Inequality's Toll on the Ovarian Clock: A 12-Country Survival Analysis of Early Menopause in South and Southeast Asia

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Abstract

Premature (<40 years) and early menopause (40–44 years) heighten women's lifetime risks of cardiovascular disease, osteoporosis, neurocognitive decline, and premature mortality. South and Southeast Asia (SSEA) exhibit among the highest prevalence of premature and early menopause worldwide, yet determinants in these settings are poorly understood. Leveraging Demographic and Health Surveys from 12 countries and a cohort of 481,048 women, we applied Kaplan–Meier estimators and Cox proportional hazards models to examine the effects of education, parity, wealth, and residence. By age 45, 5.2% of women were postmenopausal. In South Asia, no education (HR 1.37, 95% CI 1.04–1.79), having one child (HR 1.29, 1.13–1.48), and low wealth (HR 1.36, 1.26–1.47) predicted earlier menopause (all $p<0.05$). Although Southeast Asia exhibited a lower baseline hazard (HR 0.62, 0.45–0.85; $p=0.003$), the adverse effects of low education (HR 1.70, 1.31–2.19), high parity (HR 2.13, 1.45–3.13), and rural residence (HR 1.31, 1.13–1.51) were significantly stronger (all $p<0.001$). Contrary to high income countries, higher parity was linked to earlier menopause. These findings underscore that socio-demographic disadvantages accelerate ovarian ageing in SSEA and call for policies to expand girls' education, strengthen rural reproductive health services, and reduce economic inequities.

Extended abstract

Background

Menopause is defined as the final cessation of ovarian function comprising loss of reproductive hormone production and irreversible loss of fertility (Davis et al., 2023). Typically occurring between the ages of 45 and 55 years (Gold, 2011), some women experience menopause earlier than the average age, classified as premature menopause (before age 40 years) or early menopause (ages 40-44 years) (Faubion et al., 2015). Premature and early menopause have significant adverse effects on women's health and well-being, including an increased risk of cardiovascular diseases, osteoporosis, and mental health disorders (Shuster et al., 2010). The timing of menopause is generally influenced by a wide range of determinants, including genetic, biological, environmental, and socio-economic factors (Davis et al., 2023; El Khoudary et al., 2019; Schoenaker et al., 2014). Understanding the determinants of premature and early menopause is crucial, particularly in low- and middle-income countries (LMICs) where the healthcare and preventative measures are limited.

Southeast Asia is experiencing the fastest pace of population aging worldwide (United Nations, 2021). Projections indicate that regions including South Asia and Southeast Asia (SA/SEA) will see a doubling in the proportion of older persons between 2019 and 2050. Specifically, within SA/SEA, the percentage of persons aged 60 or above is expected to increase from 9.8% in 2017 to a remarkable 20.3% by 2050 (UN, 2017). Amidst this rising trend of older persons in these regions, Leone and colleagues (2023) report the highest prevalence of both premature (2.7%) and early menopause (4.5%) in SA/SEA, while in high income countries, these prevalence rates are ≥1% and 2–3%, respectively (Golezar et al., 2019). These excessive prevalence in premature and early menopause in SA/SEA underscore the urgent need to understand associated factors and develop effective public health interventions.

Research Questions

In particular, we explored the following three research questions (RQ):

RQ1: How have the distribution of menopausal timing and the SMAM evolved across successive DHS waves in SSEA?

RQ2: What are the country-wise prevalence of premature and early menopause in SSEA between 1986 and 2022?

RQ3: What are the population-averaged hazard ratios for education, parity, wealth, and place of residence on menopause timing, and how do these vary between South Asia and Southeast Asia?

Implications

Our study is the first to explore the underlying factors behind the high prevalence of premature and early menopause in SA/SEA, contributing crucial insights to global menopause research in

the context of LMICs. The findings of this study will have several important policy and research implications. First, the identification of key demographic and reproductive determinants of premature and early menopause will provide valuable insights into the underlying causes of their high prevalence in SE/SEA. This knowledge can inform the development of targeted interventions aimed at mitigating the risk of premature and early menopause, particularly among vulnerable subgroups. The regional variations identified in the study will be critical for designing country-specific strategies that account for local contexts and address the unique challenges faced by women in different parts of SE/SEA. The findings will also add to the global body of knowledge on menopause, particularly in LMICs where data has been historically scarce. This can lead to more equitable healthcare policies that address the needs of women across different socio-economic and demographic backgrounds. Overall, this study will shed light on the pattern and highlight the significant impact of demographic and reproductive factors on premature and early menopause in SA/SEA, providing a strong basis for future research and policy development aimed at improving women's reproductive health outcomes in LMICs.

Data

This study utilized 51 Demographic and Health Surveys (DHS) from 12 selected SA/SEA countries including Afghanistan, Bangladesh, Cambodia, India, Indonesia, Maldives, Myanmar, Nepal, Pakistan, Philippines, Timor-Leste, and Vietnam. These spanned surveys from 1986 to 2022 those included the question *"When did your last menstrual period start?"*. The DHS program defines a woman as post-menopausal if she meets three criteria: she is not pregnant, is not experiencing amenorrhea following childbirth (postpartum amenorrhea), and has not menstruated within the six months preceding the survey. Additionally, women who self-report being menopausal or having undergone a hysterectomy are also classified as menopausal[1].

Methods

In this study, we modified the DHS definition by extending the criterion of no menstruation from six months to twelve months. This modification aligns with established clinical and epidemiological definitions of menopause (WHO, 1996) and aims to minimize misclassification of women who may be peri-menopausal but are not yet post-menopausal (Harlow et al., 2012). We calculated the age at menopause based on the respondent's age at the interview and the reported time of their last menstrual period using all 51 surveys (Leone et al., 2023). Women who have not had a menstrual period for at least one year were considered post-menopausal. If this occurred before the age of 40, it was classified as *premature menopause*. Menopause between the ages of 40 and 44 was defined as *early menopause*. For analysis, both premature and early menopause variables were dichotomized as '1' (premature or early menopausal) and '0' (not premature or early menopausal). The socio-economic factors considered in the study to observe the patterns of premature and early menopause across population subgroups include level of

[1] Please see sampling and calculation details here https://dhsprogram.com/data/Guide-to-DHS-Statistics/Menopause.htm.

education, region/division, place of residence, wealth quintile, religion, and race/ethnicity. The demographic and reproductive factors were considered to observe the plausible determining factors of premature and early menopause including birth cohort, age at first marriage/cohabitation, age at first childbirth, number of children ever born, ideal number of children, and use of hormonal contraceptives.

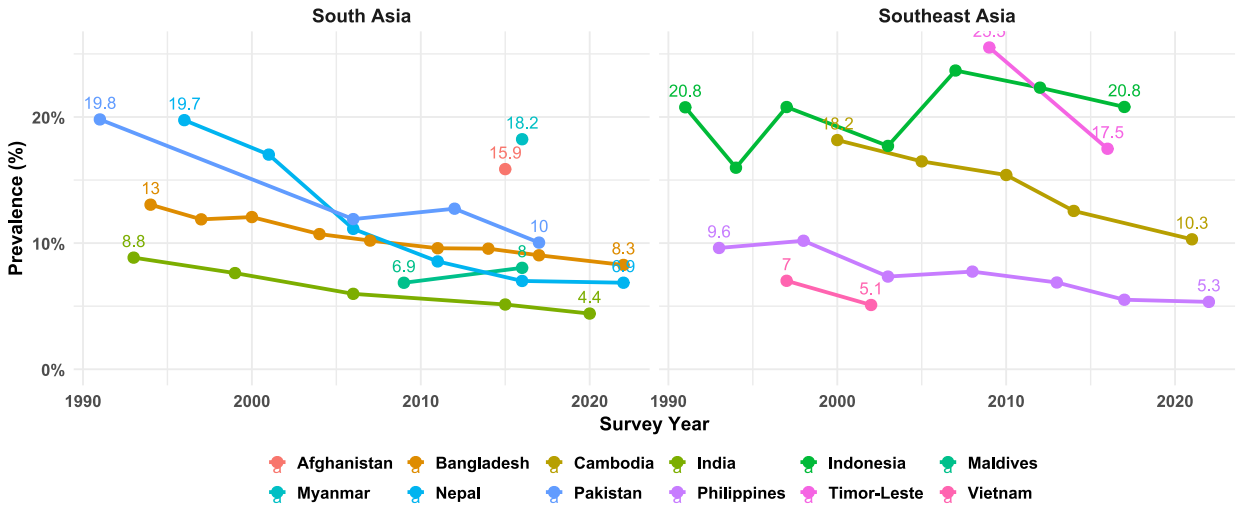
Preliminary analyses

We explored the country specific trends in prevalence of premature and early menopause. The outcome and the explanatory variables were then characterized through descriptive statistics. Subsequently, a bivariate analysis employing cross-tabulation and chi-square tests were conducted to explore the patterns and identify statistically significant associations between premature and early menopause and its hypothesized correlates.

Preliminary findings

Preliminary results revealed significant regional variations in the prevalence of premature and early menopause. Figure 1 illustrates trends in the prevalence of premature menopause across selected South Asian and Southeast Asian countries from 1986 to 2022. In South Asia, most countries exhibit a declining trend. Nepal and Pakistan had the highest prevalence in the early 1990s, nearing 20%, but experienced a sharp decline over time. Bangladesh and India followed a more gradual downward trajectory, while Afghanistan and Myanmar, with limited data points, reported a prevalence of 15.9% and 18.2%, respectively. In Southeast Asia, the trends are more heterogeneous. Indonesia exhibited fluctuating but generally high prevalence levels, with peaks exceeding 20%, while Vietnam, despite showing a decline, maintained relatively high prevalence at around 17.5% in recent years. Conversely, Cambodia and Timor-Leste demonstrated a more

Fig 1: Trends of Premature Menopause by Region



consistent decline, with Timor-Leste reaching the lowest levels by 2020.

Figure 2 presents trends in the prevalence of early menopause across selected South Asian and Southeast Asian countries from 1986 to 2022. In South Asia, trends vary across countries. Afghanistan reports a notably high prevalence of 22.1% in 2015, significantly higher than other countries in the region. Bangladesh exhibits a fluctuating trend, reaching 11.3% by 2020. Nepal and Pakistan show relatively stable prevalence levels, with Pakistan peaking at around 10% before declining slightly. India and Myanmar report consistently lower prevalence, generally below 7%, with Myanmar experiencing a slight decline over time.

In Southeast Asia, early menopause prevalence trends are more stable, with some countries showing gradual increases. Indonesia exhibits a rising trend, reaching approximately 10.3% by 2020, while Vietnam and Cambodia maintain moderate prevalence levels at around 8%. Timor-Leste and the Philippines report consistently lower prevalence, with Timor-Leste remaining below 5% over time. Overall, while some countries experience increasing trends, others show stability or slight declines.

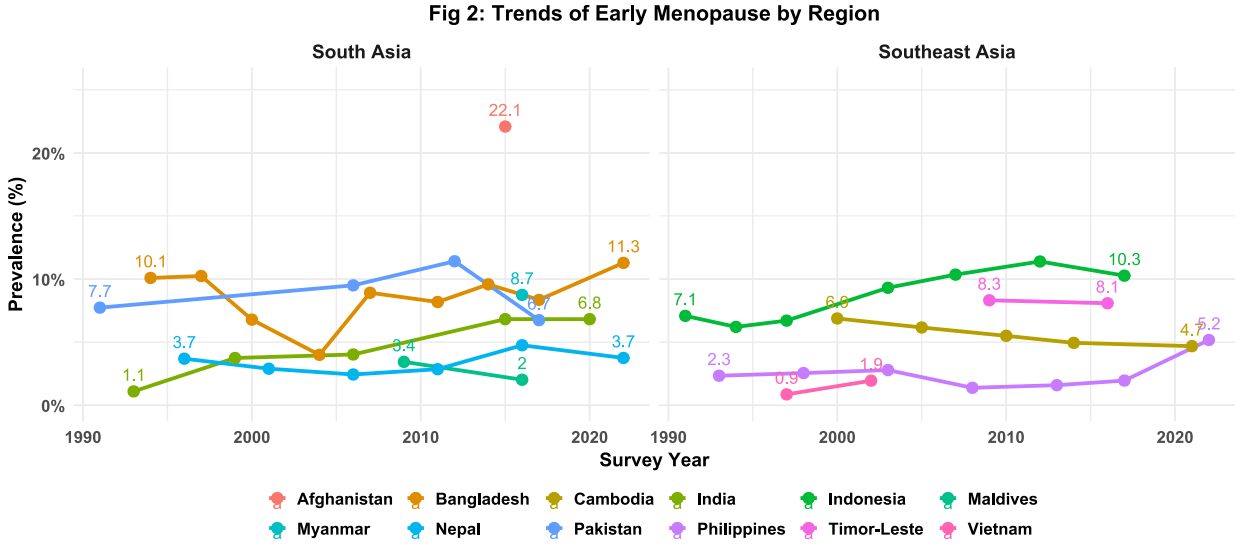
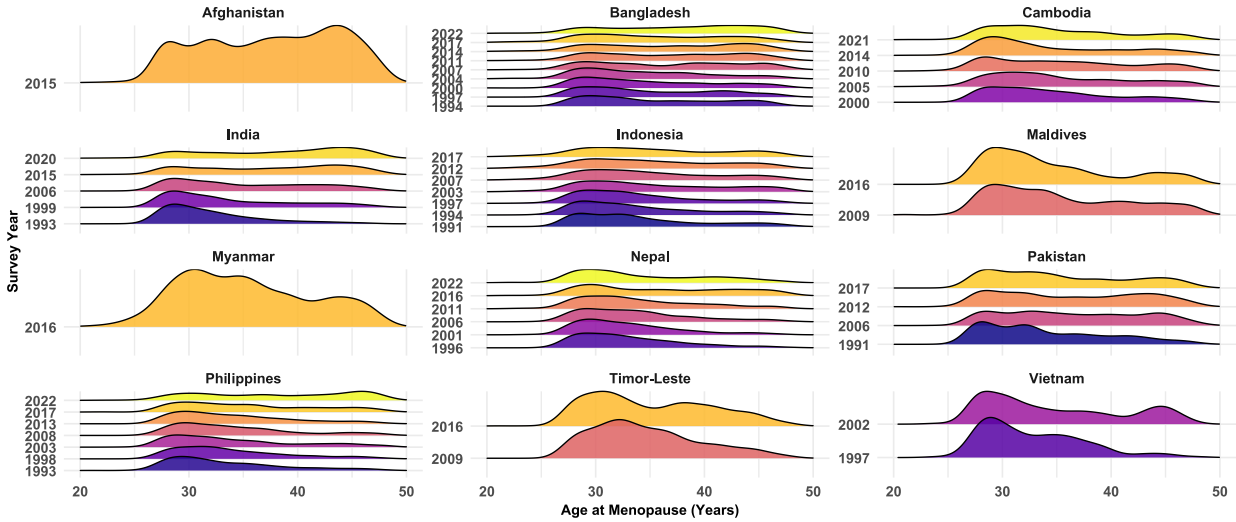


Figure 3 presents the distribution of age at menopause across multiple Asian countries, stratified by survey year. The density plots illustrate variations in menopausal age distributions over time, revealing notable country-specific trends and temporal shifts. The distribution of menopausal age in South Asian countries (Afghanistan, Bangladesh, India, Maldives, Myanmar, Nepal, and Pakistan) exhibits both stability and gradual shifts over time. Afghanistan, Myanmar, and Pakistan display relatively broad and stable distributions, with menopause occurring mostly in the late 40s. Bangladesh and Nepal, however, show a clear temporal shift, with earlier survey years (1990s and early 2000s) reflecting younger menopausal ages compared to more recent years. India, which has data from multiple survey years, exhibits a gradual broadening of the distribution, suggesting increasing variability in menopausal age, potentially influenced by demographic transitions and changing reproductive health patterns. The Maldives, with two survey years (2009 and 2016), shows a relatively stable distribution but with a concentration of cases around the mid-40s. Pakistan, despite spanning multiple decades, does not exhibit a

significant shift in menopausal age, suggesting a more stable trend compared to its South Asian counterparts.

The Southeast Asian countries (Cambodia, Indonesia, the Philippines, Timor-Leste, and Vietnam) display more pronounced variability in menopausal age distributions over time. Vietnam stands out with clear multimodal distributions in older survey years (1997 and 2002), suggesting the existence of distinct demographic subgroups experiencing menopause at different ages. This pattern could be linked to historical events, socioeconomic disparities, or variations in healthcare access. Indonesia and the Philippines, with survey data spanning multiple decades, show a broadening of distributions over time, reflecting increasing heterogeneity in menopausal age.

Fig 3: Distribution of Age at Menopause by Country



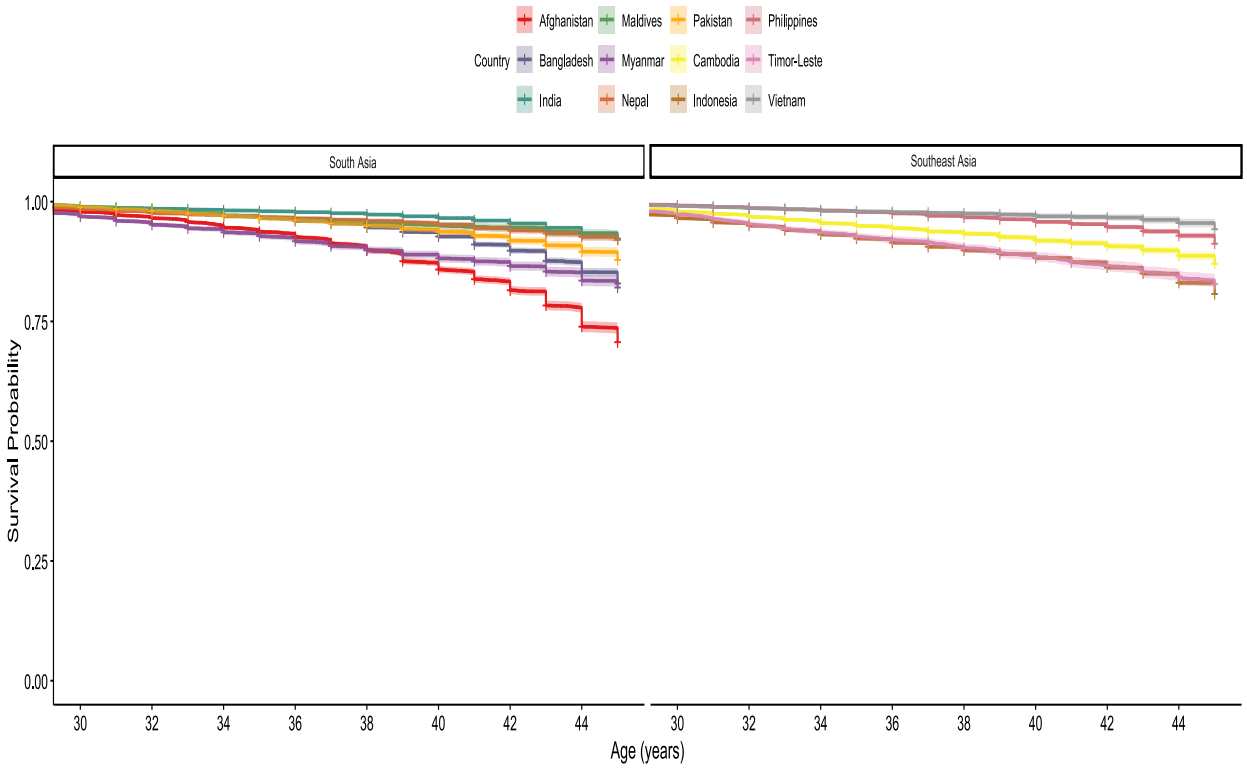
The Philippines, in particular, shows a steady upward shift. Cambodia also exhibits some variability, with a shift toward later menopausal ages in recent years, while Timor-Leste, based on limited survey years, presents a relatively concentrated distribution.

Figure 4 presents the distribution of menopausal age in Bangladesh and Indonesia, distinguishing premature menopause (<40 years, red), early menopause (40–44 years, orange), and other cases (≥45 years, green). The distribution of menopausal age in Bangladesh exhibits a right-skewed pattern, with a substantial proportion of cases classified under premature and early menopause. Notably, the prevalence of premature menopause (red) appears more pronounced in older survey years (1994–2004), suggesting a historical trend where a higher proportion of Bangladeshi women experienced menopause before the age of 40. Over time, the density of premature menopause declines, particularly in more recent survey years (2017–2022). Early menopause (orange) also follows a declining trend but remains relatively prominent across all survey years, indicating that a considerable proportion of women still experience menopause between 40 and 44 years.

The Kaplan–Meier curves for menopause timing, disaggregated by region and country (Figure 5), reveal substantial cross-country variation in the timing of menopause among women aged 30

and above. In South Asia, countries such as Afghanistan and Bangladesh show noticeably earlier declines in survival probability (i.e., earlier onset of menopause), while countries like India, Nepal, and Maldives exhibit relatively delayed declines, suggesting later menopausal timing on average. In contrast, the curves for Southeast Asian countries are more tightly clustered, although notable differences still exist—such as earlier menopausal transitions in Vietnam and Myanmar compared to more gradual declines in the Philippines and Timor-Leste.

Fig 4: Kaplan–Meier Curves for Menopause Timing by Region & Country



The steeper descent in the survival curves for certain countries (e.g., Afghanistan and Bangladesh) signals an accelerated transition into menopause, potentially reflecting underlying disparities in health, reproductive history, nutrition, or broader socioeconomic factors. Meanwhile, the more gradual slopes observed in other countries suggest later menopausal timing, possibly linked to improved maternal and reproductive health profiles, higher educational attainment, or better access to healthcare. These visible disparities not only justify a move toward multivariable analysis but also underscore the importance of accounting for both individual and contextual influences. The variation within and between regions strengthens the case for a multilevel Cox proportional hazards model that incorporates shared frailties at the community, country, and regional levels. Such an approach will enable us to quantify the extent to which unobserved heterogeneity—arising from social, cultural, environmental, or health system-level factors—explains cross-national differences in menopause timing. Moreover, this heterogeneity cautions against pooled analyses that do not correct for clustering effects.

In light of the patterns observed, validating the proportional hazards assumption becomes even more crucial, as non-proportionality could reflect varying effects of covariates over time across diverse settings. Lastly, supplementing the analysis with discrete-time event history models will help test the robustness of findings, especially given the interval-censored nature of age-at-menopause data.

Next Steps

To strengthen the cross-national comparability and analytic depth of this study, the next phase of the analysis will focus on refining both the dataset and the modeling approach. First, we will restrict the final analysis to the most recent DHS surveys conducted between 2015 and 2022 across the 12 selected countries. This will help ensure greater temporal consistency and reduce variability that may arise due to changes in survey design, recall bias, or evolving social contexts across different time periods.

Cox proportional hazard regression models will be used to estimate hazard ratios (HRs) for the predictors influencing age at menopause. The median age at which 50% of women were expected to remain in their reproductive years will be determined as the median survival time. A survival analysis approach was chosen over logit analysis due to its ability to handle censored observations, a common feature of this dataset, and its consideration of the duration from menarche to menopause (Ortiz et al., 2006). Building on the initial exploratory findings, we will then fit a multilevel Cox proportional hazards model that incorporates shared frailties at the community, regional, and national levels. This approach allows us to account for unobserved heterogeneity across different layers of social and spatial structure, acknowledging that factors influencing menopause timing extend beyond individual or household characteristics. These frailty terms will help capture contextual influences such as differences in health infrastructure, environmental conditions, and sociocultural norms that may cluster within communities or countries.

To ensure the robustness of the Cox model estimates, we will rigorously test the proportional hazards assumption. This will involve assessing Schoenfeld residuals and incorporating time-dependent covariates if necessary. Addressing any violations of this assumption is critical to ensuring the validity of the hazard ratio estimates and the reliability of our interpretations.

Finally, as a sensitivity analysis, we will replicate the analysis using discrete-time event history models. These models offer a flexible alternative, especially when dealing with time measured in intervals rather than as continuous. Comparing the results from both modeling approaches will help validate our findings and highlight any model-dependent interpretations, offering a more comprehensive understanding of the factors shaping menopausal timing across diverse South and Southeast Asian settings.

Expected Results

We anticipate that our analysis will reveal significant cross-country and regional variations in the timing of menopause among women in South and Southeast Asia. The Kaplan–Meier curves are expected to show that certain countries, particularly in South Asia, exhibit an accelerated decline in survival probability—indicating earlier menopause onset—compared to other countries with more gradual transitions.

In the multilevel Cox proportional hazards model, we expect key individual-level factors such as lower education, lower wealth, and earlier age at last childbirth to be associated with a higher hazard of early menopause. Conversely, higher education, greater wealth, and urban residence are anticipated to be protective, resulting in a lower hazard. We further expect that incorporating shared frailties at the community, country, and regional levels will reveal substantial unobserved heterogeneity, confirming that contextual factors play a critical role in shaping menopause timing.

The proportional hazards assumption, as evaluated using Schoenfeld residuals and time-dependent covariates, may indicate minor deviations for some predictors, prompting the use of sensitivity analyses with discrete-time event history models. Overall, we expect our findings to robustly support the hypothesis that both individual and contextual determinants significantly influence the timing of menopause in these regions, thereby providing actionable insights for targeted public health interventions.

Concluding remarks

Our research is the first to comprehensively investigate the elevated prevalence of premature and early menopause in South and Southeast Asia, a region often underrepresented in global menopause studies. As the world's population ages, understanding menopause in low- and middle-income countries is increasingly important for women's health and well-being. Our findings will enhance global understanding of menopause in low- and middle-income countries, offering a foundation for further research and policy development to address the rising prevalence and associated health disparities of premature and early menopause in SA/SEA.

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