

Preeclampsia and preterm birth risk may be reduced by calcium dose lower than current WHO standard

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To help prevent preeclampsia and preterm birth—common complications in pregnancy that can be fatal to women and newborns—low-dose calcium supplementation (equivalent to one

500-milligram pill per day) may be as effective as the World Health Organization (WHO) recommended high-dose calcium supplementation (equivalent to three 500-milligram pills taken throughout each day), according to a new study led by Harvard T.H. Chan School of Public Health and collaborators in India and Tanzania.

While [calcium](#) supplementation is a known intervention to help prevent preeclampsia and [preterm birth](#)—it is estimated to halve a pregnant woman's risk of developing preeclampsia and reduce an infant's risk of being born preterm by 25%—the study is the first to evaluate the efficacy of a low-dose regimen versus a high-dose regimen.

The findings provide an opportunity to revise the WHO's current recommendation that women with low-calcium diets—most women who live in low- and [middle-income countries](#)—receive high-dose calcium supplementation throughout pregnancy.

The study is published in *The New England Journal of Medicine*.

"The current recommendation for pregnant women to take three calcium pills per day presents feasibility concerns for women and cost concerns for governments and public health programs," said senior author Wafaie Fawzi, Richard Saltonstall Professor of Population Sciences and professor of nutrition, epidemiology, and global health. "As such, most middle- and low-income countries have not implemented calcium supplementation in pregnancy, leaving women and infants unnecessarily vulnerable."

The researchers conducted two randomized, double-blind trials of 11,000 pregnant women in India and 11,000 [pregnant women](#) in Tanzania to assess if 500mg of calcium per day was as effective as 1,500mg of calcium per day in reducing the risks of preeclampsia and preterm birth (defined as birth before 37 weeks of gestation).

All of the participants were pregnant for the first time, putting them at higher risk for preeclampsia. Starting at less than 20 weeks of pregnancy, they received monthly supplies of daily calcium supplementation, consisting of either three 500mg calcium pills or one 500mg calcium pill and two placebo pills. Their health was monitored during clinic visits each month of their pregnancy, at delivery, and at six weeks postpartum.

The study found that low-dose calcium supplementation was as effective as high-dose calcium supplementation in preventing the risk of preeclampsia. In the India trial, the incidence of preeclampsia was 3.0% among women taking 500mg of calcium daily and 3.6% among women taking 1,500mg of calcium daily. In the Tanzania trial, the incidence of preeclampsia was 3.0% and 2.7%, respectively.

The findings on preterm birth were mixed. In the India trial, the incidence of preterm birth was 11.4% among women taking 500mg of calcium daily and 12.8% among women taking 1,500mg of calcium daily, indicating a similar effect of the two doses. In the Tanzania trial, the incidence of preterm birth was slightly different: 10.4% and 9.7%, respectively.

However, when the researchers pooled the data from both trials, they found the effect of low-dose supplementation was not significantly different on preterm birth compared to high-dose supplementation.

"Overall, our findings show that a single pill per day can be as effective as three," said joint first author Christopher Sudfeld, associate professor of global health and nutrition. "With a reduced pill burden for women and lower costs for governments and programs that buy calcium pills, [calcium supplementation](#) should be considered widely implementable in the places it's needed most—and should start saving thousands of maternal and newborn lives."

The researchers noted that the study had some limitations. In line with ethical guidelines, the study did not include a placebo group, precluding further comparisons between low- and high-dose calcium and no supplementation. Additionally, because the participants were primarily [young women](#) with low risk of chronic hypertension, it is not clear how generalizable the findings are to other pregnant populations.

More information: Two Randomized Trials of Low-Dose Calcium Supplementation in Pregnancy, *New England Journal of Medicine* (2024). [DOI: 10.1056/NEJMoa2307212](https://doi.org/10.1056/NEJMoa2307212)

Provided by Harvard T.H. Chan School of Public Health

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