had prevalence rates exceeding the global average, with more than half of these located in high-middle- and high-SDI regions. In that year, Italy (11,139.3 [7,621.0–15,798.4]), Japan (7,978.4 [5,503.4–11,275.0]), and New Zealand (7,573.2 [5,125.5–10,765.4]) reported the highest prevalence rates and also ranked among the countries with the highest incidence rates. DALY rates increased in 201 countries, with eight (e.g., Equatorial Guinea) experiencing rises exceeding 100% relative to 1990. Patterns in DALY levels and percentage changes closely mirrored those observed for prevalence and incidence (Table S2, Data S1, and Figures S3 and S4).

Age-specific analyses showed that the burden of young PCOS in 2021 was concentrated in older adolescent and young adult age groups. Italy reported the highest prevalence rate in the 10- to 24-year age group, at 11,139.3 (7,621.0–15,798.4), with the peak observed among those aged 20–24 years (15,948.2 [11,314.8–22,113.5]), compared with 4,259.6 (2,613.6–6,405.2) among those aged 10–14 years. Italy also reported the highest overall DALY rate, at 0.8 (0.2–1.8), with 149.6 (67.0–316.5) in the 20- to 24-year age group versus 37.1 (16.1–78.3) in the 10- to 14-year age group.

### Subnational trend and heterogeneity in young PCOS burden

Beyond national-level differences, substantial subnational heterogeneity was evident (Data S1; Figures S7 and S8). Among the 20 subnational regions analyzed, South Italy (13,897.9 [9,524.9–19,891.3]) reported the highest prevalence rate in

**Table 1. The incidence, prevalence, and DALY rates of young PCOS (per 100,000 females) in 1990 and 2021, and their percentage changes, by the global and regional levels (95% UIs)**

| Location                     | Incidence              |                        |                        | Prevalence                   |                              |                        | DALY                |                      |                        |
|------------------------------|------------------------|------------------------|------------------------|------------------------------|------------------------------|------------------------|---------------------|----------------------|------------------------|
|                              | Rate                   |                        | Percentage change      | Rate                         |                              | Percentage change      | Rate                |                      | Percentage change      |
|                              | 1990                   | 2021                   |                        | 1990                         | 2021                         |                        | 1990                | 2021                 |                        |
| Global                       | 188.0<br>(106.3–309.5) | 242.5<br>(138.8–390.8) | 29.0%<br>(–38.2–168.9) | 1,633.3<br>(1,111.1–2,338.2) | 2,141.6<br>(1,467.0–3,042.8) | 31.1%<br>(–21.7–119.4) | 14.8<br>(6.5–31.4)  | 19.4<br>(8.6–40.9)   | 30.6%<br>(–56.3–290.7) |
| High SDI                     | 452.6<br>(244.6–757.7) | 543.6<br>(304.0–872.4) | 20.1%<br>(–44.0–158.2) | 3,951.4<br>(2,737.3–5,599.4) | 4,695.8<br>(3,333.7–6,530.2) | 18.8%<br>(–26.8–93.2)  | 35.9<br>(15.8–73.5) | 42.6<br>(19.1–86.9)  | 18.9%<br>(–59.2–245.8) |
| High-middle SDI              | 180.7<br>(106.0–291.9) | 274.6<br>(158.6–441.3) | 52.0%<br>(–25.5–210.2) | 1,687.9<br>(1,146.4–2,409.2) | 2,483.8<br>(1,675.7–3,544.8) | 47.2%<br>(–12.7–148.2) | 15.2<br>(6.6–31.9)  | 22.5<br>(9.9–47.7)   | 48.0%<br>(–50.7–344.4) |
| Middle SDI                   | 181.0<br>(104.6–292.9) | 295.0<br>(171.8–473.3) | 63.0%<br>(–20.3–233.0) | 1,567.7<br>(1,059.6–2,250.9) | 2,648.3<br>(1,790.1–3,758.0) | 68.9%<br>(0.1–184.9)   | 14.2<br>(6.2–30.2)  | 23.9<br>(10.5–50.9)  | 68.1%<br>(–44.6–409.7) |
| Low-middle SDI               | 111.8<br>(62.5–184.7)  | 170.5<br>(96.3–279.8)  | 52.4%<br>(–28.2–223.2) | 906.7<br>(593.6–1,323.9)     | 1,523.8<br>(1,019.8–2,212.4) | 68.1%<br>(–3.1–191.3)  | 8.4<br>(3.6–17.9)   | 13.8<br>(6.0–29.3)   | 64.6%<br>(–46.1–401.4) |
| Low SDI                      | 75.2<br>(40.4–127.4)   | 106.9<br>(59.0–176.7)  | 42.1%<br>(–35.1–211.0) | 585.2<br>(374.3–877.6)       | 870.4<br>(570.8–1,283.8)     | 48.7%<br>(–16.8–165.8) | 5.3<br>(2.3–11.3)   | 7.8<br>(3.3–16.6)    | 47.2%<br>(–52.2–353.8) |
| North Africa and Middle East | 237.5<br>(134.0–386.1) | 302.3<br>(175.3–491.6) | 27.3%<br>(–38.7–164.0) | 1,999.0<br>(1,328.0–2,906.9) | 2,728.3<br>(1,834.9–3,934.4) | 36.5%<br>(–20.5–134.2) | 18.6<br>(8.1–39.3)  | 25.0<br>(10.9–53.2)  | 33.9%<br>(–55.8–305.7) |
| South Asia                   | 94.2<br>(54.1–154.9)   | 155.3<br>(87.4–254.7)  | 64.7%<br>(–21.6–246.4) | 771.4<br>(516.3–1,119.1)     | 1,440.8<br>(968.6–2,083.6)   | 86.8%<br>(8.9–220.0)   | 7.2<br>(3.1–15.2)   | 13.0<br>(5.5–27.2)   | 80.9%<br>(–40.5–449.9) |
| Western Europe               | 508.8<br>(316.7–788.3) | 583.3<br>(357.1–905.7) | 14.6%<br>(–39.8–118.7) | 5,005.2<br>(3,434.4–7,070.1) | 5,244.5<br>(3,594.5–7,444.1) | 4.8%<br>(–36.9–74.1)   | 45.6<br>(20.2–95.7) | 48.2<br>(21.3–100.3) | 5.6%<br>(–64.3–212.6)  |
| Central Europe               | 27.0<br>(14.0–46.9)    | 32.7<br>(18.3–53.1)    | 21.1%<br>(–45.1–169.7) | 228.7<br>(135.0–362.3)       | 300.1<br>(193.3–447.7)       | 31.2%<br>(–30.9–149.6) | 2.1<br>(0.8–4.5)    | 2.7<br>(1.1–5.8)     | 30.2%<br>(–58.7–310.0) |
| Eastern Europe               | 28.5<br>(14.7–51.7)    | 37.5<br>(19.4–66.9)    | 31.8%<br>(–45.0–215.4) | 229.8<br>(138.3–370.8)       | 295.1<br>(180.7–466.1)       | 28.4%<br>(–34.6–152.2) | 2.2<br>(0.8–4.8)    | 2.8<br>(1.1–6.2)     | 27.8%<br>(–62.1–330.5) |
| East Asia                    | 112.8<br>(61.9–191.5)  | 224.0<br>(124.4–369.6) | 98.5%<br>(–8.5–330.5)  | 1,101.8<br>(732.8–1,607.2)   | 1,947.1<br>(1,286.7–2,832.8) | 76.7%<br>(1.9–206.7)   | 9.8<br>(4.2–20.7)   | 17.4<br>(7.6–37.0)   | 78.0%<br>(–41.8–443.1) |
| Central Asia                 | 51.0<br>(27.3–86.4)    | 70.6<br>(38.2–116.2)   | 38.5%<br>(–37.2–205.5) | 436.4<br>(271.4–662.7)       | 616.2<br>(391.7–907.1)       | 41.2%<br>(–22.9–158.9) | 4.0<br>(1.7–8.5)    | 5.6<br>(2.3–12.2)    | 40.8%<br>(–55.5–346.1) |
| Southeast Asia               | 228.6<br>(122.7–383.4) | 419.9<br>(234.2–691.4) | 83.7%<br>(–15.5–299.0) | 1,885.0<br>(1,264.0–2,759.5) | 3,723.5<br>(2,512.8–5,362.5) | 97.5%<br>(15.4–238.1)  | 17.5<br>(7.5–36.0)  | 34.1<br>(14.8–71.9)  | 95.6%<br>(–35.0–488.9) |
| High-income                  | 442.8<br>(230.1–757.8) | 578.3<br>(312.1–928.8) | 30.6%<br>(–41.1–191.0) | 3,964.9<br>(2,676.4–5,755.0) | 4,781.1<br>(3,417.3–6,556.0) | 20.6%<br>(–26.7–98.6)  | 36.0<br>(15.6–72.7) | 43.4<br>(19.6–88.0)  | 20.6%<br>(–58.3–248.4) |
| North America                | 87.2<br>(49.1–147.6)   | 87.2<br>(49.8–143.3)   | 0.0%<br>(–52.9–112.2)  | 711.9<br>(451.3–1,075.3)     | 822.0<br>(532.5–1,212.7)     | 15.5%<br>(–36.1–108.4) | 6.5<br>(2.7–14.3)   | 7.5<br>(3.1–16.5)    | 15.3%<br>(–64.0–269.1) |
| Andean Latin America         | 404.3<br>(244.5–635.4) | 504.5<br>(312.5–774.6) | 24.8%<br>(–34.9–139.2) | 3,216.2<br>(2,129.5–4,618.4) | 4,616.3<br>(3,095.2–6,680.3) | 43.5%<br>(–16.4–146.3) | 28.3<br>(12.2–61.4) | 40.7<br>(17.7–85.8)  | 43.9%<br>(–52.8–338.9) |
| Central Latin America        | 429.5<br>(272.1–649.0) | 436.6<br>(280.8–655.9) | 1.6%<br>(–44.3–85.2)   | 3,618.3<br>(2,425.4–5,168.3) | 4,127.5<br>(2,795.9–5,857.5) | 14.1%<br>(–32.4–92.4)  | 32.3<br>(14.4–68.9) | 36.7<br>(16.4–77.5)  | 13.6%<br>(–61.9–238.2) |

(Continued on next page)

Table 1. Continued

| Location                    | Incidence                |                          |                        | Prevalence                   |                              |                        | DALY                 |                      |                        |
|-----------------------------|--------------------------|--------------------------|------------------------|------------------------------|------------------------------|------------------------|----------------------|----------------------|------------------------|
|                             | Rate                     |                          | Percentage change      | Rate                         |                              | Percentage change      | Rate                 |                      | Percentage change      |
|                             | 1990                     | 2021                     |                        | 1990                         | 2021                         |                        | 1990                 | 2021                 |                        |
| Southern Latin America      | 184.1<br>(97.8–310.9)    | 280.5<br>(152.7–468.0)   | 52.4%<br>(–31.3–237.4) | 1,459.4<br>(974.1–2,174.6)   | 2,450.7<br>(1,669.9–3,566.7) | 67.9%<br>(–2.7–189.9)  | 13.4<br>(5.8–27.9)   | 22.5<br>(9.7–46.1)   | 68.0%<br>(–44.0–402.7) |
| Central Sub-Saharan Africa  | 66.4<br>(35.3–113.0)     | 102.9<br>(56.7–172.8)    | 54.8%<br>(–30.1–242.7) | 523.3<br>(330.7–794.6)       | 817.1<br>(529.2–1,226.5)     | 56.2%<br>(–14.3–184.3) | 4.7<br>(1.9–10.0)    | 7.3<br>(3.1–15.4)    | 56.4%<br>(–50.5–393.6) |
| Eastern Sub-Saharan Africa  | 78.0<br>(41.1–133.8)     | 100.3<br>(53.9–168.0)    | 28.6%<br>(–42.8–188.6) | 610.6<br>(387.7–915.4)       | 820.7<br>(532.3–1,216.2)     | 34.4%<br>(–25.4–142.0) | 5.5<br>(2.3–11.6)    | 7.3<br>(3.1–15.6)    | 33.5%<br>(–56.8–312.2) |
| Western Sub-Saharan Africa  | 74.8<br>(39.7–127.7)     | 107.4<br>(57.7–178.9)    | 43.7%<br>(–35.7–220.5) | 592.0<br>(375.8–895.2)       | 868.9<br>(560.9–1,282.9)     | 46.8%<br>(–18.8–165.2) | 5.4<br>(2.3–11.5)    | 7.9<br>(3.3–16.7)    | 46.7%<br>(–52.9–356.5) |
| Southern Sub-Saharan Africa | 129.0<br>(70.8–213.9)    | 161.0<br>(89.3–265.7)    | 24.9%<br>(–42.1–169.1) | 1,080.2<br>(702.7–1,607.7)   | 1,364.0<br>(885.8–2,012.5)   | 26.3%<br>(–29.1–124.7) | 9.9<br>(4.2–21.3)    | 12.4<br>(5.2–26.9)   | 25.3%<br>(–59.8–291.4) |
| Australasia                 | 669.9<br>(359.2–1,105.8) | 764.8<br>(411.5–1,288.3) | 14.2%<br>(–48.3–152.6) | 5,537.1<br>(3,806.4–7,698.3) | 6,282.1<br>(4,268.6–8,962.2) | 13.5%<br>(–31.7–88.6)  | 49.3<br>(21.2–101.2) | 56.0<br>(24.2–116.4) | 13.4%<br>(–62.1–239.5) |
| High-income Asia Pacific    | 768.6<br>(374.6–1,338.5) | 836.3<br>(430.9–1,380.5) | 8.8%<br>(–53.5–156.1)  | 5,794.0<br>(3,951.7–8,302.6) | 6,725.5<br>(4,620.4–9,497.2) | 16.1%<br>(–30.4–93.5)  | 51.8<br>(21.8–107.3) | 60.1<br>(25.6–125.5) | 15.9%<br>(–61.9–252.5) |
| Caribbean                   | 167.1<br>(98.4–270.4)    | 207.9<br>(123.7–333.6)   | 24.4%<br>(–38.3–150.4) | 1,603.2<br>(1,042.8–2,335.4) | 2,019.4<br>(1,318.6–2,929.1) | 26.0%<br>(–28.2–120.7) | 14.8<br>(6.3–31.9)   | 18.4<br>(8.0–39.6)   | 24.5%<br>(–59.7–283.4) |
| Oceania                     | 195.3<br>(110.8–316.1)   | 270.7<br>(157.6–437.1)   | 38.6%<br>(–32.7–185.4) | 1,619.9<br>(1,068.8–2,355.6) | 2,301.5<br>(1,526.2–3,317.2) | 42.1%<br>(–17.9–145.6) | 14.5<br>(6.2–30.7)   | 20.3<br>(8.8–42.9)   | 40.2%<br>(–54.1–327.5) |

Abbreviations: PCOS, polycystic ovary syndrome; DALY, disability-adjusted life year; UIs, uncertainly intervals.

2021, while North West England (26.6% [-25.8–115.9]) experienced the most rapid increase in prevalence from 1990 to 2021. The highest DALY rate in 2021 and the greatest percentage increase were likewise observed in these two regions.

From 1990 to 2021, 94.6% of the 652 subnational locations exhibited upward trends in prevalence rates. The most rapid increases were observed in West Papua (137.1% [37.3–310.2]), Siquijor (131.5% [29.0–315.5]), and Southeast Sulawesi (129.9% [34.6–292.5]). Among the top 100 subnational locations with the largest percentage increases, 51% were located in the Philippines, 31% in Indonesia, and 17% in China, with 87.0% located in low- and middle-SDI regions. In contrast, among the 100 subnational locations with the highest prevalence rates in 2021, 41% were in Japan, 21% in Italy, and 21% in the UK, with 85% located in high-middle- and high-SDI regions. Across all 652 subnational locations, the highest prevalence rates of young PCOS were observed in Basilicata (17,955.8 [12,248.4–25,558.3]), Molise (17,839.4 [12,062.5–25,453.7]), and Wakayama (16,627.5 [11,194.8–24,368.5]).

From 1990 to 2021, incidence rates increased in 89.0% of subnational locations. Among the 100 subnational locations with the largest increases in incidence rates, the majority were located in the Philippines (42%), Indonesia (29%), and China (28%). Within China, the provinces of Henan (146.6% [12.4–440.9]), Hebei (144.7% [9.6–447.4]), and Jiangsu (139.7% [6.9–438.1]) recorded the highest subnational increases in incidence. In 2021, the 100 subnational locations with the highest incidence rates were primarily located in Japan (46%), Italy (21%), and the US (18%). The highest subnational rates were observed in Wakayama (2,372.6 [970.8–4,490.3]), Tottori (2,359.3 [969.0–4,368.4]), and Akita (1,970.5 [910.2–3,479.5]).

For DALY rates, 94.3% of subnational locations showed upward trends from 1990 to 2021, with the largest increases observed in the same regions as those observed for prevalence. The most rapid increases among the 100 locations were observed in West Papua (134.2% [-23.5–616.2]), Siquijor (130.8% [-25.7–615.5]), and Southeast Sulawesi (127.9% [-25.1–593.1]). Among the 100 subnational locations with the highest DALY rates in 2021, Japan (41%), Italy (21%), and the UK (18%) predominated. The highest DALY rates were recorded in Basilicata (160.9 [69.1–342.9]), Molise (159.7 [68.7–334.3]), and Wakayama (146.5 [63.9–310.6]) (Data S1, Figures S5 and S6, and Tables S3–S20).

In 2021, age-specific analyses at the subnational level were consistent with global patterns. In Basilicata, the prevalence rate was 24,225.2 (16,904.5–33,930.6) among those aged 20–24 years, compared with 7,318.0 (4,547.4–10,945.2) among those aged 10–14 years. Corresponding DALY rates were 222.9 (97.2–476.1) and 63.9 (27.1–133.0) for these age groups, respectively.

### Absolute and relative inequalities in young PCOS burden

Considerable absolute and relative inequalities in young PCOS burden persisted and worsened, with a concentration in economically advantaged regions. From 1990 to 2021, global absolute inequality in the prevalence rate increased by 30.6%, with the slope inequality index (SII) rising from 2,054.1 (1,654.6–2,453.5) to 2,683.3 (2,127.8–3,238.8). Over the same

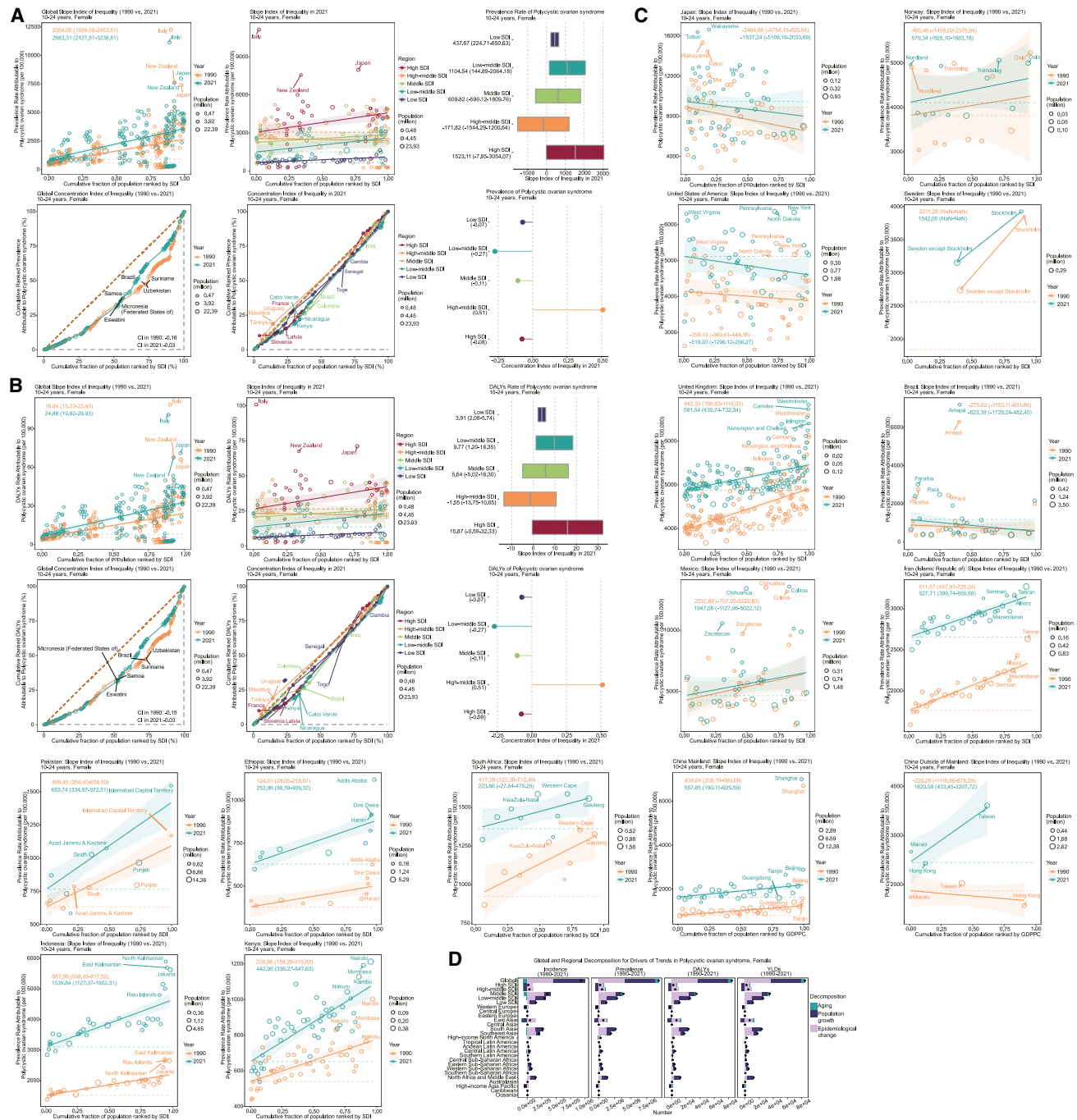
period, absolute inequality in the incidence rate increased by 33.9%, with the SII rising from 287.8 (163.1–254.5) to 279.6 (214.5–344.8). Similarly, global absolute inequality in DALY rate worsened by 24.5%, with the SII increasing from 18.8 (15.2–22.5) in 1990 to 24.9 (19.8–29.9) in 2021.

In 2021, absolute inequalities in incidence, prevalence, and DALY rates were most pronounced in high-SDI region, with the SII reaching 178.6 (-12.7–369.9), 1,523.1 (-7.9–3,054.1), and 15.9 (-0.6–32.3), respectively, primarily driven by Italy, New Zealand, and Japan. Conversely, relative inequality in prevalence rates followed an opposite global pattern, with the concentration index (CI) decreasing from -0.16 in 1990 to -0.03 in 2021. However, heterogeneity across SDI regions persisted. In 2021, the highest CI for prevalence was observed in the high-middle-SDI region (0.51), while the lowest were observed in the low- and high-SDI regions. Incidence and DALY rates showed similar global and regional patterns (Figures 2A and 2B).

At the national level, absolute inequality in incidence, prevalence, and DALY rates increased in eight countries in 2021 and decreased in six others. For prevalence, the SII increased to -519.9 (-1,296.1 –256.2) in the US (101.4% increase), 579.3 (-525.1–1683.8) in Norway (25.8% increase), -623.4 (-1,729.2–482.4) in Brazil (126.2% increase), 653.7 (335.0–972.5) in Pakistan (42.3% increase), 1,539.8 (1,127.4–1,952.3) in Indonesia (123.8% increase), 254.0 (98.6–409.3) in Ethiopia (104.8% increase), 443.0 (338.3–547.6) in Kenya (86.9% increase), 557.9 (190.1–925.6) in China Mainland (27.2% increase), and 1,820.6 (433.5–3,207.7) in China Outside of Mainland (926.5% increase). By 2021, young PCOS burden was primarily concentrated in subnational locations with higher socio-economic status in Norway, Sweden, the UK, Mexico, Iran, Pakistan, Indonesia, Ethiopia, Kenya, South Africa, and China. In contrast, in Brazil, the US, and Japan, the burden was primarily concentrated in lower socio-economic status subnational locations (Figure 2C, Data S1, and Figures S9–S11).

### Gap between observed performance and achievable frontier of young PCOS burden

The frontier analysis revealed that high-income regions performed well below the achievable frontier levels of young PCOS burden relative to their SDI. In 2021, 96.6% of the 204 countries and territories failed to reach the frontier for prevalence and incidence rates, with Italy exhibiting the largest deviation from the frontier (Figures 3A–3D and Table 2). In 2021, only seven countries (3.4%) reached the frontier, the majority of which were located in low-SDI region. Among the 88 high- and high-to-middle SDI countries, only three reached the frontier, including Bosnia and Herzegovina (frontier deviation: 99.3 [-3.9–249.6]), Ukraine (100.6 [-3.5–260.5]), and Czechia (103.3 [-0.7–253.2]). In 2021, the largest frontier deviations in prevalence rates were observed in Italy (10,982.2 [7,463.9–15,641.2]), Japan (7,821.1 [5,346.2–11,117.7]), New Zealand (7,416.0 [4,968.3–10,608.2]), and Australia (5,850.9 [3,925.8–8,458.0]). For DALY rates, 45 countries reached the frontier, primarily located in low-SDI region. From 1990 to 2021, 98.5%, 99.0%, and 98.5% of the 204 countries and territories experienced increases in frontier deviations for incidence, prevalence, and DALYs, respectively, with the Maldives recording the largest



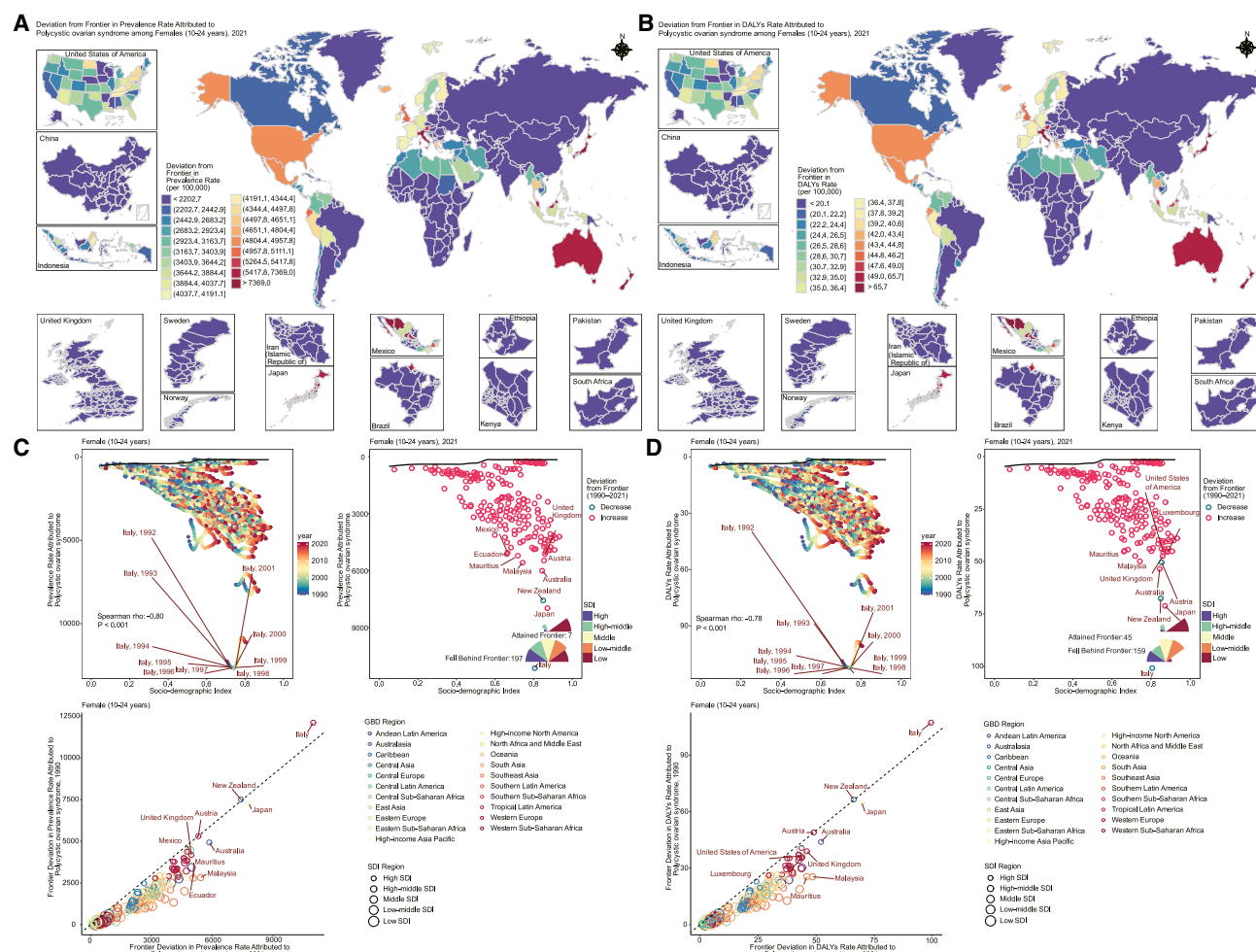
**Figure 2. Health inequality and decomposition analysis of young PCOS, from 1990 to 2021**

(A) Absolute cross-country inequality in young PCOS prevalence rates at the global (left) and regional (right) levels, measured by the SII and ranked by SDI. Negative SII values indicate higher burdens among socio-economically disadvantaged populations, whereas positive values indicate the opposite. Left: Global changes from 1990 to 2021. Right: Inequalities across the five SDI regions in 2021.

(B) Absolute cross-country inequality in young PCOS DALY rates at the global (left) and regional (right) levels, measured by the SII.

(C) Absolute within-country inequality in young PCOS prevalence rates at the national level, measured by the SII.

(D) Decomposition analysis of changes in global and regional young PCOS burden, including incidence, prevalence, DALYs, and YLLs. Stacked bars show the contributions of population growth, population aging, and epidemiological changes. Black dots indicate the observed net change after summing all components.



**Figure 3. Global frontier analysis of young PCOS burden in 2021**

(A) Deviation from the achievable frontier for young PCOS prevalence rates in 2021.

(B) Deviation from the achievable frontier for young PCOS DALY rates in 2021.

(C) Frontier analysis of young PCOS prevalence rates. The frontier represents the minimal prevalence rate theoretically achievable at a given SDI level and is shown as a solid black line. Top left: Annual prevalence rates for 204 countries (colored by year) relative to the frontier. Top right: Countries' prevalence rates in 2021, colored by whether the gap from the frontier has increased (red) or decreased (green) since 1990. Bottom left: Comparison of frontier deviations between 1990 and 2021.

(D) Frontier analysis of young PCOS DALY rates, following the same analytical framework as in (C).

increases across all three metrics (Table 2, Data S1, and Figures S12–S15).

At the subnational level in 2021, 68.8% of the 494 subnational locations failed to reach the frontier for prevalence rates (Figure 4 and Table 3). Japan accounted for the largest share (42.0%) of the 100 subnational locations with the greatest frontier deviations, whereas Indonesia accounted for the largest share (33.0%) of locations with the greatest increases in frontier deviation between 1990 and 2021. In 2021, none of the subnational locations in the US, Iran, Indonesia, Ethiopia, and China achieved the frontier prevalence rates. For DALY rates, 31.2% of subnational locations failed to reach the frontier in 2021. From 1990 to 2021, 96.6%, 97.6%, and 97.6% of subnational locations experienced increases in frontier deviations for incidence, prevalence, and DALYs, respectively, with Wakayama

recording the largest increases across all three burden metrics. In 2021, Japan accounted for 41% of the 100 subnational locations with the largest deviations, whereas Indonesia accounted for 33.0% of those with the greatest increases over time (Table 3, Data S1, and Figures S14–S16).

### Decomposition of drivers underlying changes in young PCOS burden

A decomposition analysis was conducted to quantify the contributions of population growth, population aging, and epidemiological change to changes in young PCOS burden. Globally, increases in DALY rates were primarily driven by population growth (50.9%) and epidemiological change (42.8%), while aging contributed comparatively little (6.3%). Marked regional heterogeneity was observed. Epidemiological change emerged as the dominant

**Table 2. Frontier deviation in incidence, prevalence, and DALY rates attributed to young PCOS across 204 countries and territories**

| PCOS       |                                                                    | 10–24 years |
|------------|--------------------------------------------------------------------|-------------|
| Incidence  | countries behind frontiers n (%)                                   | 197 (96.6%) |
|            | country with the largest deviation in 2021                         | Italy       |
|            | number of countries with increasing deviation from frontiers n (%) | 201 (98.5%) |
|            | country with the largest decrease in deviation from 1990 to 2021   | Italy       |
|            | country with the largest increase in deviation from 1990 to 2021   | Maldives    |
| Prevalence | countries behind frontiers n (%)                                   | 197 (96.6%) |
|            | country with the largest deviation in 2021                         | Italy       |
|            | number of countries with increasing deviation from frontiers n (%) | 202 (99.0%) |
|            | country with the largest decrease in deviation from 1990 to 2021   | Italy       |
|            | country with the largest increase in deviation from 1990 to 2021   | Maldives    |
| DALYs      | countries behind frontiers n (%)                                   | 159 (77.9%) |
|            | countries with the largest deviation in 2021                       | Italy       |
|            | number of countries with increasing deviation from frontiers n (%) | 201 (98.5%) |
|            | country with the largest decrease in deviation from 1990 to 2021   | Italy       |
|            | country with the largest increase in deviation from 1990 to 2021   | Maldives    |

Abbreviations: PCOS, polycystic ovary syndrome; DALY, disability-adjusted life year.

driver of increasing PCOS burden in several regions, including East Asia, Central Asia, Southeast Asia, high-income North America, Southern Latin America, and the Caribbean. By contrast, population growth exerted a strong offsetting effect in Western Europe, Central Europe, and high-income Asia Pacific.

Across SDI levels, epidemiological change contributed positively to DALY rates in all regions, with the largest contribution observed in the high-SDI region, while population growth contributed negatively in high- and high-to-middle-SDI regions (Figure 2D). At the national level, population growth contributed negatively to changes in young PCOS prevalence in countries such as Japan, Poland, Iran, and China, whereas epidemiological change was the primary driver in countries including the UK, the US, Norway, Sweden, Indonesia, South Africa, and the Philippines. In contrast, population growth remained a major contributor to increasing burden in several low- and middle-income countries, including Nigeria, Pakistan, Ethiopia, Brazil, Mexico, and Kenya (Data S1 and Figure S25).

### Deep-learning forecasts of young PCOS burden to 2040

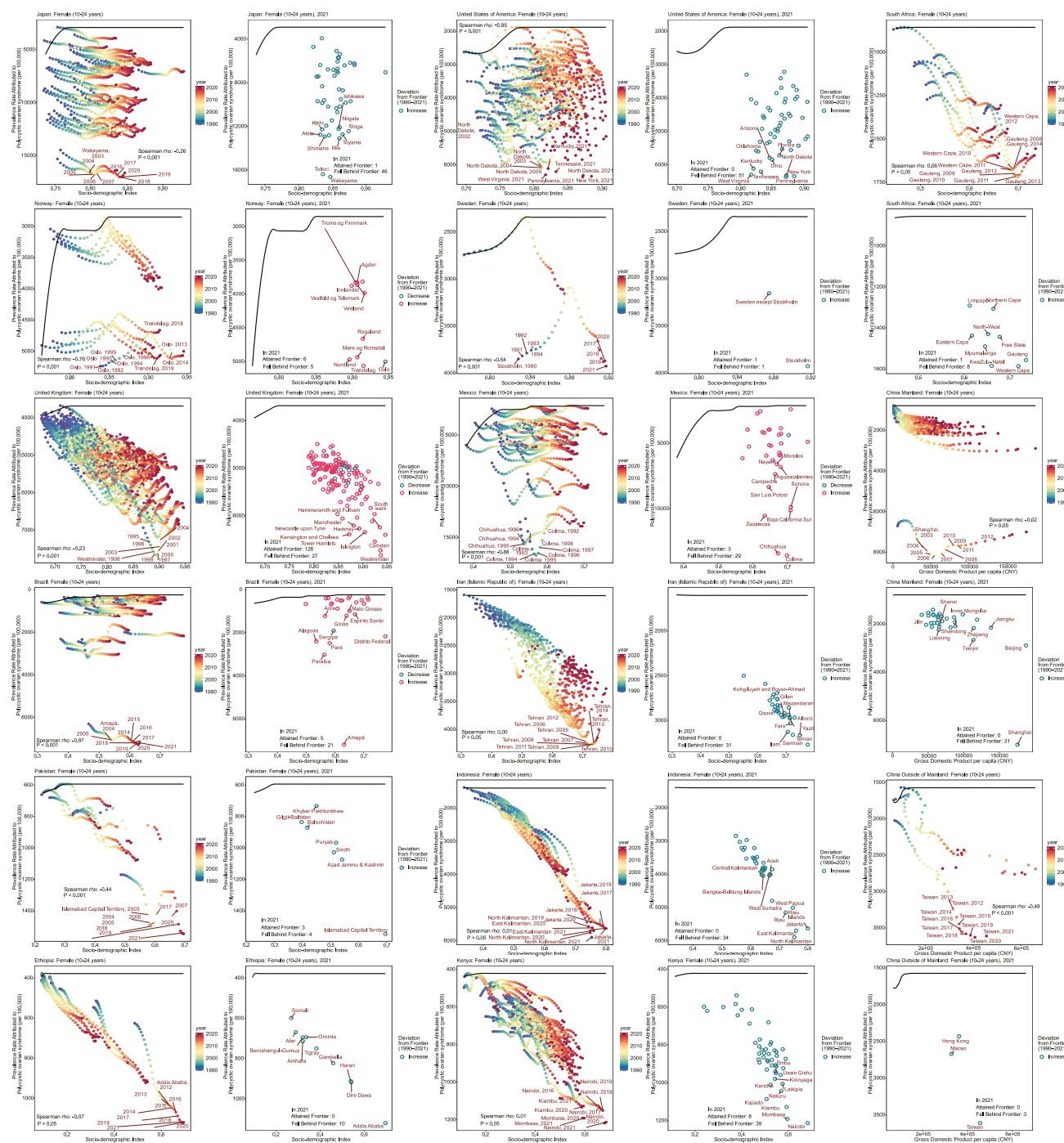
Using an advanced deep-learning framework incorporating attention mechanisms,<sup>20–22</sup> we generated forecasts of the young

PCOS burden through 2040 across 953 locations. These forecasts assume that historical trends will continue in the absence of substantial changes in public health interventions before 2040. The model demonstrated strong forecasting performance, with low error metrics, namely mean absolute percentage error (MAPE) (0.10% [0.10%–0.11%]) and mean squared percentage error (MSPE) (0.03% [0.03%–0.03%]). Relative to 2021, the global young PCOS burden is forecasted to increase by 2040. Specifically, the global prevalence rate is forecasted to rise by 5.7% (3.6–7.7) to 2,262.9 (2,219.5–2,306.3), the incidence rate by 5.5% (3.8–7.3) to 256.0 (251.8–260.2), and the DALY rate by 10.8% (10.4–11.1) to 21.5 (21.4–21.6) (Figure 5). In the 20- to 24-year age group, the global prevalence rate is forecasted to increase by 8.7% (6.8–10.6), reaching 3,755.8 (3,690.3–3,821.3) by 2040.

From 2021 to 2040, prevalence, incidence, and DALY rates of young PCOS are forecasted to increase across all SDI regions. The high-SDI region is forecasted to experience the highest increases, with prevalence rising by 14.7% (13.2–16.2), incidence by 12.8% (10.1–15.5), and DALY rates by 21.7% (20.5–23.0). By 2040, the high-SDI region is forecasted to have the highest rates among the five SDI regions, with prevalence, incidence, and DALY rates reaching 5,387.2 (5,316.3–5,458.1), 613.2 (598.7–627.7), and 51.9 (51.4–52.4), respectively. Among the 21 GBD regions, high-income Asia Pacific is forecasted to have the largest prevalence rate of young PCOS in 2040, at 7,000.8 (6,925.4–7,076.1). Consistent with earlier patterns, the burden of PCOS is also forecasted to remain highest in the 20- to 24-year age group by 2040 (Data S1 and Figures S17–S19).

At the national level, 90.1% of the 204 countries and territories are forecasted to experience increases in prevalence rates between 2021 and 2040. The largest percentage increases are forecasted for the US (34.3% [31.8–36.7]), Nepal (24.1% [17.9–30.4]), and Sudan (21.2% [18.1–24.2]). Nevertheless, the highest absolute prevalence rates in 2040 are expected to occur in Italy (11,290.3 [11,251.4–11,329.2]), Japan (7,963.0 [7,931.4–7,994.6]), and New Zealand (7,867.3 [7,778.5–7,956.0]). In nearly all countries and territories (99.0%), prevalence rates are forecasted to increase in the 20- to 24-year age group by 2040, with the largest increases predicted in the US (45.3% [42.7–47.9]), Sweden (22.8% [19.8–25.8]), and Angola (20.3% [17.1–23.5]). DALY rates are forecasted to rise in 85.8% of countries and territories by 2040, with the steepest increases expected in the US (52.9% [49.7–56.2]), Sudan (47.7% [45.7–49.7]), and Nepal (37.8% [36.6–39.0]). By contrast, the highest DALY rates in 2040 are forecasted to occur in Italy (104.7 [104.5–104.9]), Japan (75.7 [75.5–75.8]), and New Zealand (75.7 [75.3–76.1]). Additionally, 97.1% of countries and territories are forecasted to experience higher DALY rates in the 20- to 24-year age group by 2040 (Data S1 and Figures S20–S22).

At the subnational level, 90.0% of the 460 subnational locations with available SDI values are forecasted to experience increases in prevalence rates by 2040. Among the 100 subnational locations with the most pronounced upward trends, 50 are expected to be in the US, 25 in Kenya, and 17 in Indonesia. The highest increases are forecasted to occur in Rhode Island (58.1% [49.3–66.8]), Michigan (48.2% [44.0–52.4]), and Delaware (46.3% [39.7–52.9]). Among the 100 subnational locations with the highest forecasted



**Figure 4. Frontier analysis of young PCOS burden at national and subnational levels in 2021**

Frontier analysis of young PCOS prevalence rates at the subnational level. The frontier represents the minimal prevalence rate theoretically achievable at a given SDI level and is shown as a solid black line. Top left: Annual prevalence rates for subnational locations (colored by year) relative to the frontier. Top right: subnational locations' prevalence rates in 2021, colored by whether the gap from the frontier has increased (red) or decreased (green) since 1990. Bottom left: Comparison of frontier deviations between 1990 and 2021.

prevalence rates in 2040, 41 are expected to be in Japan, 29 in the US, 13 in Mexico, and 13 in the UK. The highest prevalence rates are projected for Wakayama (16,603.6 [16,522.3–16,685.0]), Tot-

tori (16,344.7 [16,252.5–16,436.9]), and Colima (14,213.0 [13,969.0–14,457.1]). Similarly, 82.0% of subnational locations are forecasted to experience increases in DALY rates by 2040.

**Table 3. Frontier deviation in incidence, prevalence, and DALY rates attributed to young PCOS across 494 subnational locations**

| PCOS       |                                                                                       | 10–24 years            |
|------------|---------------------------------------------------------------------------------------|------------------------|
| Incidence  | subnational units behind frontiers n (%)                                              | 330 (66.8%)            |
|            | subnational units with the largest deviation in 2021                                  | Wakayama               |
|            | number of subnational units with increasing deviation from frontiers n (%)            | 477 (96.6%)            |
|            | subnational unit with largest decrease in deviation from 1990 to 2021                 | Colima                 |
|            | subnational unit with largest increase in deviation from 1990 to 2021                 | Aomori                 |
|            | country with largest proportion in top 100 2021 deviation subnational units           | Japan (40.0%)          |
|            | country with largest proportion in top 100 2021 increased deviation subnational units | United Kingdom (50.0%) |
| Prevalence | subnational units behind frontiers n (%)                                              | 340 (68.8%)            |
|            | subnational units with the largest deviation in 2021                                  | Wakayama               |
|            | number of subnational units with increasing deviation from frontiers n (%)            | 482 (97.6%)            |
|            | subnational unit with largest decrease in deviation from 1990 to 2021                 | Sergipe                |
|            | subnational unit with largest increase in deviation from 1990 to 2021                 | Aomori                 |
|            | country with largest proportion in top 100 2021 deviation subnational units           | Japan (42.0%)          |
|            | country with largest proportion in top 100 2021 increased deviation subnational units | Indonesia (33.0%)      |
| DALYs      | subnational units behind frontiers n (%)                                              | 154 (31.2%)            |
|            | subnational units with the largest deviation in 2021                                  | Wakayama               |
|            | number of subnational units with increasing deviation from frontiers n (%)            | 482 (97.6%)            |
|            | subnational unit with largest decrease in deviation from 1990 to 2021                 | Sergipe                |
|            | subnational unit with largest increase in deviation from 1990 to 2021                 | Aomori                 |
|            | country with largest proportion in top 100 2021 deviation subnational units           | Japan (41.0%)          |
|            | country with largest proportion in top 100 2021 increased deviation subnational units | Indonesia (33.0%)      |

Abbreviations: PCOS, polycystic ovary syndrome; DALYs, disability-adjusted life years.

Among the 100 subnational locations with the steepest upward trends in DALY rates, 50 are expected to be in the US, 22 in Indonesia, and 12 in Kenya. The steepest increases in DALY rates are projected to occur in Rhode Island (84.6% [79.8–89.4]), Michigan (68.9% [66.3–71.6]), and Mississippi (65.0% [61.0–69.0]) (Data S1 and Figures S23 and S24).

## DISCUSSION

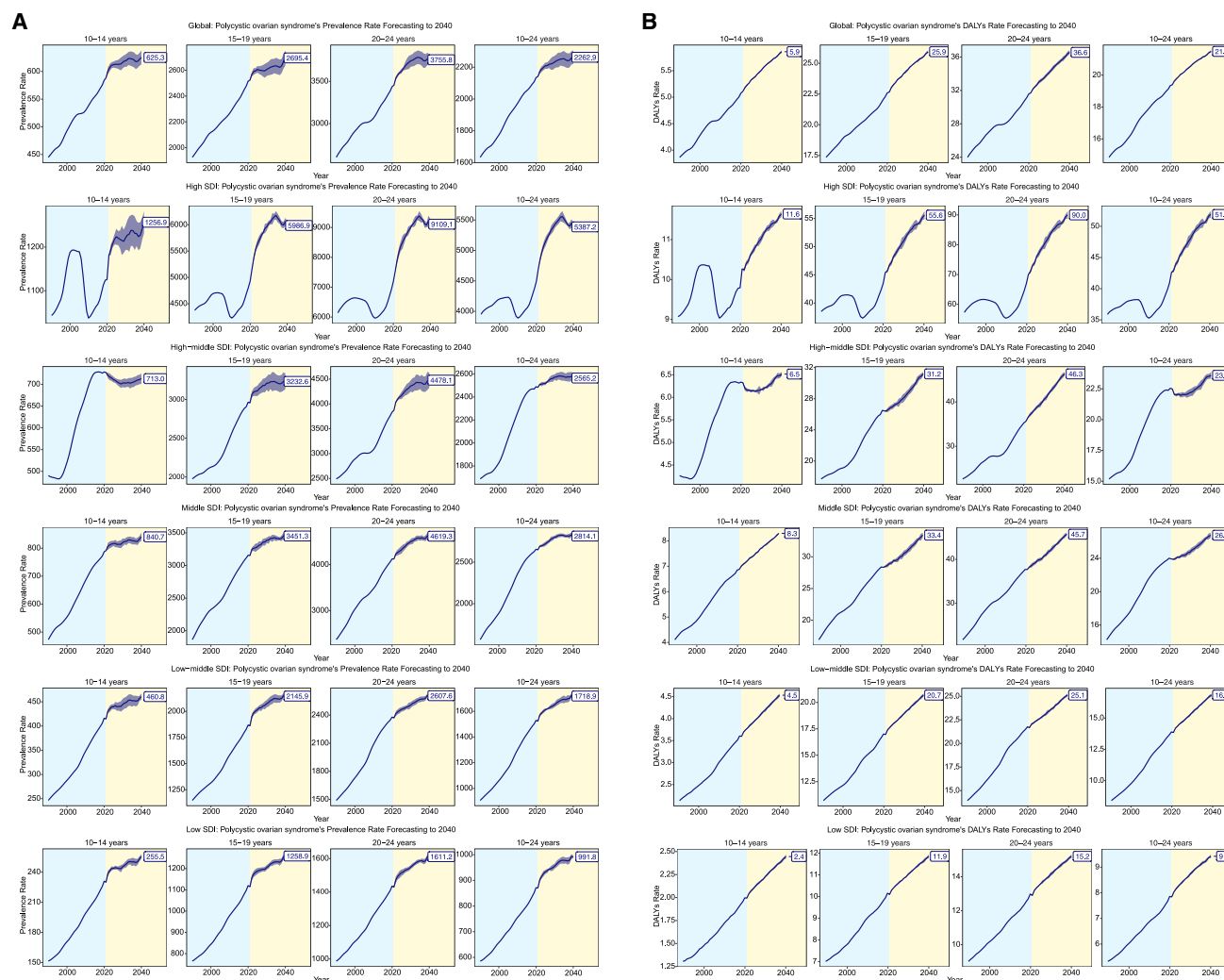
This study provides, to our knowledge, the most comprehensive and granular analysis of the global burden of PCOS among young females age 10–24 years to date, encompassing the broadest geographic scope of 953 global to subnational locations and the longest time frame, spanning 1990 to 2021. Our study have five principal findings: 1) The burden of young PCOS increased substantially over the past three decades in more than 95% of the 953 global to subnational locations, especially in the 20- to 24-year age group; 2) In 2021, high-SDI areas bore the highest young PCOS prevalence, reaching 24,225.2 (16,904.5–33,930.6) per 100,000 females in Basilicata, Italy, while the sharpest growth was observed in low- and middle-SDI areas; 3) Disparities in the observed burden of young PCOS across levels of socio-economic development have widened globally, with higher prevalence concentrated in high-SDI countries, while in countries such as Brazil, the US, and Japan, subnational regions with relatively lower SDI exhibited higher burdens; 4) Frontier analysis highlighted substantial and worsening deviations in young PCOS prevalence, with 96.6% of countries failing to achieve the estimated frontier levels

in 2021. Nearly all countries (99.0%) and most subnational locations (97.6%) experienced increasing frontier deviation between 1990 and 2021, illuminating vast opportunities for improvement; 5) The attention-based deep-learning algorithm forecasts a substantial global rise in the young PCOS burden by 2040, particularly in high-SDI region, subnational locations within the US, and among young adults aged 20–24 years, with sufficient predictive performance.

## Widespread global increase in PCOS burden among young females, particularly ages 20–24

The consistent widespread surges in young PCOS burden across global to subnational locations indicate a genuine global health concern, rather than isolated regional phenomena. Several factors are likely contributing to this trend, including evolving diagnostic criteria,<sup>23</sup> improved disease awareness and diagnosis,<sup>24</sup> rising obesity prevalence,<sup>25</sup> environmental exposures,<sup>26</sup> and lifestyle changes associated with urbanisation.<sup>27</sup> Of particular concern is the parallel quadrupling of obesity rates among young people between 1990 and 2022, from 1.7% to 6.9%.<sup>25</sup> Evidence from Mendelian randomization studies indicates that higher BMI causally increases the risk of PCOS, rather than suggesting a bidirectional relationship.<sup>28</sup> This causal link, together with the concurrent rise in both obesity and PCOS prevalence, constitutes a substantial and growing public health challenge.<sup>3,29</sup>

Age-stratified analyses consistently showed that women aged 20–24 years experienced substantially higher PCOS burden than younger adolescents across all regions. This age-specific pattern likely reflects both the natural progression of the



**Figure 5. Forecasts of young PCOS burden from 2020 to 2040**

(A) Forecasted prevalence rates of young PCOS at the global and SDI-regional levels from 2022 to 2040, generated using a state-of-the-art, attention-based deep-learning model.

(B) Forecasted DALY rates of young PCOS over the same period and regions, using the same modeling framework. Solid lines represent mean predictions, and shaded areas indicate UIs where applicable.

PCOS, polycystic ovary syndrome; DALY, disability-adjusted life years; SDI, socio-demographic index; UIs, uncertainty intervals.

condition and the typical timing of diagnosis. Diagnosing PCOS in young adolescents remains challenging because several defining features overlap with normal pubertal development, including menstrual irregularity and acne.<sup>30–34</sup> Additionally, clinical manifestations of PCOS often become more pronounced and readily recognizable in late adolescence and early adulthood, contributing to higher diagnostic rates in the 20- to 24-year age group. Delayed diagnosis has been associated with adverse reproductive outcomes,<sup>34</sup> underscoring the importance of timely identification during this critical life stage.

### Increasing socio-economic inequalities of young PCOS burden

High-income regions exhibited the highest young PCOS burden in 2021, with particularly elevated rates observed in Italy, Japan,

and New Zealand. This concentration may reflect improved healthcare access,<sup>35</sup> more widespread screening,<sup>36</sup> and more systematic diagnostic practices, rather than true biological differences in underlying disease prevalence.<sup>37</sup> Regional genetic architecture likely plays a role,<sup>38</sup> as the heritability of PCOS was estimated at over 70% in twin studies.<sup>39</sup> For instance, the high prevalence in Italy aligns with evidence of specific genetic predispositions, including identified roles of melanocortin receptor<sup>40</sup> and vasopressin receptor genes<sup>41</sup> in Italian families. Notably, substantial subnational heterogeneity exists within high-income countries, with Basilicata and Molise, Italy, recording the world's highest provincial young PCOS prevalence. This pattern highlights substantial subnational disparities in the observed young PCOS burden within affluent nations, with relatively disadvantaged regions exhibiting higher reported

prevalence.<sup>42</sup> This likely reflects a combination of limited healthcare access, less healthy dietary patterns dominated by processed foods, higher obesity rates in lower-income communities, and potential environmental exposures from industrial activities.<sup>43–45</sup> Similar subnational patterns observed in Japan and New Zealand further highlight the importance of tailored subnationally targeted interventions, especially in under-resourced settings within otherwise high-income countries.

While the high-SDI region exhibited the highest absolute prevalence rates, low- and middle-SDI regions experienced the most pronounced increases (>60% for both prevalence and incidence). Our inequality analyses further showed that absolute inequality in the distribution of reported young PCOS burden increased globally (particularly within the high-SDI region), yet relative inequality decreased as lower-SDI areas experienced more rapid growth in burden. One possible explanation is that, in high-income countries where healthcare access is relatively equitable, the increasing burden among socio-economically disadvantaged populations may be partly driven by higher obesity rates and metabolic risk profiles.<sup>46</sup> Conversely, in many low- and middle-income countries, access to PCOS diagnosis remains concentrated among more affluent populations, potentially leading to under-ascertainment and masking of the true burden of young PCOS in disadvantaged groups.<sup>47,48</sup>

These regional patterns are closely tied to broader socio-economic and environmental changes. Economic transitions are often accompanied by dietary shifts toward energy-dense, nutrient-poor foods and reductions in physical activity,<sup>49</sup> fueling obesity and PCOS risk.<sup>50</sup> Psychosocial stressors and environmental disruptions may further influence PCOS pathogenesis.<sup>51</sup> Industrialization also increases exposure to endocrine-disrupting chemicals (EDCs) such as bisphenol A, perfluorooctanoic acid (PFOA), di (2-ethyl hexyl) phthalate (DEHP), and organochlorine insecticides, which have been implicated in elevated PCOS risk,<sup>51</sup> particularly in rapidly developing countries, including Indonesia, Kenya, and Ethiopia.<sup>52</sup> This interpretation is supported by our decomposition analyses, which indicate that epidemiological changes contributed substantially to increases in PCOS incidence, prevalence, and DALY rates globally and across most regions, accounting for a large share of the observed temporal changes.

### Surging young PCOS burden by 2040

Our proposed approach adapts an advanced attention-based deep-learning architecture built on iTransformer-based frameworks to address limitations inherent to traditional forecasting methods such as ARIMA and BAPC models.<sup>17–19</sup> Traditional methodologies are constrained by assumptions of stationarity, limited capacity to capture complex, non-linear temporal relationships, and a tendency to produce overly smoothed forecasts. These constraints render them inadequate for capturing the multifactorial, non-linear dynamics that characterize the burden of young PCOS. In contrast, our iTransformer-based pipeline learns complex historical patterns from multiple variables simultaneously, rather than relying on single-variable input, enabling more flexible and adaptive modeling of disease dynamics. Through its self-attention mechanism, the model integrates information across time and covariates to capture

evolving patterns in the data.<sup>20–22</sup> In our application, this approach achieved low prediction errors, with MAPE of 0.10% and MSPE of 0.03%, supporting its suitability for forecasting PCOS burden under the current analytical framework.

Given the particularly concerning trends observed in the high-SDI region and among the 20- to 24-year age group, these forecasts challenge the assumption that economic development alone necessarily translates into improved population health outcomes.<sup>53</sup> High-SDI regions already exhibit the highest prevalence of young PCOS and are expected to maintain a substantial burden in the coming decades. Notably, 50 of the top 100 fastest-growing subnational locations in young PCOS prevalence are located in the US, implying that nearly all states may experience remarkable increases in burden over time. Subnationally, Michigan exemplifies an environment where young PCOS prevalence is forecasted to rise rapidly. PCOS has been associated with unhealthy lifestyle factors and exposure to environmental pollutants,<sup>54</sup> and industrial and environmental exposures (e.g., EDCs in water or food sources)<sup>55</sup> may contribute to hormonal dysregulation, thereby exacerbating the increase in PCOS burden in Michigan's urban and industrial areas. PCOS is not only a leading cause of infertility but also a catalyst for long-term metabolic sequelae. Women with PCOS have an approximately 2.5-fold higher risk of developing type 2 diabetes and are at higher cardiovascular disease risk.<sup>56</sup> Therefore, the widespread increase in young PCOS burden may foreshadow a broader wave of metabolic and cardiovascular complications in the coming decades. High-SDI settings, particularly in the US, must respond urgently. Based on our findings, public health authorities should implement tailored prevention and management strategies to mitigate the long-term health impacts for their local population.

### Substantial frontier deviations indicate significant room for improvement

Despite the forecasted rise in the young PCOS burden, our frontier analysis reveals considerable inefficiencies in health system performance and illuminates substantial opportunities for improvement. In 2021, a striking 96.6% of the 204 countries examined fell below the achievable frontier for both prevalence and incidence rates, as estimated by their SDI. Notably, only seven countries, predominantly low-SDI countries, attained the benchmarks performance. By contrast, high-SDI countries, which are generally expected to possess more advanced healthcare infrastructures and resources,<sup>57</sup> were frequently observed to underperform relative to the frontier. It is important to note that deviations from the global SDI-prevalence relationship may arise from differences in disease ascertainment, diagnostic practices, healthcare utilization, and reporting intensity across settings. Accordingly, SDI-based frontier estimates should be interpreted as conditional benchmarks, rather than as evidence of causal effects. For example, none of the states in the US reached the prevalence frontier in 2021, underscoring substantial unrealized potential, even within resource-rich health settings. Comparisons with similar frontier analyses in chronic conditions, such as chronic kidney disease and adolescent diabetes,<sup>58,59</sup> suggest that rising obesity prevalence and other metabolic risk factors may erode the potential benefits of

improved healthcare access and advanced clinical management. Collectively, these findings point to missed opportunities for strengthening preventive strategies and early intervention to mitigate future disease burden.

Furthermore, the finding that a few low-SDI countries appear to have attained the estimated achievable frontiers is likely a result of detection bias,<sup>60</sup> reflecting underdiagnosis, rather than genuinely superior disease management. This interpretation underscores persistent challenges, including limited healthcare access, diagnostic inconsistencies, and insufficient public health infrastructure. Addressing these gaps requires a shift toward more effective prevention and management strategies. In particular, moving beyond traditional diagnostic frameworks, such as the original NIH criteria,<sup>2</sup> toward more inclusive, evidence-based guidelines that can be harmonized across settings may help improve case identification and comparability. These findings stress an urgent need to bridge the gap between observed outcomes and the best achievable control of young PCOS. Targeted strategies, such as enhanced screening programs, early detection, increasing patient and healthcare professional awareness, and standardizing diagnostic practices, are essential steps. Additionally, greater attention to environmental factors and endocrine disruptors may offer complementary avenues for prevention.<sup>61</sup> Together, the frontier-based efficiency framework presented here provides a clear roadmap for reducing the future young PCOS burden. Policies that prioritize early-life interventions and cross-sectoral collaboration may help underperforming regions, particularly high-income countries, progress toward more equitable and effective PCOS management.<sup>1,2,62</sup>

Our study provides comparable estimates with an unprecedented geographic coverage (953 locations) and an extended time frame (1990–2021), employing standardized modeling approaches applied consistently from global to local levels. These estimates offer valuable insights, particularly for many sublocations where data on PCOS among young individuals are otherwise unavailable, by enabling meaningful assessments of relative burden and temporal trends that cannot be derived from heterogeneous single-country or single-study sources. Such comparability is especially informative for health system planning in under-resourced regions. Additionally, our advanced deep-learning framework captures complex non-linear patterns that traditional forecasting methods may overlook.<sup>20</sup> Its performance, validated by low error metrics despite inherent uncertainties, enables more nuanced forecasts of future young PCOS burden. Finally, the integration of multiple analytical approaches, including inequality analysis, frontier analysis, and forecasting, provides a robust foundation for characterizing the dynamics of young PCOS burden, strengthens the interpretability of our findings, and offer a valuable framework for future research and for informing resource allocation across diverse global settings.

Our standardized, globally comparable estimates reveal a rising burden and widening inequalities in young PCOS across the majority of global to local settings, particularly among women aged 20–24 years. While high-SDI locations bore the heaviest burden in 2021, low- and middle-SDI locations experienced more rapid increases, reflecting complex interactions among

healthcare access, genetic susceptibility, and environmental determinants. Although the young PCOS burden is expected to continue surging in the coming decades, our frontier analysis identifies a clear and attainable pathway for improvement. These findings may inform prioritization of investments in prevention and management strategies, especially obesity reduction, timely diagnosis, and appropriate clinical management of young PCOS. Looking ahead, well-designed longitudinal cohort studies will be essential to improve understanding of the natural history of PCOS, support harmonized diagnostic practices, and inform more effective and equitable global responses to this growing public health challenge.

### Limitations of the study

This study has several limitations. Underdiagnosis of PCOS is well established,<sup>63</sup> and diagnostic uncertainty is particularly pronounced in younger populations. The evolving diagnostic criteria, from the 1990 NIH guidelines to more recent standards, further complicate the interpretation of temporal trends and may contribute to underestimation when more restrictive definitions are applied.<sup>2,23,30</sup> Importantly, the diagnosis of PCOS in adolescents aged 10–14 years is inherently challenging. Irregular menstrual cycles are frequently part of normal pubertal development,<sup>64</sup> and current diagnostic criteria exclude such irregularity within one year of menarche, with the average age of menarche being approximately 12 years.<sup>65</sup> As a result, distinguishing physiological variation from pathological features in this age group is difficult,<sup>64</sup> and some symptoms captured in epidemiological data may not reflect clinically confirmed PCOS.<sup>66</sup> In this context, prevalence estimates for the 10- to 14-year age group in the present study represent population-level modeled estimates, rather than individual-level clinical diagnoses. These estimates are likely driven predominantly by cases occurring in later adolescence (e.g., ages 13–14 years), in combination with age aggregation and diagnostic uncertainty inherent to pubertal development. Accordingly, prevalence estimates reported for the 10- to 14-year age group should not be interpreted as reflecting routine clinical diagnosis during early puberty, but rather as epidemiological signals without direct clinical actionability. Although age-stratified analyses were conducted, findings for this age group warrant cautious interpretation, particularly within population-level modeling frameworks that lack individual-level clinical information. Additionally, GBD 2021 estimates are subjected to inherent limitations related to data quality and completeness, particularly in low-income and conflict-affected settings, where reporting delays and constrained surveillance systems may affect precision.<sup>67,68</sup> A related limitation is the substantial heterogeneity in data availability and registry coverage across regions. In settings without comprehensive national registries, lower estimated PCOS prevalence likely reflects underascertainment, rather than a genuinely lower disease burden; consequently, regional patterns, particularly areas with low reported prevalence in global maps, should be interpreted with caution. Furthermore, comparisons between 1990 and 2021 may be influenced by temporal improvements in diagnostic practices, surveillance capacity, and data collection, such that part of the observed change may reflect enhanced case detection, rather than true epidemiological shifts. Residual uncertainty

related to data availability and quality, therefore, cannot be fully eliminated. Additionally, while our forecasting model assumes a business-as-usual scenario, it may not fully capture the effects of unexpected events such as pandemics or conflicts, which could alter future disease trajectories.

## RESOURCE AVAILABILITY

### Lead contact

Requests for further information and resources should be directed to and will be fulfilled by the lead contact, Queran Lin ([queran.lin18@alumni.imperial.ac.uk](mailto:queran.lin18@alumni.imperial.ac.uk)).

### Materials availability

This study did not generate new unique reagents.

### Data and code availability

- Data: All original data used in this study are publicly available from the GBD 2021 portal (<http://ghdx.healthdata.org/gbd-results-tool>). The specific data resource identifiers are listed in the [key resources table](#). All processed datasets reported in this article will be shared by the [lead contact](#) upon request.
- Code: This paper does not report original code. The modeling framework and deep learning forecasting architecture are described in detail within the [STAR Methods](#) and [supplemental information](#). All computational scripts required to reanalyze the data reported in this article are available from the [lead contact](#) upon request.
- Any additional information: Any additional information required to reanalyze the data reported in this article is available from the [lead contact](#) upon request.

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## AUTHOR CONTRIBUTIONS

Conceptualization, Q.L., W.J., and P.Y.; methodology, Y. Wu, W.C., M.C., and S. Luo; investigation, Y. Wu, W.C., M.C., S. Luo, R.J.N., M.B.K., L.M., H.Z., S.N.S.S., S.R., D.A.E., and L.P.; writing – original draft, Y. Wu and W.C.; writing – review & editing, Y. Wu, W.C., M.C., S. Luo, R.J.N., M.B.K., L.M., H.Z., S.N.S.S., S.R., D.A.E., L.P., K.D., S.M., L. Zheng, X.S., Y. Zeng, Y. Zuo, B.H., F.L., M.X., T.S., G.C., Y. Chen, Y. Wang, Y.L., D.W., Y. Wan, N.W. C.L., W.P., R.Z. T.Y., Y.X., K.C., J. Zhao, S. Li, L. Zheng, L.T., Y. Zeng, L.S., N.M.H., C.C.Z., F.Y., Y. Chu, X.J., P.W., L.W., Y.Y., J.C., Z.W., Y.T., J. Zhang, D.Y., S.W., and H.T.; resources, Q.L., W.J., and P.Y.; supervision, P.Y., D.Y., S.W., A.M., H.T., W.J., and Q.L.

## DECLARATION OF INTERESTS

The authors declare no competing interests.

## STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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  - Decomposition analysis
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## SUPPLEMENTAL INFORMATION

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## STAR★METHODS

### KEY RESOURCES TABLE

| REAGENT or RESOURCE                            | SOURCE                     | IDENTIFIER                                                                                            |
|------------------------------------------------|----------------------------|-------------------------------------------------------------------------------------------------------|
| Software and algorithms                        |                            |                                                                                                       |
| R Project for Statistical Computing (v4.2.0)   | The R Foundation           | <a href="https://www.r-project.org/">https://www.r-project.org/</a>                                   |
| Python Programming Language (v3.9.19)          | Python Software Foundation | <a href="https://posit.co/downloads/">https://posit.co/downloads/</a>                                 |
| Other                                          |                            |                                                                                                       |
| Global Burden of Disease Study 2021 (GBD 2021) | IHME                       | <a href="http://ghdx.healthdata.org/gbd-results-tool">http://ghdx.healthdata.org/gbd-results-tool</a> |

### EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

Omitted as our study does not involve biological models.

### METHOD DETAILS

#### Definitions

PCOS is a complex endocrine and metabolic disorder affecting women worldwide. Diagnosis is based on the International Evidence-Based PCOS Guideline, which incorporates clinical or biochemical hyperandrogenism, ovulatory dysfunction, and/or specific ovarian morphological characteristics or elevated anti-Müllerian hormone levels.<sup>69</sup> Over recent decades, diagnostic criteria for PCOS have evolved from consensus-based definitions to evidence-based frameworks that are more inclusive of phenotypic heterogeneity, with important implications for estimates of disease prevalence and incidence across populations. In the GBD 2021 study, however, PCOS was defined using a historical and comparatively narrower case definition, based on the National Institutes of Health (NIH) criteria as recommended by the American College of Obstetricians and Gynaecologists (ACOG). This definition requires the presence of chronic anovulation and hyperandrogenism, established through hormonal measurements or clinical findings, after exclusion of secondary causes.<sup>70</sup>

In this study, we estimated the burden of PCOS among females aged 10–24 years, categorized as “young people” according to the World Health Organization.<sup>71–73</sup> Analyses were conducted using age-stratified groups of 10–14, 15–19, and 20–24 years, consistent with standard GBD age-grouping conventions and encompassing key stages of youth development. Prevalence estimates for each age group reflect population-level modeled estimates rather than individual-level clinical diagnoses. Given the diagnostic complexity of PCOS in early adolescence, estimates for the 10–14-year age group should be interpreted with caution. These estimates may be influenced by age-band aggregation within the modeling framework and by limited diagnostic certainty at younger ages, with case ascertainment more likely to occur toward later adolescence within this age band. Individual-level data on age at diagnosis are not available within the GBD framework.

#### Data source, processing, and estimation of the young PCOS burdens

The detailed methodology of the GBD study, including data collection, estimation procedures, and assessments of model performance, has been comprehensively described in the GBD 2021 capstones publications and their [supplemental information](#).<sup>67,68</sup> In the present study, we generated comparable estimates of prevalence, incidence, and DALYs (calculated as the sum of years of life lost and years lived with disability, capturing both premature mortality and non-fatal health loss) for PCOS among females aged 10–24 years across 953 locations worldwide from 1990 to 2021. Estimates were stratified by age group and geographic location. The geographic hierarchy comprised 1 global entity; 21 GBD regions (e.g., High-income Asia Pacific); 56 international regions (e.g., High-SDI, European Union); 204 countries and territories (e.g., United Kingdom [UK]); 20 subnational regions (e.g., England); and 652 subnational locations (e.g., Kensington and Chelsea) across 18 specific countries: Brazil, China (Taiwan was included as both territory and a Chinese province), Ethiopia, Indonesia, Italy, Iran, Japan, Kenya, Nigeria, Norway, Pakistan, the Philippines, Poland, South Africa, Sweden, Mexico, the UK, and the US.<sup>68</sup> Detailed information on the GBD geographic hierarchy is provided in [Tables S1](#) and [S2 of Methods S1](#). GBD 2021 non-fatal estimates were derived from 75,459 data sources, including disease registries, clinical informatics systems, epidemiological surveillance records, household surveys, and published scientific literature.<sup>68,74</sup> Within the GBD 2021 analytical framework, PCOS prevalence estimates were informed by multiple data sources, including population-based registries where available, administrative health databases, epidemiological surveys, and published studies. Data availability and completeness varied substantially across regions and over time; consequently, in settings lacking comprehensive national registries, estimates relied more heavily on non-registry data and model-based inference. Additional details regarding data sources are available through the GBD 2021 Sources Tool (<https://ghdx.healthdata.org/gbd-2021/sources>). This study adhered to the

Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) to ensure methodological transparency and rigor throughout the research process.

To ensure internal consistency across data sources, observations with known or suspected biases were adjusted using advanced statistical approaches implemented within the GBD framework, including meta-regression—Bayesian, regularized, and trimmed (MR-BRT) models.<sup>68,74</sup> The socio-demographic index (SDI) is a composite measure of social and economic development that integrates indicators of average educational attainment, income per capita, and total fertility rates.<sup>68,74</sup> SDI was used to contextualize PCOS burden across varying levels of socio-demographic development, enabling assessment of health inequalities and identification of settings with potential need for targeted intervention. Detailed SDI classifications for all countries and subnational locations included in this study are provided in [Tables S3](#) and [S4](#) of [Methods S1](#). Percentage changes in the incidence, prevalence, and DALYs of young PCOS between 1990 and 2021 were calculated by subtracting estimates for 1990 from those for 2021 and dividing the difference by the corresponding 1990 values.

### Attentive deep-learning-empowered forecast

To forecast future prevalence, incidence, and DALYs of young PCOS, we adapted the Inverted Transformer (iTransformer), an attention-based deep-learning architecture designed for multivariate time-series forecasting and previously applied to disease burden projections.<sup>20–22</sup> This model leverages self-attention mechanisms to capture complex dependencies and interactions across multiple temporal input dimensions. Compared with conventional architectures, the iTransformer incorporates structural modifications designed for time-series data. In contrast to trend-based approaches such as Joinpoint regression, which identify discrete inflection points,<sup>75</sup> the iTransformer is designed to learn continuous and potentially non-linear temporal patterns directly from historical trajectories, without requiring predefined breakpoints.<sup>20</sup> Given that GBD estimates represent smoothed, model-based time series, this data-driven framework is well-suited for consistently characterizing temporal dynamics across locations.<sup>68</sup> A detailed description of the forecasting methodology is provided in [Methods S1](#), Section 3. It employs a self-attention mechanism, in which the attention for a set of queries  $Q$ , keys  $K$ , and values  $V$  was calculated as follows:

$$\text{Attention}(Q, K, V) = \text{softmax}\left(\frac{QK^T}{\sqrt{d_k}}\right)V$$

Here,  $d_k$  denotes dimensionality of the key vector. This scaled dot-product attention was further enhanced by multi-head attention:

$$\text{MultiHead}(Q, K, V) = \text{Concat}(\text{head}_1, \dots, \text{head}_h)W^O,$$

where  $\text{head}_i = \text{Attention}(QW_i^Q, KW_i^K, VW_i^V)$ . Herein,  $W_i^Q$ ,  $W_i^K$ ,  $W_i^V$  denote the parameter matrices for the  $i$ -th attention head, and  $W^O$  represents the output linear transformation matrix used to combine the outputs of all heads. Following the attention layers, each Transformer layer included a feed-forward network (FFN), modified with a Gaussian Error Linear Unit (GELU) activation, between two linear transformations:

$$\text{FFN}(z) = \left(0.5 \times (zW_1 + b_1) \left(1 + \tanh\left(\sqrt{\frac{2}{\pi}}(zW_1 + b_1 + \phi(zW_1 + b_1)^3)\right)\right)\right)W_2 + b_2$$

In this context,  $W_1$  and  $b_1$  represent the weight matrix and bias vector for the initial linear transformation, while  $W_2$  and  $b_2$  represent those for the second transformation. The GELU activation function is defined as  $\text{GELU}(u) = u \times \Phi(u)$ , where  $\Phi(u)$  denotes the cumulative distribution function of the standard normal distribution.

During the forecasting procedure, we randomly divided the multivariate time series input data in half into training and test sets based on location and age.

To ensure comparability of input features and stable model performance, all training inputs were standardized before model fitting. Model training and optimisation were performed exclusively on the training set using a five-fold cross-validation, with 10% of the training set reserved as a validation set within each fold. The iTransformer was trained under a supervised learning framework, using 13 years of historical input data (1990–2002) to forecast outcomes over the subsequent 19-year period (2003–2021). Model performance was iteratively refined by comparing predicted values with observed estimates over the forecasting window. This training strategy enabled extension of forecasts through 2040 across 691 global to subnational locations with available SDI values. The forecast horizon was limited to 2040 based on data availability and the model performance considerations over a shorter time span. To assess the robustness of long-term forecasting under the current trend scenario, forecasting was repeated five times as part of a sensitivity analysis. The held-out test dataset was kept entirely independent from model training and validation and was used solely for final performance evaluation, quantified using mean absolute percentage error (MAPE) and mean squared percentage error (MSPE).

### Patient engagement and protocol approvals

This study utilized openly collected data and conducted in-depth analysis without involving any personally identifiable information. Patients did not participate in determining the research questions, designing and executing experiments, or measuring results, hence

patient consent was not necessary. Furthermore, this study strictly adhered to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) in every step of analyzing and reporting the global burden of young PCOS.

## QUANTIFICATION AND STATISTICAL ANALYSIS

### Inequality analysis

The Slope Inequality Index (SII) and Concentration Index (CI) were used as standardized measures to assess inequalities in the young PCOS burden globally, and across 14 countries with available subnational SDI or GDP per capita (GDPPC) data. The SII captures absolute health inequality by estimating the difference in PCOS burden between the most and least advantaged locations using weighted regression models, in which location-specific burden estimates are regressed against a relative rank derived from the cumulative distribution of SDI values.<sup>76,77</sup> In contrast, the CI quantifies relative inequality by measuring the degree to which PCOS burden is disproportionately concentrated among more or less advantaged populations. The CI was constructed using numerical integration of the concentration curve, which plots the cumulative proportion of young PCOS burden against the cumulative population share, ranked by SDI, to quantify relative inequality.<sup>77</sup> A negative value of SII or CI indicates that a higher SDI level is associated with a lower young PCOS burden, whereas positive values indicate the opposite pattern. Larger absolute values of either index reflect a larger magnitude of inequality.<sup>77,78</sup>

### Frontier analysis

To assess the lowest achievable disease burden (frontier) across varying levels of development, we constructed frontiers describing the association between SDI or GDPPC (for China only) and the rates of prevalence, incidence, and DALYs of young PCOS. Frontier analysis was applied to establish benchmarks for young PCOS burden, enabling comparisons of countries and subnational locations against the best-performing peers operating at similar levels of socioeconomic and demographic development.<sup>79,80</sup> For each location, we calculated a frontier deviation, defined as the gap between the observed burden and the potentially achievable burden after accounting for SDI. Frontiers were delineated using the free disposal hull (FDH) method, a non-parametric and non-linear data envelopment approach. To address uncertainty and to estimate average burden levels across the SDI continuum, we performed 1,000 bootstrap resampling iterations, with locations randomly sampled with replacement. The resulting frontier was smoothed using locally weighted polynomial regression (LOESS) with a first-degree polynomial and a span parameter of 0.2. To minimize distortion of the frontier boundary, locations with exceptionally low burdens (ultra-efficient observations) were excluded as outliers. The frontier deviation, was ultimately quantified as the absolute distance between each location's burden estimate and the achievable frontier boundary.<sup>79</sup> Within this framework, SDI was used as a comparative benchmark to normalize frontier performance across locations, rather than to imply a uniform or monotonic relationship between PCOS burden and development level within individual countries.<sup>79,81</sup>

### Decomposition analysis

We performed a decomposition analysis to quantify the relative contributions of population growth, population ageing, and epidemiological change to temporal changes in PCOS burden. Following established GBD decomposition frameworks, changes in PCOS incidence, prevalence, and DALYs were partitioned into components attributable to population growth, population ageing, and epidemiological change.<sup>67,80</sup> This approach allowed us to disentangle the demographic and epidemiological drivers underlying observed changes in PCOS burden over time.

### Statistical evaluation and software

Comprehensive methodology details, including data collection procedures, analytical strategies, uncertainty intervals (UIs) estimation, and model validation, are provided in [Methods S1](#). Additional results are presented in figures and tables in [Data S1](#), which is available via Google Drive: [https://drive.google.com/file/d/1DbC4k9HSmoVEwunqPWq1S6\\_JX4YLsoow/view?usp=drive\\_link](https://drive.google.com/file/d/1DbC4k9HSmoVEwunqPWq1S6_JX4YLsoow/view?usp=drive_link). All rates reported in this study are expressed per 100,000 females. Statistical analyses and data visualizations were conducted using R software (version 4.2.0), and forecasting analyses were performed using Python (version 3.9.19). All data were anonymized and aggregated at the population level, with no personally identifiable information included. Therefore, ethical approval and informed consent were not required.