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## The association of age at menarche and cardio-vascular events: systematic review and meta-analysis

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This study aimed to evaluate the association between age at menarche and cardiovascular (CV) events through a systematic review and meta-analysis of observational studies. A comprehensive literature search covering studies published from January 1, 2000, to October 31, 2023, was conducted in PubMed, MEDLINE, Embase, and Scopus. Twenty-nine observational studies involving 4,931,160 adult women aged 18 years or older were included. The meta-analysis revealed a J-shaped association between age at menarche and CV events. Individuals with menarche at 12-13 years exhibited the lowest risk, while those with younger (≤ 11 years) or older ages (14–15 years and  $\geq$  16 years) showed an increased risk. Notably, individuals with age at menarche of 16 years and older had the highest risk of CV events. The pooled odds of CV mortality in age at menarche categories 14–15 years and ≥ 16 years were 37% (OR: 1.37, 95% CI 1.14-1.64, I2:76.9%) and 64% (OR: 1.64, 95% CI 1.20-2.24, I2:87%) higher than referent age at menarche 12-13 years. No statistically significant difference was found in CV mortality risk between individuals with age at menarche  $\leq$  11 years and those with age at menarche 12-13 years. The ORs for coronary heart disease were significantly higher for age at menarche  $\geq$  16 years (35%) increase), while no significant difference was found for age at menarche ≤ 11 years or 14–15 years compared to age at menarche 12-13 years. Regarding stroke, the ORs for age at menarche  $\leq$  11, 14–15, and  $\geq$  16 years were significantly higher (7%, 24%, and 94% increase, respectively) compared to age at menarche 12–13 years. Dose–response meta-analysis and one-stage random-effect cubic splinemodels confirmed the J-shaped risk pattern. Meta-regression indicated that age and BMI were not significant sources of heterogeneity. Sensitivity analyses and the absence of publication bias further supported the robustness of the findings. This study concludes that age at menarche is independently associated with CV events, with a J-shaped pattern. The findings underscore the significance of considering menarche age as an independent risk factor for CV events. Further research is warranted to validate these findings and explore potential underlying mechanisms.

**Image:** Pooled Odds Ratio (OR) and 95% confidence interval (CI) of cardiovascular (CV) events b age at menarche.

## Biography

As a seasoned reproductive health specialist, Samira Behboudi-Gandevani bring a wealth of expertise in research and education to my role as an Associate Professor at Nord University, Norway. With over 100 papers published in prestigious international journals, her contributions to the field span a wide range of topics, including reproductive health maternal health, women's cardiovascular risk factors, and high risk pregnancy. Her research endeavors aim to advance understanding and promote evidencebased practices in reproductive health, addressing critical issues to improve outcomes for individuals and communities worldwide.