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Age disparity in the burden of premenstrual syndrome: A five-year lag between incidence and prevalence peaks

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Letter

Age disparity in the burden of premenstrual syndrome: A five-year lag between incidence and prevalence peaks

Dear Editor,

Premenstrual syndrome (PMS) is a prevalent chronic condition affecting women's health periodically. Symptoms recur during the luteal phase of the menstrual cycle and typically subside shortly after the onset of menstruation. While not a life-threatening condition, it can substantially impair work efficiency, cognitive function, interpersonal relationships, and overall quality of life. Most previous studies have focused on describing the magnitude of PMS burden using single indicators or restricted age ranges[1–2], while less attention has been paid to the alignment between disease onset and accumulated health loss across the life course. This gap restricts a comprehensive understanding of the natural history of PMS and its long-term health implications. When the peak incidence of the disease aligns with the peak burden, public health resources can be effectively targeted toward the same high-risk age group. Conversely, a mismatch between these peaks necessitates the implementation of distinct strategies for disease prevention and disease management, tailored to different life stages.

In the present study, we used the Global Burden of Disease Study 2021 (GBD 2021) to obtain incidence, prevalence, disability-adjusted life years (DALYs), and corresponding age-standardized rates (ASRs) of PMS among women aged 10–54 years globally from 1990 to 2021. In this database, we chose DALYs because they represent the standard summary measure of disease burden in the GBD framework. Since PMS is non-fatal, DALYs consist entirely of years lived with disability (YLDs) and are therefore numerically identical. Moreover, five sociodemographic index (SDI) zones and 21 regions based on geographical locations were used. The SDI is a comprehensive indicator of a country or region's development status, calculated based on data such as per capita income, average education level, and fertility rate, with a range of 0–1, where higher values indicate better development status. The 95% uncertainty intervals (UI) for each of the above indicators were directly obtained from the database. The Joinpoint Regression Program (version 5.0.2) was applied using annual data from 1990 to 2021 with the grid search method and permutation tests to identify temporal breakpoints. Results are presented as annual percent change (APC) and the average annual percent change (AAPC), with 95% confidence intervals (CIs). Ages were divided into different groups: 10–14 years, 15–19 years, 20–24 years, 25–29 years, 30–34 years, 35–39 years, 40–44 years, 45–49 years, and 50–54 years. We primarily compared the age distribution patterns of various indicators, focusing on identifying the age peaks for incidence rates, prevalence rates, and DALY rates. In addition, we employed restricted cubic splines (RCS) to model the relationship between ASR and SDI, with six knots automatically allocated at the 5th, 23rd, 41st, 59th, 77th, and 95th percentiles of the SDI distribution (SDI knot values: 0.311, 0.482, 0.563, 0.627, 0.729, 0.834) for curve fitting. All RCS analyses and data visualization were implemented in R (version 4.5.2), using the rms package for RCS modeling, the rms::robcov function for cluster-robust variance estimation, and the ggplot2 package for visualization. The shaded bands in the RCS curves represented cluster-robust 95% confidence intervals of the predicted ASR values. A sensitivity analysis was performed using cluster-robust standard errors implemented with the robcov function in the rms package, with location as the clustering variable, was performed to assess the impact of within-region correlation.

We found that the incident cases of PMS increased by

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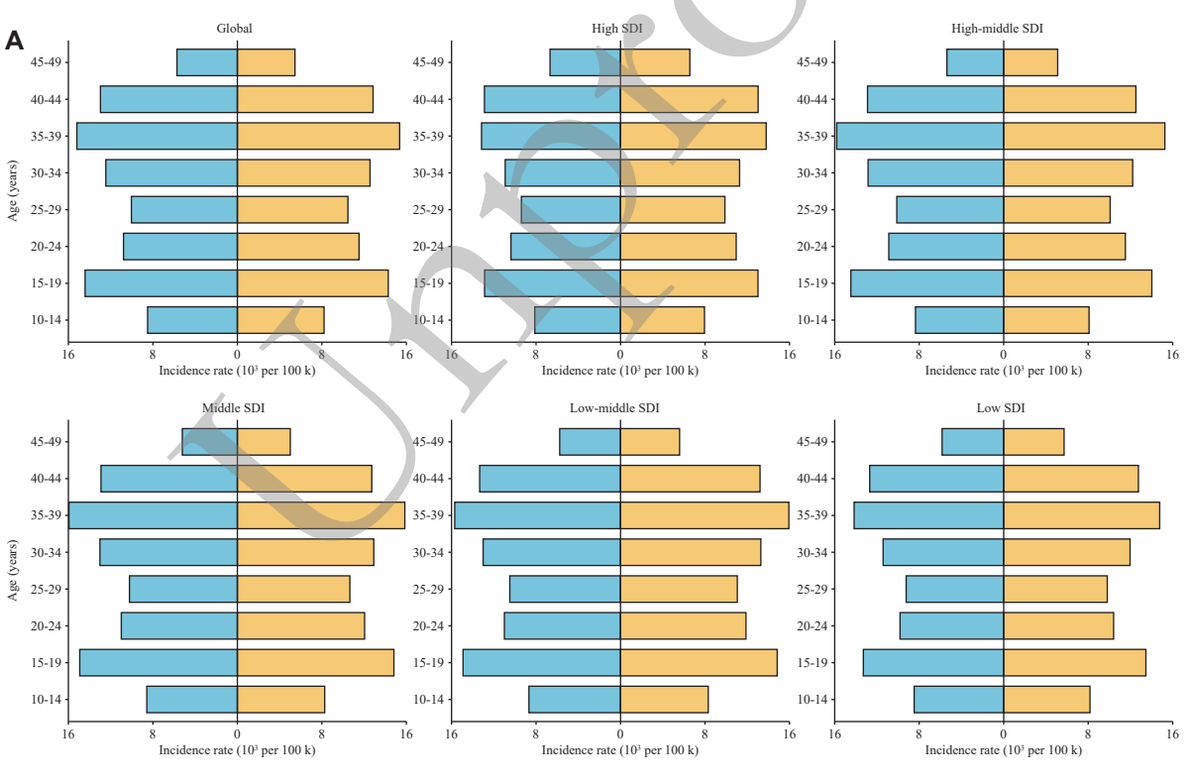
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42.9% from 182.2 (95% UI: 144.8–218.1) million in 1990 to 259.1 (206.1–312.9) million in 2021 globally. The age-standardized incidence rate (ASIR) was on the increase with an AAPC of 0.025 (95% CI: 0.022–0.027) (***Supplementary Table 1***). Prevalent cases of PMS increased by 49.1% from 651.4 (95% UI: 538.3–765.5) million in 1990 to 971.2 (95% UI: 795.3–1 152.8) million in 2021 globally. The AAPC of age-standardized prevalence rate (ASPR) indicated an upward trend, with an AAPC of 0.024 (95% CI: 0.021–0.027) (***Supplementary Table 2***). A similar upward trend was observed for ASR-DALYs, with an AAPC of 0.022 (95% CI: 0.019–0.024) (***Supplementary Table 3***). Joinpoint regression revealed a common three-phase trend for all three metrics across SDI subgroups: an initial stable period, a decline during 2000–2015, followed by a rebound (***Supplementary Fig. 1***). Detailed segment endpoints and *P* values are provided in ***Supplementary Tables 4–6***.

Globally, different burden indicators of PMS display markedly distinct age distribution characteristics (***Fig. 1***). Regarding incidence rates, a remarkably consistent age distribution pattern is observed both globally and across different SDI regions. Notably, the 35–39 age group exhibits the highest incidence rate, representing the most significant peak in all five SDI regions. The second highest incidence is found in the 15–19 age group, while the 40–44 age group also demonstrates a relatively high incidence rate. In contrast, the age distribution pattern for prevalence rates differs substantially from that of incidence rates. In both 1990 and 2021, the 40–44 age group consistently shows the highest prevalence rate, followed by the 35–39 age group. Furthermore, the age distribution of the DALYs rate closely resembles that of the prevalence rate, with both reaching a global peak in the 40–44 age group.

RCS analysis revealed an M-shaped association between SDI and ASR from 1990 to 2021 (***Fig. 2*** and ***Supplementary Fig. 2***). Likelihood ratio tests (LRTs) were conducted to statistically verify nonlinearity by contrasting linear and six-knot RCS regression models for ASIR, ASPR and ASR-DALYs. All LRT *P* values were < 0.001, confirming significant M-shaped nonlinear relationships between SDI and all PMS burden indicators. In the cluster-robust sensitivity analysis, all nonlinear terms remained significant (ASIR: F = 4.72, ASPR: F = 4.75, ASR-DALYs: F = 5.01; all $P < 0.001$). For ASR-DALYs, South Asia, Southeast Asia, Eastern Europe, Central Europe, Tropical Latin America, and Central Latin America demonstrated higher-than-expected PMS burden relative to their SDI levels. Western Sub-Saharan Africa and North Africa and Middle East presented a lower-than-expected PMS burden during this period. The trends of ASIR and ASPR were similar to those of ASR-DALYs.



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Fig. 1 **The incidence rate, prevalence rate, and disability-adjusted life years rate of premenstrual syndrome among different age groups across various socio-demographic index regions in 1990 and 2021.** A: The incidence rate. B: The prevalence rate. C: The disability-adjusted life years rate. All subfigures adopt butterfly bidirectional bar design: leftward blue bars represent values from 1990, whereas rightward yellow bars correspond to data in 2021; a single Y-axis (age) and a single X-axis (rate) are used without dual-Y axis. Abbreviation: SDI, socio-demographic index.

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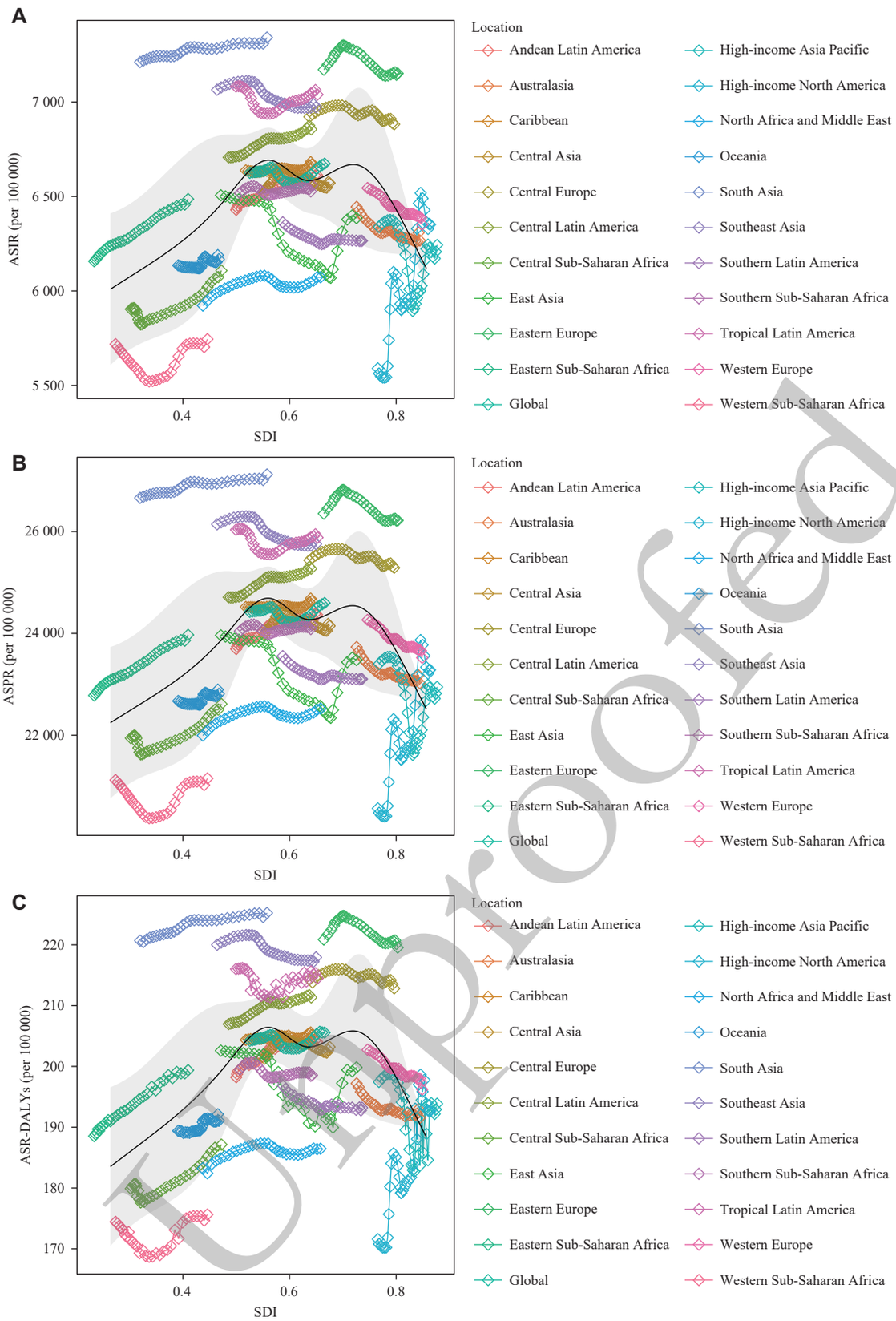


Fig. 2 **Correlation between the age-standardized rate and socio-demographic index for premenstrual syndrome in 21 regions during the 1990-2019 period.** A: Age-standardized incidence rate. B: Age-standardized prevalence rate. C: Age-standardized disability-adjusted life years rate. Solid lines represent restricted cubic spline fits with six knots based on cluster-robust variance estimation using the rms::robcov function; shaded areas indicate cluster-robust 95% confidence intervals. *P* for nonlinearity (likelihood ratio test) < 0.001 for all panels. Abbreviations: ASIR, age-standardized incidence rate; ASPR, age-standardized prevalence rate; ASR-DALYs, age-standardized disability-adjusted life years rate; SDI, socio-demographic index.

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From a women's health perspective, this study reveals a notable mismatch between the timing of PMS onset and the period of greatest accumulated health loss. Although PMS incidence peaks among women aged 35–39 years, the highest prevalence and disability-adjusted life years are observed later, at ages 40–44 years. This onset-burden lag suggests that women experience a prolonged period of symptom accumulation before reaching the stage of maximal functional impairment. The peak incidence observed between the ages of 35 and 39 may correlate with the accelerated decline in ovarian reserve function during this period[3], resulting in relative progesterone insufficiency or an imbalance in the estrogen-to-progesterone ratio during the luteal phase. The peak burden accumulation observed between the ages of 40 and 44 may result from a dual effect. First, the persistent symptoms accumulated over preceding years may continue to worsen. Second, the pronounced hormonal fluctuations characteristic of the early transitional phase of perimenopause begin to compound, thereby intensifying the severity and frequency of symptoms and increasing the prevalence and DALY rates[4].

This lag effect confirms the characteristics of PMS as a chronic, non-fatal and periodically occurring disease[5–6]. When intervention strategies are primarily based on prevalence rates or the distribution of DALYs, they often concentrate on stages where the disease burden has already accumulated significantly, potentially overlooking the critical early prevention window. Conversely, strategies based solely on incidence rates may fail to account for the long-term functional impairments experienced by middle-aged women. Therefore, interventions for PMS should adopt a phased and precise approach grounded in the life-course perspective. For individuals aged 35 to 39, public health initiatives should prioritize early identification, health education, and preventive interventions to reduce disease onset. For those aged 40 to 44, the clinical and social support systems should emphasize comprehensive symptom management, psychological support, and functional rehabilitation.

Additionally, a notably high incidence was found in the 15–19 age group, likely associated with immaturity of the hypothalamic-pituitary-ovarian axis during puberty, combined with academic and social stressors[7–8]. Supporting this, Liao *et al*[9] analyzed the relationship between PMS and school bullying in 10 042 girls, finding that girls who experienced bullying were more likely to develop PMS (OR = 3.15, 95% CI: 2.75–3.60). These findings emphasize that PMS prevention and management should adopt a life-course approach rather than focus on a single age group. Early identification and psychosocial support during adolescence are essential for reducing the risk of disease onset and alleviating long-term burdens.

Furthermore, our study revealed an M-shaped pattern in ASR with increasing SDI, with peaks corresponding to the low-middle and high-middle SDI regions. In high-middle SDI countries, the second peak may be attributed to heightened psychological stress and increased health awareness. Lifestyle factors such as high-intensity work, stress burden, obesity, and dietary imbalances, combined with enhanced health awareness among women and well-established healthcare systems, may collectively contribute to the rising disease burden observed in recent years. In summary, the M-shaped distribution of PMS burden across SDI levels reflects a complex interaction between socioeconomic development and the accessibility of menstrual health resources. This further suggests that PMS is not solely a biological concern; rather, it constitutes a public health issue intricately woven into the social fabric and life course of women.

Several limitations should be considered. First, the GBD framework may not fully account for racial and ethnic variations. Second, the lack of detailed data on etiology and risk factors for PMS restricts a more profound interpretation of observed trends and age-specific patterns. Third, estimates for certain regions and countries may lack robust quality assurance. Additionally, future studies could adopt mixed-effects models to further account for the panel structure.

Collectively, our key finding is a systematic onset-burden lag effect: the peak incidence of PMS occurs at ages 35–39, while the peak burden (measured by prevalence and DALYs) manifests later, at ages 40–44. It underscores that effective public health and clinical strategies must be tailored to specific life stages, with distinct priorities for prevention (targeting the 35-39 years) versus management (addressing the 40–44 years).

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Yours sincerely,

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Author contributions

Yiran Liu: Conceptualization; Methodology; Software; Writing-Original Draft. **Tianle Cheng:** Software; Validation; Data Curation. **Guiping Wan:** Data Curation, Supervision; Project administration. **Weiwei Tang:** Supervision; Writing-Reviewing & Editing; Funding acquisition. All authors reviewed the drafted manuscript for critical content and all authors approved the final version of the manuscript.

Additional information

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