

## Abstract

---

### Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia

Rolnik DL, Wright D, Poon LC, et al.  
*n engl j med.* 2017; 377;7 [nejm.org](http://nejm.org)

**Background:** Preterm preeclampsia is an important cause of maternal and perinatal death and complications. It is uncertain whether the intake of low-dose aspirin during pregnancy reduces the risk of preterm preeclampsia.

**Methods:** In this multicenter, double-blind, placebo-controlled trial, we randomly assigned 1776 women with singleton pregnancies who were at high risk for preterm preeclampsia to receive aspirin, at a dose of 150 mg per day, or placebo from 11 to 14 weeks of gestation until 36 weeks of gestation. The primary outcome was delivery with preeclampsia before 37 weeks of gestation. The analysis was performed according to the intention-to-treat principle.

**Results:** A total of 152 women withdrew consent during the trial, and 4 were lost to follow up, which left 798 participants in the aspirin group and 822 in the placebo group. Preterm preeclampsia occurred in 13 participants (1.6%) in the aspirin group, as compared with 35 (4.3%) in the placebo group (odds ratio in the aspirin group, 0.38; 95% confidence interval, 0.20 to 0.74;  $P = 0.004$ ). Results were materially unchanged in a sensitivity analysis that took into account participants who had withdrawn or were lost to follow-up. Adherence was good, with a reported intake of 85% or more of the required number of tablets in 79.9% of the participants. There were no significant between-group differences in the incidence of neonatal adverse outcomes or other adverse events.

**Conclusions:** Treatment with low-dose aspirin in women at high risk for preterm preeclampsia resulted in a lower incidence of this diagnosis than placebo.

### Collaborative Group. Antiplatelet agents for prevention of pre-eclampsia: a meta-analysis of individual patient data.

Askie LM, Duley L, Henderson-Smart DJ, Stewart LA; PARIS

*Lancet.* 2007 May 26;369(9575):1791-8. <https://www.ncbi.nlm.nih.gov/pubmed/17512048>

**Background:** Pre-eclampsia is a major cause of mortality and morbidity during pregnancy and

childbirth. Antiplatelet agents, especially low-dose aspirin, might prevent or delay pre-eclampsia, and thereby improve outcome. Our aim was to assess the use of antiplatelet agents for the primary prevention of pre-eclampsia, and to explore which women are likely to benefit most.

**Methods:** We did a meta-analysis of individual patient data from 32,217 women, and their 32,819 babies, recruited to 31 randomised trials of pre-eclampsia primary prevention.

**Findings:** For women assigned to receive antiplatelet agents rather than control, the relative risk of developing pre-eclampsia was 0.90 (95% CI 0.84-0.97), of delivering before 34 weeks was 0.90 (0.83-0.98), and of having a pregnancy with a serious adverse outcome was 0.90 (0.85-0.96). Antiplatelet agents had no significant effect on the risk of death of the fetus or baby, having a small for gestational age infant, or bleeding events for either the women or their babies. No particular subgroup of women was substantially more or less likely to benefit from antiplatelet agents than any other.

**Interpretation:** Antiplatelet agents during pregnancy are associated with moderate but consistent reductions in the relative risk of pre-eclampsia, of birth before 34 weeks' gestation, and of having a pregnancy with a serious adverse outcome

### Antiplatelet agents for preventing and treating pre-eclampsia.

Knight M, Duley L, Henderson-Smart DJ, King JF. *Cochrane Database Syst Rev.* 2000;(2):CD000492. <https://www.ncbi.nlm.nih.gov/pubmed/10796208>

**Background:** Pre-eclampsia is associated with deficient intravascular production of prostacyclin, a vasodilator, and excessive production of thromboxane, a platelet-derived vasoconstrictor and stimulant of platelet aggregation. These observations led to the hypotheses that antiplatelet agents, and low dose aspirin in particular, might prevent or delay the development of pre-eclampsia.

**Objectives:** To assess the effectiveness and safety of antiplatelet agents when given to women at risk of developing pre-eclampsia, and to those with established pre-eclampsia.

**Search Strategy:** This review drew on the search strategy developed for the Pregnancy and Childbirth Group as a whole. The Cochrane Controlled Trials Register was also searched, The Cochrane Library 1999 Issue 1, Embase was searched from 1994-1999 and hand searches were performed of the congress proceedings of the International and European Societies for the Study of Hypertension in Pregnancy.

**Selection Criteria:** All randomised trials comparing antiplatelet agents with either placebo or no antiplatelet agent during pregnancy. Quasi random study designs were excluded. Participants were pregnant women considered to be at risk of developing pre-eclampsia, and those with pre-eclampsia before delivery. Women treated postpartum were excluded. Interventions were any comparisons of an antiplatelet agent (such as low dose aspirin or dipyridamole) with either placebo or no antiplatelet agent.

**Data Collection And Analysis:** Assessment of trials for inclusion in the review and extraction of data was performed independently and unblinded by two reviewers. Data were entered into the Review Manager software and double checked.

**Main Results:** Forty two trials involving over 32,000 women were included in this review, with 30,563 women in the prevention trials. There is a 15% reduction in the risk of pre-eclampsia associated with the use of antiplatelet agents [32 trials with 29,331

women; relative risk (RR) 0.85, 95% confidence interval (0.78, 0.92); Number needed to treat (NNT) 89, (59, 167)]. This reduction is regardless of risk status at trial entry or whether a placebo was used, and irrespective of the dose of aspirin or gestation at randomisation. Twenty three trials (28,268 women) reported preterm delivery. There is a small (8%) reduction in the risk of delivery before 37 completed weeks [RR 0.92, (0.88, 0.97); NNT 72 (44, 200)]. Baby deaths were reported in 30 trials (30,093 women). Overall there is a 14% reduction in baby deaths in the antiplatelet group [RR 0.86, (0.75, 0.98); NNT 250 (125, >10000)]. Small for gestational age babies were reported in 25 trials (20,349 women), with no overall difference between the groups, RR 0.92, (0.84, 1.01). There were no significant differences between treatment and control groups in any other measures of outcome. Five trials compared antiplatelet agents with placebo or no antiplatelet agent for the treatment of pre-eclampsia. There are insufficient data for any firm conclusions about the possible effects of these agents when used for treatment of pre-eclampsia.

**Reviewer's Conclusions:** Antiplatelet agents, in this review largely low dose aspirin, have small-moderate benefits when used for prevention of pre-eclampsia. Further information is required to assess which women are most likely to benefit, when treatment should be started, and at what dose.