

Measuring the global disease burden of polycystic ovary syndrome in 194 countries: Global Burden of Disease Study 2017

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STUDY QUESTION: What is the current burden of polycystic ovary syndrome (PCOS) at the global, regional, and country-specific levels in 194 countries and territories according to age and socio-demographic index (SDI)?

SUMMARY ANSWER: Slight increases in age-standardized incidence of PCOS and associated disability-adjusted life-years (DALYs) were evidenced among women of reproductive age (15–49 years) from 2007 to 2017 at the global level, and in most regions and countries.

WHAT IS KNOWN ALREADY: No detailed quantitative estimates of the PCOS incidence and DALYs by age and SDI in these 194 countries and territories have been published previously.

STUDY DESIGN, SIZE, DURATION: An age- and SDI-stratified systematic analysis of the PCOS incidence and DALYs across 194 countries and territories has been performed.

PARTICIPANTS/MATERIALS, SETTING, METHODS: We used data from the Global Burden of Diseases, Injuries and Risk Factors Study (GBD) 2017 to estimate the total and age-standard PCOS incidence rates and DALYs rates among women of reproductive age in both 2007 and 2017, and the trends in these parameters from 2007 to 2017.

MAIN RESULTS AND THE ROLE OF CHANCE: Globally, women of reproductive age accounted for 1.55 million (95% uncertainty intervals (UIs): 1.19–2.08) incident cases of PCOS and 0.43 million (0.19–0.82) associated DALYs. The global age-standardized PCOS incidence rate among women of reproductive age increased to 82.44 (64.65–100.24) per 100 000 population in 2017, representing an increase of 1.45% (1.43–1.47%) from 2007 to 2017. The rate of age-standardized DALYs increased to 21.96 (12.78–31.15) per 100 000 population in 2017, representing an increase of 1.91% (1.89–1.93%) from 2007 to 2017. Over the study period, the greatest increase in the age-standardized PCOS incidence and DALYs rates were observed in the middle-SDI and high-middle SDI regions, respectively. At the GBD regional level, the highest age-standardized incidence and DALY rates in 2017 were observed in Andean Latin America, whereas the largest percentage increases in both rates from 2007 to 2017 were observed in Tropical Latin America. At the national level, Ecuador, Peru, Bolivia, Japan, and Bermuda had the highest age-standardized incidence rates and DALYs rates in both 2007 and 2017. The highest increases in both the age-standardized incidence rates and DALYs rates from 2007 to 2017 were observed in Ethiopia, Brazil, and China.

LIMITATIONS, REASONS FOR CAUTION: Although the GBD (2017) study aimed to gather all published and unpublished data, the limited availability of data in some regions might have led to the estimation of wide UIs. Additionally, the PCOS phenotype is complicated and the diagnostic criteria are constantly changing. Consequently, the incidence of PCOS might have been underestimated.

WIDER IMPLICATIONS OF THE FINDINGS: Knowledge about the differences in the PCOS burden across various locations will be valuable for the allocation of resources and formulation of effective preventive strategies.

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Introduction

Polycystic ovary syndrome (PCOS) is among the most common endocrine disorders and a major cause of anovulatory infertility in women of reproductive age (15–49 years) (Szilágyi and Szabó, 2003; Balen et al., 2016). Globally, the estimated prevalence of PCOS ranges between 5% and 15% (Azziz, 2016). Compelling evidence suggests that women with PCOS have significantly higher risks of obesity, dyslipidemia, impaired glucose tolerance, and long-term complications such as diabetes, endometrial cancer, and cardiovascular disease (Lim et al., 2012; Wild 2012; Peigné and Dewailly, 2014).

Previous efforts to monitor the PCOS epidemic have focused mainly on reporting the prevalence of disease (Yildiz et al., 2012; Ding et al., 2017; Wolf et al., 2018). However, the annual incidence of PCOS, defined as the rate of new cases per year, provides a better reflection of the epidemiological changes associated with this disease (Guang, 2009). The disability-adjusted life-years (DALYs), a comprehensive measurement of premature mortality and disability, are an advantageous measure that can be compared directly across geographical areas (Capone, 2019).

Globally, the age-standardized prevalence of infertility and associated DALYs among women increased by 0.370% and 0.396% per year, respectively, from 1990 to 2017 (Sun et al., 2019). As PCOS is the most common cause of anovulatory infertility in women (Balen et al., 2016), a better understanding of the current burden of PCOS is essential for the primary prevention of infertility.

To our knowledge, no detailed quantitative estimates of the PCOS incidence and associated DALYs by age and socio-demographic index (SDI) across countries and territories has been published. Therefore, we aimed to provide a comprehensive estimate of the age- and SDI-stratified PCOS incidence at the global, regional, and national levels using data collected from 194 countries and territories during the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD, 2017). Here, we present: the estimated PCOS incidence and DALYs for women of reproductive age; the age-standardized PCOS incidence and DALYs in this population in both 2007 and 2017; and the trends in both variables from 2007 to 2017.

Materials and methods

Overview

GBD (2017) used all of the most recent and available sources of epidemiological survey data and optimized, standardized methods for a comparative assessment of health losses and associated risk factors for 282 causes of death, 354 causes of years lived with disability (YLDs), and 359 causes of DALYs in 194 countries and territories from 1990

to 2017. Details of the methodology of GBD (2017) have been published elsewhere (GBD, 2017; GBD Disease and Injury Incidence and Prevalence Collaborators, 2018; Yadgir et al., 2020). GBD (2017) was divided into 21 regions and 7 GBD super-regions based on the geographic distribution of the 194 included countries and territories.

Data sources

The GBD study used data from both literature reports and epidemiological surveillance. In addition to data sources derived from the scientific literature, surveys, and monitoring, the GBD (2017) also included new sources of data such as hospital discharge records, outpatient visits, and health insurance claims records.

Estimation of incidence and DALYs

For this study, the parameters of PCOS incidence and DALYs were used. The age-standardized rates and the estimated annual percentage changes in the PCOS incidence and DALYs among women of reproductive age were considered quantitative trends representative of the two parameters of PCOS. The age-standardized incidence is defined as the number of cases per 100 000 persons, and the age-standardized DALYs is defined as the number of YLDs and the years of life lost (YLLs) per 100 000 persons after age standardization. The DALYs were derived by summing the YLLs and YLDs thereby incorporating both the fatal and nonfatal burdens (GBD, 2017; DALYs and HALE Collaborators, 2018).

Socio-demographic index

In this study, the results were aggregated by the SDI, which is an aggregative index of development estimated for each geographic entity. This index is computed using the mean of the scaled values of total population fertility, the educational level of residents older than 15 years and the per capita personal income (United Nations Development Programme, 2015). The 194 countries and territories were segmented into five SDI quintiles (low, low-middle, middle, high-middle, and high) according to the SDI of each country in 2017.

Statistical analysis

The GBD used the Bayesian meta-regression tool disMOD-MR 2.1 to determine the causes and sequelae of the YLD results. Cause of death ensemble modeling was the principal method used to estimate the mortality and YLLs. We used a global standard (World Health Organization (WHO) 2000–2025) to calculate the age-standardized rate in women of reproductive age (Ahmad et al., 2001). The data are reported as estimates with 95% uncertainty intervals (UIs) where relevant. The findings are also presented according to the SDIs of various

regions, as calculated by GBD (2017). We used R version 3.3.1 (R Foundation, Vienna, Austria, <https://www.r-project.org/>) and Microsoft Excel version 1803 (Microsoft Corporation, Redmond, Washington, <https://www.microsoft.com/>) to draw the figures.

Results

The PCOS burden at the global level

In 2017, 1.55 million (95% UI: 1.19–2.08) incident cases of PCOS among women of reproductive age (15–49 years) were reported globally, representing an increase of 4.47% (2.86–6.37%) from 2007 to 2017. The global age-standardized incidence rate of PCOS among women of reproductive age was 82.44 (64.65–100.24) per 100 000 population in 2017, which represents an increase of 1.45% (1.43–1.47%) from 2007 to 2017 (Table I; Fig. 1A and C).

In 2017, the total number of DALYs due to PCOS among women of reproductive age was 0.43 (95% UI: 0.19–0.82) million worldwide, representing a 12.08% (11.10–13.07%) increase from 2007 to 2017. The global age-standardized DALY rate due to PCOS among women of reproductive years was 21.96 (12.78–31.15) per 100 000 population in 2017, representing an increase of 1.91% (1.89–1.93%) from 2007 to 2017 (Table I; Fig. 1B and D).

The PCOS burden at the SDI quintile level

The PCOS incidence varied by SDI quintile in our analysis. In 2017, the highest age-standardized incidence rate was observed in the high-SDI quintile (91.54 (95% UI: 72.79–110.30) per 100 000 population) across all seven super-regions, whereas the lowest age-standardized incidence rate was observed across the low-SDI quintiles (71.36 (54.81–87.92) per 100 000 population). The percentage change in the age-standardized incidence rate among women of reproductive age increased in all of the SDI quintiles over the study period. The highest increase in the age-standardized incidence rate was observed in the middle-SDI quintiles, which exhibited an increase of 4.61% (4.57–4.65%) from 2007 to 2017 (Table I; Fig. 1A and C).

Similarly, the highest rate of age-standardized DALYs in 2017 was observed in the middle-SDI quintiles (23.73 (95% UI: 14.18–33.28) per 100 000 population), and the lowest was observed in the low-SDI quintiles (18.63 (10.17–27.09) per 100 000 population). The percentage change in the age-standardized DALYs rates over the study period also increased in all of the SDI quintiles, although the steepest increase from 2007 to 2017 was observed in the high-middle SDI quintiles (3.82% (3.77–3.87%)) (Table I; Fig. 1B and D).

The PCOS burden at the regional level

In 2017, the highest age-standardized PCOS incidence rates were observed in the geographic regions of Andean Latin America (220.50 (95% UI: 191.39–249.60) per 100 000 population), high-income Asia Pacific (151.10 (127.00–175.19) per 100 000 population) and Caribbean (140.15 (116.94–163.35) per 100 000 population). The lowest age-standardized incidence rate was observed in Southern Latin America (52.91 (38.65–67.17)) per 100 000 population (Table I; Fig. 1A). The largest increases in the age-standardized incidence rates from 2007 to 2017 were observed in Tropical Latin America (4.29%

(4.17–4.41%)), East Asia (3.70% (3.65–3.75%)), and Eastern Sub-Saharan Africa (2.76% (2.67–2.85%)). In contrast, only North Africa and the Middle East (–0.61% (–0.68% to –0.54%)) and southern Latin America (–0.22% (–0.44–0.00%)) exhibited downward trends in the age-standardized PCOS incidence rates from 2007 to 2017 (Table I; Fig. 1C).

The regions of Andean Latin America with (57.66 (95% UI: 42.77–72.54) per 100 000 population), Caribbean (38.53 (26.37–50.70) per 100 000 population) and high-income Asia Pacific (36.57 (24.71–48.42) per 100 000 population) had the highest age-standardized DALYs rates in 2017, whereas Southern Latin America had the lowest age-standardized DALYs rate (13.33 (6.17–20.48) per 100 000 population) (Table I; Fig. 1B). Tropical Latin America (4.58% (4.46–4.70%)), East Asia (3.62% (3.58–3.66%)), and Eastern Sub-Saharan Africa (2.77% (2.67–2.87%)) had the steepest increases in the age-standardized DALYs rates from 2007 to 2017, whereas only North Africa and the Middle East exhibited a downward trend during this period (–1.05% (–1.12% to –0.98%)) (Table I; Fig. 1D).

Countries with the highest PCOS burdens in 2017

At the national level, the top five countries in terms of the age-standardized incidence rates of PCOS in 2017 were Ecuador (242.54 (95% UI: 212.01–273.06) per 100 000 population), Peru (211.59 (183.08–240.10) per 100 000 population), Bolivia (208.75 (180.43–237.07) per 100 000 population), Japan (170.13 (144.74–195.89) per 100 000 population) and Bermuda (145.93 (122.26–169.61)). In contrast, Argentina (53.75 (39.38–68.12) per 100 000 population), Uruguay (53.26 (38.95–67.56) per 100 000 population) and Chile (50.69 (36.73–64.64) per 100 000 population) had the lowest age-standardized incidence rates in 2017 (Supplementary Table S1, Fig. 2 and Supplementary Fig. S1A). The percentage changes in the age-standardized PCOS incidence rates from 2007 to 2017 varied greatly between countries, with the steepest increases in Brazil (4.33% (4.09–4.57%)), Ethiopia (3.80% (3.08–4.52%)) and China (3.63% (3.45–3.81%)), and the steepest decreases in Afghanistan (–2.91% (–3.72% to –2.11%)) and Austria (–5.68% (–7.08% to –4.27%)) (Supplementary Table S1 and Supplementary Fig. S1C).

The top five countries in terms of the PCOS-associated age-standardized DALYs rates in 2017 were Ecuador (63.45 (95% UI: 47.84–79.07) per 100 000 population), Peru (55.65 (41.03–70.27) per 100 000 population), Bolivia (54.85 (40.33–69.36) per 100 000 population), Japan (41.33 (28.73–53.93) per 100 000 population), and Barbados (40.66 (28.16–53.16) per 100 000 population). In contrast, the lowest age-standardized DALYs rates were in Argentina (13.50 (6.30–20.71) per 100 000 population), and Chile (12.87 (5.84–19.91) per 100 000 population) (Supplementary Table S1, Fig. 2 and Supplementary Fig. S1B). Brazil (4.61% (3.71–5.51%)), China (3.68% (3.02–4.33)) and Ethiopia (3.58% (0.19–6.97%)) exhibited the steepest increases in the age-standardized DALYs from 2007 to 2017, whereas Egypt (–4.23% (–5.91% to –2.55%)) and Austria (–5.43% (–9.77% to –1.09%)) exhibited the greatest decreases during the study period (Supplementary Table S1 and Supplementary Fig. S1D).

Table 1 Incidence and disability-adjusted life-years (DALYs) counts in 2007 and 2017, percentage change in incidence and DALYs counts during 2007–2017, and their age-standardized rate (per 100 000) for polycystic ovary syndrome by socio-demographic index (SDI) and world regions among women of reproductive age (15–49 years).

Location	Numbers (95% UI)		Age-standardized rate (per 100 000) (95% UI)	
	2007	2017	2007	2017
Global				
Incidence	1 487 950.25 (1 135 872.28, 1 998 276.87)	1 554 508.65 (1 190 519.23, 2 081 418.38)	81.27 (63.60, 98.93)	82.44 (64.65, 100.24)
DALYs	380 399.74 (169 627.31, 738 136.40)	426 360.81 (189 150.84, 820 947.93)	4.47 (2.86, 6.37)	21.96 (12.78, 31.15)
Low SDI				
Incidence	199 632.20 (150 238.02, 273 541.87)	263 878.44 (198 563.50, 362 006.64)	70.30 (53.86, 86.73)	71.36 (54.81, 87.92)
DALYs	43 555.26 (19 146.81, 83 925.86)	57 774.72 (25 561.48, 111 062.24)	18.26 (9.89, 26.64)	18.63 (10.17, 27.09)
Low-middle SDI				
Incidence	327 978.23 (246 644.92, 448 294.82)	383 031.55 (290 394.44, 520 223.34)	79.99 (62.46, 97.52)	80.08 (62.54, 97.62)
DALYs	76 738.41 (33 920.71, 148 125.42)	94 287.33 (42 151.22, 182 743.15)	21.31 (12.26, 30.36)	21.58 (12.47, 30.68)
Middle SDI				
Incidence	470 180.16 (358 949.44, 631 058.61)	464 654.32 (358 192.14, 621 137.52)	87.28 (68.97, 105.59)	91.31 (72.58, 110.03)
DALYs	120 532.95 (53889.93, 232 385.38)	132 342.09 (58 811.72, 254 410.64)	22.92 (13.54, 32.30)	23.73 (14.18, 33.28)
High-middle SDI				
Incidence	276 668.44 (212 573.07, 373 036.24)	237 616.88 (186 054.64, 315 908.95)	78.72 (61.33, 96.10)	82.17 (64.40, 99.93)
DALYs	75 336.74 (33276.57, 144 988.74)	78 116.45 (34 608.27, 150 496.72)	20.64 (11.74, 29.54)	21.43 (12.36, 30.50)
High SDI				
Incidence	207 750.78 (163 211.08, 273597.69)	200 422.81 (157 764.15, 263 724.28)	89.52 (70.97, 108.06)	91.54 (72.79, 110.30)
DALYs	62 705.24 (28224.46, 119 797.35)	62 307.20 (27 976.30, 118 446.98)	23.60 (14.08, 33.12)	23.72 (14.18, 33.27)
Southeast Asia, East Asia, and Oceania				
Incidence	428 433.76 (328 285.51, 579 082.03)	383 967.68 (298 783.75, 511 655.00)	76.03 (58.94, 93.12)	79.55 (62.07, 97.03)
DALYs	113 564.29 (49 952.57, 219 430.27)	116 975.66 (51 486.14, 224 242.44)	19.70 (11.00, 28.40)	20.43 (11.57, 29.28)
East Asia				
Incidence	278 948.79 (213 985.06, 377 047.83)	229 532.49 (179 381.08, 306 404.54)	71.15 (54.62, 87.68)	73.78 (56.94, 90.61)
DALYs	74 851.25 (32 621.80, 144 474.15)	74 505.80 (32 718.76, 143 308.71)	18.22 (9.85, 26.59)	18.88 (10.36, 27.40)
Southeast Asia				
Incidence	147 258.67 (112 187.28, 197 523.46)	151 685.88 (115 471.09, 204 958.95)	86.88 (68.61, 105.15)	87.93 (69.55, 106.31)
DALYs	38 183.23 (16 982.06, 73 712.78)	41 781.10 (18 437.92, 80 492.58)	23.30 (13.84, 32.76)	23.62 (14.09, 33.15)
Oceania				
Incidence	2226.29 (1671.31, 3037.14)	2749.30 (2059.61, 3787.93)	79.85 (62.34, 97.37)	79.92 (62.40, 97.44)
DALYs	529.81 (238.26, 1011.61)	688.76 (307.61, 1334.54)	21.53 (12.44, 30.63)	21.74 (12.60, 30.88)

(continued)

Table 1 Continued

Location	Numbers (95% UI)			Age-standardized rate (per 100 000) (95% UI)		
	2007	2017	Percentage change 2007–2017	2007	2017	Percentage change, 2007–2017
Central Europe, Eastern Europe, and Central Asia						
Incidence	81 082.63 (62 799.19, 108537.28)	63 426.50 (49 474.50, 84 449.89)	-21.78 (-23.89, -19.32)	75.35 (58.34, 92.37)	77.23 (60.00, 94.45)	2.49 (2.40, 2.58)
DALYs	21 176.33 (9332.38, 40 795.12)	20 388.68 (9026.24, 39 393.69)	-3.72 (-5.74, -1.64)	19.25 (10.65, 27.86)	19.77 (11.06, 28.49)	2.7 (2.62, 2.78)
Central Asia						
Incidence	20 449.52 (15 533.62, 27 821.62)	18 258.94 (13 954.53, 24 727.46)	-10.71 (-14.77, -6.61)	81.65 (63.94, 99.36)	83.03 (65.17, 100.89)	1.69 (1.51, 1.87)
DALYs	4685.41 (2066.08, 9112.86)	5249.38 (2321.00, 10 176.88)	12.04 (7.61, 16.81)	21.25 (12.22, 30.29)	21.65 (12.53, 30.76)	1.84 (1.66, 2.02)
Central Europe						
Incidence	20 043.90 (15 535.40, 26 912.27)	16 279.80 (12 686.24, 21 781.54)	-18.78 (-22.36, -14.71)	73.42 (56.62, 90.21)	74.45 (57.54, 91.37)	1.41 (1.23, 1.59)
DALYs	5544.35 (2439.22, 10 728.02)	5167.68 (2266.17, 9996.02)	-6.79 (-10.77, -2.89)	18.64 (10.17, 27.10)	18.98 (10.44, 27.52)	1.86 (1.70, 2.02)
Eastern Europe						
Incidence	40 589.22 (31 758.37, 54 136.04)	28 887.76 (22 700.83, 38 166.54)	-28.83 (-31.19, -26.12)	72.93 (56.19, 89.66)	74.63 (57.70, 91.56)	2.33 (2.20, 2.46)
DALYs	10 946.57 (4902.75, 21 203.04)	9971.62 (4411.37, 19 160.29)	-8.91 (-11.24, -6.68)	18.81 (10.31, 27.30)	19.26 (10.66, 27.86)	2.43 (2.31, 2.55)
High income						
Incidence	194 561.32 (152 440.62, 256 251.01)	192 055.20 (150 868.72, 253 339.33)	-1.29 (-2.83, 0.30)	88.74 (70.28, 107.21)	89.60 (71.05, 108.16)	0.97 (0.91, 1.03)
DALYs	58 613.24 (26 276.15, 112 177.94)	57 976.79 (26 066.16, 111 051.88)	-1.09 (-2.66, 0.61)	23.68 (14.14, 33.22)	23.70 (14.16, 33.24)	0.07 (0.01, 0.13)
High-income Asia Pacific						
Incidence	49 266.02 (37 617.76, 65 602.91)	48 438.27 (37 232.52, 64 531.60)	-1.68 (-4.64, 2.38)	149.31 (125.36, 173.26)	151.10 (127.00, 175.19)	1.2 (1.05, 1.35)
DALYs	16 171.42 (7171.58, 30 700.23)	15 273.64 (6749.92, 29 242.97)	-5.55 (-7.93, -2.67)	36.48 (24.64, 48.32)	36.57 (24.71, 48.42)	0.24 (0.11, 0.37)
Australasia						
Incidence	6155.36 (4618.69, 8424.21)	6452.47 (4845.83, 8756.70)	4.83 (-3.69, 14.20)	110.88 (90.24, 131.52)	113.04 (92.20, 133.88)	1.95 (1.58, 2.32)
DALYs	1741.75 (763.00, 3363.95)	1946.65 (866.68, 3785.98)	11.76 (2.84, 21.11)	27.98 (17.61, 38.35)	28.53 (18.06, 39.00)	1.96 (1.62, 2.30)
Western Europe						
Incidence	69 750.01 (53 555.19, 94 647.15)	68 405.03 (52 393.42, 93 926.28)	-1.93 (-4.34, 0.72)	82.83 (64.99, 100.67)	83.67 (65.74, 101.60)	1.01 (0.91, 1.11)
DALYs	24 499.55 (10 829.05, 47 935.59)	23 614.45 (10 417.48, 46 218.85)	-3.61 (-6.10, -0.90)	24.31 (14.65, 33.98)	24.42 (14.73, 34.10)	0.42 (0.33, 0.51)
Southern Latin America						
Incidence	8336.37 (6471.27, 11186.20)	8570.98 (6587.18, 11 604.68)	2.81 (-3.21, 8.62)	53.02 (38.75, 67.30)	52.91 (38.65, 67.17)	-0.22 (-0.44, 0.00)
DALYs	2031.75 (908.71, 3912.24)	2263.61 (1015.86, 4317.20)	11.41 (4.02, 19.74)	13.28 (6.14, 20.42)	13.33 (6.17, 20.48)	0.36 (0.14, 0.58)
High-income North America						
Incidence	61 053.57 (47 527.68, 77 033.94)	60 188.45 (46 910.09, 75 586.52)	-1.42 (-3.91, 1.20)	75.36 (58.34, 92.37)	77.26 (60.03, 94.49)	2.52 (2.42, 2.62)
DALYs	14 168.77 (6383.82, 27 012.26)	14 878.45 (6653.55, 28 311.35)	5.01 (1.91, 8.66)	17.78 (9.52, 26.05)	18.19 (9.83, 26.55)	2.31 (2.21, 2.41)
Latin America and Caribbean						
Incidence	199 764.41 (151 393.75, 269 122.82)	211 874.26 (162 170.23, 284 331.72)	6.06 (3.97, 8.13)	134.77 (112.02, 157.53)	138.77 (115.69, 161.86)	2.97 (2.90, 3.04)
DALYs	49 848.31 (22 341.51, 95 973.70)	58 157.78 (26 094.93, 111 671.78)	16.67 (14.36, 18.75)	35.88 (24.14, 47.62)	37.14 (25.20, 49.09)	3.51 (3.44, 3.58)

(continued)

Table 1 Continued

Location	Numbers (95% UI)			Age-standardized rate (per 100 000) (95% UI)		
	2007	2017	Percentage change 2007–2017	2007	2017	Percentage change, 2007–2017
Caribbean						
Incidence	16 582.68 (12 327.10, 22 521.73)	16 700.09 (12 541.18, 22 903.84)	0.71 (–4.16, 5.21)	137.93 (114.91, 160.95)	140.15 (116.94, 163.35)	1.61 (1.36, 1.86)
DALYs	43 163.37 (19 411.55, 83 648.84)	46 391.19 (20 688.30, 90 246.69)	7.48 (3.08, 12.06)	37.86 (25.80, 49.92)	38.53 (26.37, 50.70)	1.77 (1.51, 2.03)
Andean Latin America						
Incidence	33 277.48 (24 509.89, 44 829.50)	35 911.16 (26 913.38, 47 712.18)	7.91 (1.92, 14.50)	215.57 (186.79, 244.35)	220.50 (191.39, 249.60)	2.29 (2.07, 2.51)
DALYs	75 113.1 (33 312.24, 145 163.32)	91 442.26 (40 988.92, 175 034.49)	21.74 (15.51, 27.94)	56.32 (41.61, 71.03)	57.66 (42.77, 72.54)	2.37 (2.14, 2.60)
Central Latin America						
Incidence	79 369.75 (59 975.29, 107 841.32)	86 131.86 (65 590.64, 117 089.86)	8.52 (5.47, 11.54)	121.79 (100.16, 143.42)	124.23 (102.38, 146.07)	2 (1.89, 2.11)
DALYs	19 155.96 (8535.30, 36 924.45)	22 626.49 (10 167.91, 43 664.24)	18.12 (14.89, 21.35)	32.22 (21.09, 43.34)	33.08 (21.80, 44.35)	2.68 (2.57, 2.79)
Tropical Latin America						
Incidence	70 534.48 (53 437.16, 95 529.21)	73 131.15 (55 814.91, 98 279.57)	3.68 (0.71, 7.01)	126.77 (104.70, 148.84)	132.20 (109.66, 154.74)	4.29 (4.17, 4.41)
DALYs	18 864.67 (8441.90, 36 468.85)	21 747.84 (9704.51, 42 492.11)	15.28 (12.03, 19.02)	34.50 (22.99, 46.01)	36.08 (24.31, 47.85)	4.58 (4.46, 4.70)
North Africa and Middle East						
Incidence	137 417.97 (103 442.50, 187 454.13)	146 841.88 (111 240.49, 201 218.05)	6.86 (3.79, 10.37)	96.52 (77.26, 115.78)	95.93 (76.74, 115.13)	–0.61 (–0.68, –0.54)
DALYs	34 806.84 (15 589.09, 67 473.78)	41 679.47 (18 629.58, 80 951.06)	19.75 (16.37, 22.98)	27.19 (16.97, 37.41)	26.91 (16.74, 37.07)	–1.05 (–1.12, –0.98)
South Asia						
Incidence	310 238.18 (235 047.86, 422 489.91)	372 249.85 (282 540.84, 505 083.95)	19.99 (17.60, 22.66)	73.59 (56.78, 90.40)	74.99 (58.02, 91.97)	1.91 (1.87, 1.95)
DALYs	74 553.26 (33 077.61, 143 605.11)	93 021.93 (41 396.20, 177 805.34)	24.77 (22.15, 27.69)	19.52 (10.86, 28.18)	19.99 (11.23, 28.76)	2.43 (2.39, 2.47)
Sub-Saharan Africa						
Incidence	136 451.98 (102 873.39, 186 441.22)	184 093.27 (139 492.92, 251 768.60)	34.91 (32.15, 37.80)	62.29 (46.82, 77.76)	63.53 (47.91, 79.15)	1.99 (1.93, 2.05)
DALYs	27 837.46 (12 048.79, 53 659.27)	38 160.50 (16 599.65, 73 886.42)	37.08 (33.57, 40.32)	15.38 (7.69, 23.07)	15.71 (7.94, 23.48)	2.13 (2.07, 2.19)
Central Sub-Saharan Africa						
Incidence	15 826.41 (11 897.94, 21 548.13)	21 291.62 (16 129.03, 29 465.92)	34.53 (28.81, 40.89)	62.95 (47.40, 78.50)	63.96 (48.29, 79.64)	1.6 (1.44, 1.76)
DALYs	3 175.14 (1380.99, 6067.53)	4403.28 (1944.75, 8449.43)	38.68 (29.74, 47.63)	15.49 (7.78, 23.21)	15.80 (8.01, 23.59)	1.95 (1.77, 2.13)
Eastern Sub-Saharan Africa						
Incidence	52 224.72 (39 156.24, 71 776.27)	72 008.54 (53 868.67, 98 443.47)	37.88 (35.03, 41.20)	61.86 (46.45, 77.28)	63.57 (47.94, 79.20)	2.76 (2.67, 2.85)
DALYs	10 306.15 (4496.43, 19 749.89)	14 506.41 (6335.20, 27 902.80)	40.75 (37.05, 44.87)	15.27 (7.61, 22.93)	15.70 (7.93, 23.46)	2.77 (2.67, 2.87)
Southern Sub-Saharan Africa						
Incidence	13 083.91 (10 008.68, 17 725.55)	12 868.66 (9966.94, 17 150.83)	–1.65 (–5.37, 2.28)	61.71 (46.31, 77.10)	62.89 (47.35, 78.43)	1.92 (1.73, 2.11)
DALYs	2827.47 (1220.24, 5457.44)	3217.11 (1408.95, 6176.36)	13.78 (9.47, 18.55)	15.10 (7.48, 22.72)	15.42 (7.72, 23.11)	2.1 (1.90, 2.30)
Western Sub-Saharan Africa						
Incidence	55 316.94 (41 625.92, 75 533.59)	77 924.45 (58 795.17, 107 092.76)	40.87 (35.06, 46.38)	62.66 (47.14, 78.17)	63.45 (47.84, 79.06)	1.26 (1.17, 1.35)
DALYs	11 528.70 (5059.38, 22 207.71)	16 033.70 (6979.91, 31 395.51)	39.08 (31.83, 46.18)	15.52 (7.80, 23.25)	15.75 (7.97, 23.53)	1.49 (1.40, 1.58)

DALYs, disability-adjusted life-years; SDI, socio-demographic index.

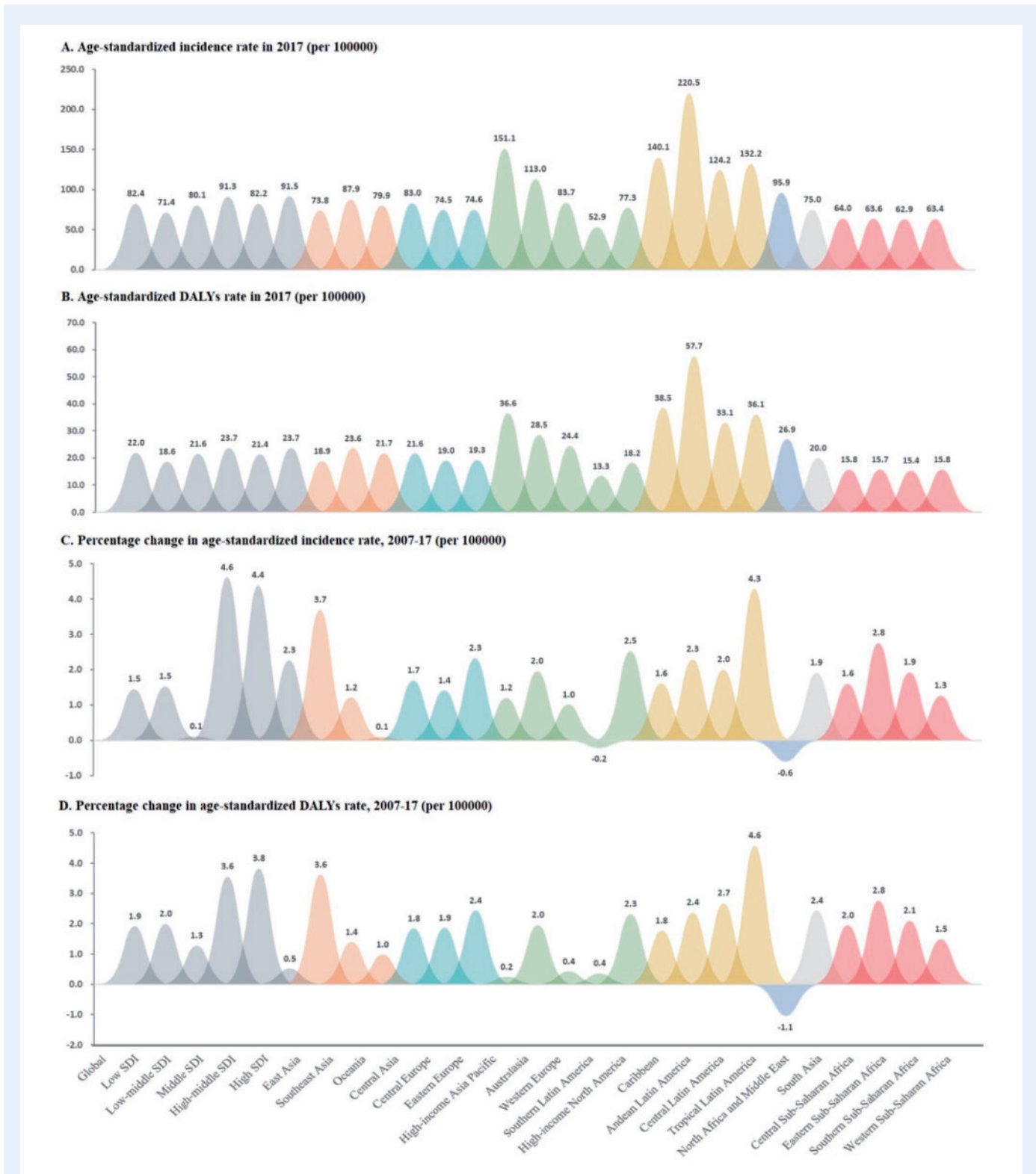


Figure 1. Age-standardized rates of incidence and disability-adjusted life-years (DALYs) in 2017, percentage change in age-standardized incidence rate and DALYs rate among women in reproductive age (15–49 years) for polycystic ovary syndrome during 2007–2017 by socio-demographic index (SDI) and world regions. (A) Age-standardized incidence rate among women in reproductive age for polycystic ovary syndrome (PCOS) in 2017 by SDI and world regions. (B) Age-standardized DALYs rate among women in reproductive age for PCOS in 2017 by SDI and world regions. (C) Percentage change in age-standardized incidence rate among women in reproductive age for PCOS during 2007–2017 by SDI and world regions. (D) Percentage change in age-standardized DALYs rate among women in reproductive age for PCOS during 2007–2017 by SDI and world regions.

Age-standardized incidence rate in 2007	Leading Countries In 2007	Leading Countries In 2017	Age-standardized incidence rate in 2017	Percentage change in age-standardized incidence rate, 2007-17	Percentage change in age-standardized DALY's rate, 2007-17	SDI Quintile
239.94	1. Ecuador	1. Ecuador	242.54	1.08%	1.34%	High SDI
207.15	2. Peru	2. Peru	211.59	2.14%	1.15%	High-middle SDI
205.12	3. Bolivia	3. Bolivia	208.75	1.77%	1.78%	Middle SDI
168.50	4. Japan	4. Japan	170.31	1.07%	0.23%	High-middle SDI
147.37	5. Bermuda	5. Bermuda	145.93	-0.98%	-0.55%	Low-middle SDI
145.37	6. Virgin Islands, U.S.	6. Barbados	144.88	0.26%	-0.02%	High-middle SDI
144.51	7. Barbados	7. Saint Vincent and the Grenadines	142.40	2.19%	0.68%	High-middle SDI
140.63	8. Antigua and Barbuda	8. Virgin Islands, U.S.	142.38	-2.06%	-1.00%	High-middle SDI
140.29	9. Grenada	9. Grenada	141.74	1.03%	0.48%	Middle SDI
139.35	10. Saint Vincent and the Grenadines	10. The Bahamas	141.38	2.26%	0.86%	High-middle SDI
138.72	11. Dominica	11. Antigua and Barbuda	141.31	0.48%	0.12%	High-middle SDI
138.26	12. The Bahamas	12. Haiti	140.65	1.83%	0.77%	Low-middle SDI
138.13	13. Haiti	13. Dominica	140.52	1.30%	0.62%	Middle SDI
138.01	14. Puerto Rico	14. Saint Lucia	140.44	2.33%	0.93%	High-middle SDI
137.94	15. Dominican Republic	15. Belize	140.42	1.83%	0.79%	Low-middle SDI
137.90	16. Belize	16. Jamaica	140.33	2.42%	0.89%	Low-middle SDI
137.73	17. Cuba	17. Trinidad and Tobago	140.22	2.00%	0.64%	Middle SDI
137.68	18. Suriname	18. Suriname	140.14	1.78%	0.70%	Low-middle SDI
137.48	19. Trinidad and Tobago	19. Paraguay	139.94	2.75%	1.08%	Middle SDI
137.24	20. Saint Lucia	20. Dominican Republic	139.88	1.41%	0.71%	Low-middle SDI

Figure 2. Top 20 countries of age-standardized rate and percentage change in age-standardized by incidence and disability-adjusted life-years among women of reproductive age (15–49 years) for polycystic ovary syndrome, 2007–2017.

The SDI-specific PCOS burdens across different age groups

Figure 3 shows the SDI-specific PCOS burdens across different age groups, ranging from 15 to >70 years, in 2017 and the percentage changes from 2007 to 2017 across these age groups. Globally, the incident cases peaked in the 15–19-year-old age group in all SDI quintiles. The DALY cases peaked in the 20–24-year-old age group in the low-SDI and low-middle-SDI quintiles, in the 25–29-year-old age group in the middle-SDI quintiles and in the 30–34-year-old age group in the high-middle-SDI quintiles.

Regional-specific trends based on the SDI

Supplementary Fig. S2 demonstrates the observed age-standardized incidence and DALY rates at the global and regional levels from 2007 to 2017 and the prospective rates according to the SDI values of the global regions. The expected pattern is essentially nonlinear, with a peak at approximately 0.66 of the SDI value and a subsequent decrease as the SDI value increases.

Discussion

In this study, we comprehensively reported the overall and age-standardized PCOS incidence rates and associated DALYs rates among women of reproductive age at the global, regional, and national levels between 2007 and 2017. In 2017, there were 1.55 million incident PCOS cases, and 0.43 million associated DALYs. Globally, the age-standardized incidence rate and DALY increased slightly (1.45% and 1.91%, respectively) from 2007 to 2017.

To date, no study has investigated the incidence of PCOS comprehensively. Epidemiological studies have reported conflicting results

regarding the prevalence of this condition, likely due to the use of different inclusion criteria, sample sizes, ethnicities, study designs, and defined regions (Ding *et al.*, 2017). Heterogeneity in the clinical manifestations of PCOS associated with different ethnicities, the application of inconsistent diagnostic criteria across ethnic groups, and variability in the knowledge of health providers also contributed to the variations in prevalence (Witchel *et al.*, 2020). Thus, consistent and convenient diagnostic criteria are needed for an accurate estimation of the PCOS incidence and prevalence across different ethnicities.

The slight increase in the PCOS incidence may be related to increases in both population growth and aging. Additionally, changes in the diagnostic criteria of PCOS over the past decades might partially account for the slight increase. For example, the incidence of PCOS was estimated to increase significantly when using the Rotterdam criteria, which remain the most widely used PCOS diagnostic criteria worldwide (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004). The recent increases in obesity rates might also contribute to the increased incidence of PCOS, as previous research confirmed that the prevalence of PCOS was 2–3 times higher among obese women relative to their non-obese counterparts (Yildiz *et al.*, 2012; Mu *et al.*, 2019). Notably, 68–75% of patients with PCOS remain undiagnosed even after visiting many medical institutions (Futterweit, 1999; March *et al.*, 2010; Wolf *et al.*, 2018), indicating that the incidence of this condition is probably underestimated (Ding *et al.*, 2017).

We observed that the PCOS burden also varied among the SDI quintiles. The greatest increases in the PCOS incidence and DALYs were observed in the middle-SDI and high-middle-SDI quintiles, respectively. These results reflect the higher detection rates, advanced healthcare infrastructure and primary healthcare in these regions. In contrast, the lowest age-standardized PCOS incidence rates and DALYs were observed in the low-SDI quintiles and are indicative of

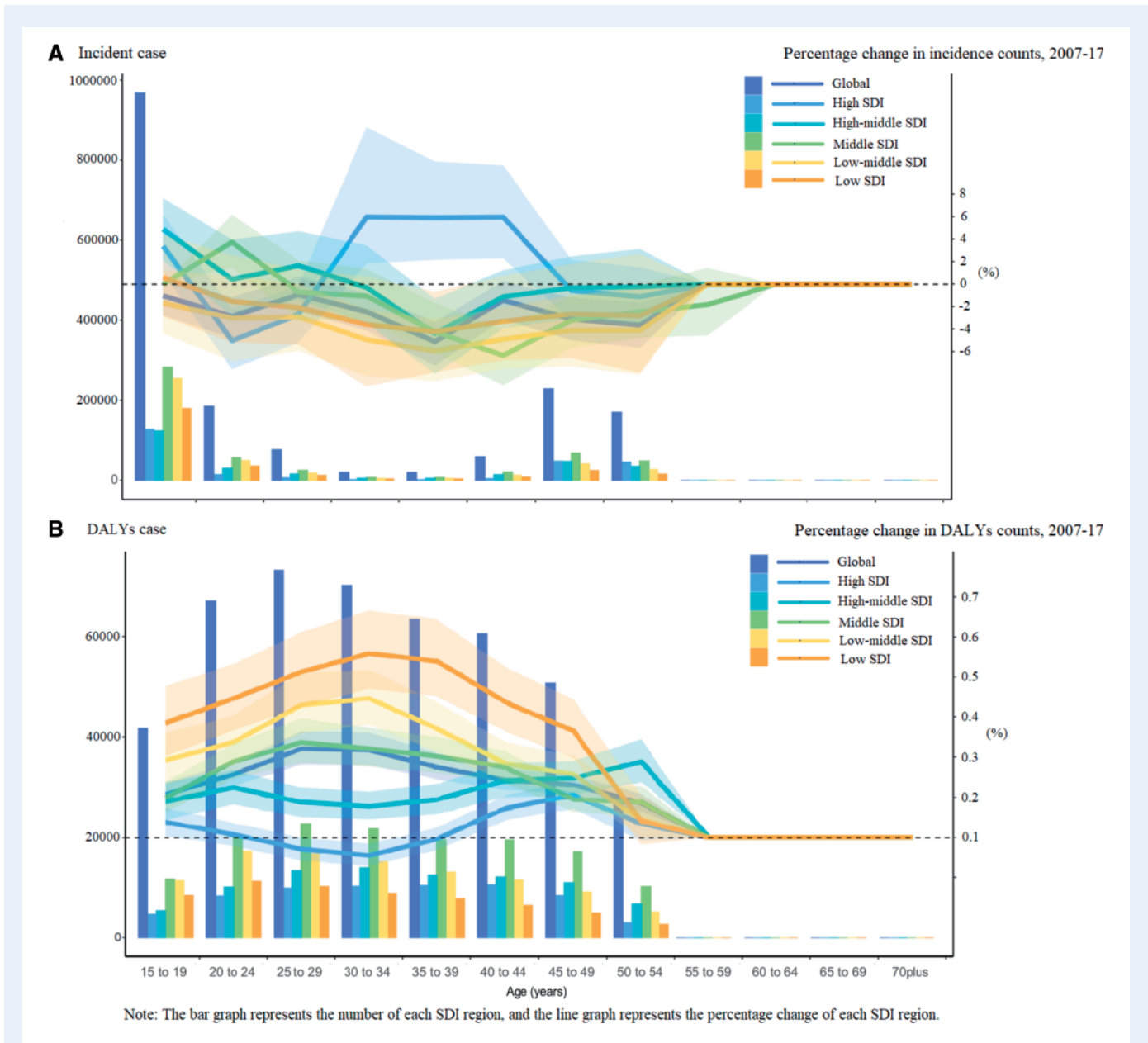


Figure 3. Age-socio-demographic index (SDI)-specific counts in 2017 and percentage change counts of polycystic ovary syndrome (PCOS), 2007–2017 of incidence and disability-adjusted life-years (DALYs) across different age groups from 15 to over 70 years old. (A) Age-SDI-specific incidence counts in 2017 and their percentage change counts of PCOS during 2007–2017. (B) Age-SDI-specific DALYs counts in 2017 and their percentage change counts of PCOS during 2007–2017.

the lower detection rates in this region. For example, ultrasonography, which is commonly used to diagnose PCOS, is limited in Africa in terms of both availability and affordability (Chima and Mamdoo, 2015). In summary, health resource allocation to resource-limited regions needs to be improved.

Regionally, Andean Latin America had both the highest age-standardized PCOS incidence and the highest DALYs, and this outcome was mainly attributable to Ecuador, Peru, and Bolivia. The Ministries of Health in these countries and Colombia have initiated national plans targeted at improving women’s health awareness and

health-seeking behavior related to gynecology (Johnson et al., 2018). In Ecuador, the ‘Health on the Go’ project within the 10-Year Health Plan (2015–2025) facilitated the identification of the clinical characteristics of PCOS and thus contributed to the increased incidence rates and DALYs (Roldós et al., 2017). Japan was the only developed country among the leading countries in terms of the age-standardized incidence and DALYs in both 2007 and 2017. This result is probably due to the complete health service system in Japan, the implementation of new revised diagnostic criteria for women of Japanese ethnicity, the extensive use of psychotropic drugs and the high prevalence of

female-to-male (FTM) trans-sexuality (Baba *et al.*, 2007, 2011; Watanabe and Kikuchi, 2014).

Tropical Latin America reported the highest increases in both the age-standardized PCOS incidence and DALYs during the study period. These increases were mostly attributable to Brazil, where urban industrialization has led to increases in obesity in all age groups (Canella *et al.*, 2014, 2015). The Brazilian public health system (SUS) provides comprehensive resources and technical guarantees for PCOS detection, and devotes attention to women's health by implementing interventions such as the maternal and child program (Thumé *et al.*, 2011; Prates *et al.*, 2017).

In contrast, decreases in the PCOS incidence and DALYs were observed in southern Latin America and in North Africa and the Middle East. Southern Latin America also reported the lowest age-standardized incidence and DALYs, which might be due to the fragile and fragmented health systems, poor health awareness, and absolute population decreases in this region (James *et al.*, 2019). Decreases in the PCOS incidence and DALYs in North Africa and the Middle East over the study period were mainly due to lower detection rates, which were a consequence of decreased resources in low-to middle-income countries in this region (Naal *et al.*, 2020). The decreases were exacerbated by international conflicts and the emigration of many experienced health workers (Miseda *et al.*, 2017; Naal *et al.*, 2020).

At the national level, Ethiopia and China exhibited the steepest increases in the PCOS incidence. Ethiopia has the fastest growing economy in Africa and a rapidly growing population. This country is experiencing simultaneous increases in factors associated with PCOS, including obesity, the exposure of farmers to chemical pesticides and a high prevalence of epilepsy (Fix *et al.*, 2020). The efforts of Ethiopia's Health Development Army, a women-centered community movement aimed at improving healthcare behaviors and practices among women, have improved the early detection of PCOS (Damtew *et al.*, 2018; Rieger *et al.*, 2019). In China, two programs have been introduced to protect women's health rights: the Program for China's Women Development (2001–2010) and the Program for China's Women Development (2011–2020) (Wang, 2001; House, 2011). The 'Healthy China 2030' initiative also aims to accelerate the prevention, treatment, and management of fertility-related diseases (Chen *et al.*, 2019). In contrast, the largest decrease in the PCOS incidence was observed in Afghanistan, and this finding was probably due to a low detection rate in a turbulent social environment. Taken together, the data suggest that PCOS is mainly concentrated in low- and middle-income countries, and therefore the increased screening and management of PCOS in these countries should be prioritized.

In addition, we observed the highest PCOS incidence among women aged 15–19 years, consistent with the observation that PCOS usually begins during puberty (Ehrmann *et al.*, 1995; Apter, 1998). However, it is difficult to diagnose PCOS during adolescence (Legro *et al.*, 2013), as the manifestations overlap with the physiological changes of puberty (Witchel *et al.*, 2019). Currently, there is no universal standard for the diagnosis of PCOS in adolescents (Witchel *et al.*, 2015). The DALYs peaked in different age groups across the SDI quintiles, suggesting that effective interventions and treatments should target different age groups according to the SDI quintile.

The stability of the global age-standardized PCOS incidence and DALYs over time suggests that the epidemiology of PCOS has not changed. However, the high degrees of variability and inconsistency

between the different diagnostic criteria present great challenges to an accurate estimation of the PCOS incidence. Currently, the etiology of PCOS remains unclear. As the clinical manifestations of PCOS vary greatly between women of different ethnic backgrounds, ethnicity-specific guidelines should be established that emphasize the racial differences in screening and diagnostic outcomes, management priorities, and responses to treatment (Ding *et al.*, 2017).

PCOS is a well-documented lifespan disorder. Accordingly, a personalized diagnostic approach and treatment should be promoted during different life stages (Teede *et al.*, 2018a). The recent International PCOS Guidelines promote the prevention, screening and treatment of PCOS during a woman's reproductive life (Teede *et al.*, 2018b; Peña *et al.*, 2020). The primary interventions comprise healthy lifestyle behaviors and avoidance of excessive weight gain, whereas secondary prevention relies on the early screening of girls at higher risk for PCOS. This guideline also promotes uniform diagnostic criteria, a timely and accurate diagnosis, enhanced education for health professionals and patients, improved screening and diagnosis protocols and the earliest treatment for PCOS-related complications (Conway *et al.*, 2014; Teede *et al.*, 2018a).

To the best of our knowledge, this is the first study to comprehensively assess the PCOS incidence and DALYs at the global, regional and national levels based on data from GBD (2017), which was the first well-rounded study to incorporate several data sources on the incidence of PCOS. We first used DALYs to estimate the PCOS burden, as this measure allows direct comparisons across different regions and countries (Capone, 2019). We also estimated the PCOS incidence and DALYs based on the SDI, which was reconstructed to better reflect the development of each country in GBD 2017 (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). Our findings will be valuable for resource allocation and priority settings at the global, regional, and national levels.

The following limitations should be acknowledged. First, although the GBD (2017) study aimed to gather all available data, some regions have limited available data. This may have led to widely estimated UIs. Second, the GBD (2017) study used increased hospital medical records (GBD 2017 DALYs and HALE Collaborators, 2018, 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). As previously reported, this may result in selection bias that favors people who access health care services (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). Furthermore, it is complicated to evaluate the PCOS phenotype, and multiple procedures are required, including clinical and laboratory assessments, pelvic ultrasonography, and multiple clinic visits (Escobar-Morreale, 2018). Therefore, the PCOS incidence might be underestimated. However, detection bias would lead to a higher estimated PCOS incidence in areas with better healthcare access and health awareness, thus there should be caution over resource allocation in these areas of 'high risk'. In addition, the diagnostic criteria are constantly changing, which contributes to inconsistencies when determining the PCOS incidence.

In conclusion, the global age-standardized PCOS incidence and DALYs rates increased slightly from 2007 to 2017, and these increases were probably related to population growth, resource availability, healthcare access, health awareness, and obesity. The highest increases in the PCOS age-standard incidence and DALYs rates from 2007 to 2017 were observed in the middle-SDI quintile, high-middle-SDI quintiles, tropical Latin America and countries such as Ethiopia,

Brazil, and China. Effective interventions and strategies should be established accordingly.

Supplementary data

Supplementary data are available at *Human Reproduction* online.

Data availability

The data underlying this article are available in the Global Health Data Exchange at <http://ghdx.healthdata.org/ihme> data.

Authors' roles

J.J.L, M.L.J, Y.H.H, Q.H.W, and L.Y.H participated in the study design, analysis, and in the interpretation of data. J.J.L, X.W, S.C.J and L.Y.H reviewed relevant medical literature. J.J.L and L.Y.H prepared the first draft of this manuscript. All coauthors interpreted the data and contributed to subsequent drafts of the manuscript, and all authors have seen and approved the final version.

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Conflict of interest

No potential conflicts of interest relevant to this article were reported.

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