| **Study, Year**  **Study quality** | **Study design** | **Country** | **N randomized or included** | **Preeclampsia risk criteria** | **Dose**  **Time of initiation and stopping treatment** | **Preeclampsia incidence reported** |
| --- | --- | --- | --- | --- | --- | --- |
| Ayala, 201259  Good | RCT | Spain | 350 | Receiving medical care at a high-risk unit. High risk includes: family or personal history of PE; chronic HTN; CVD; endocrine, metabolic, or bleeding disease; history of spontaneous abortion; multiple pregnancy; obesity; or age. | 100 mg daily  12 to 16 weeks; delivery | Yes |
| Benigni,198960  Fair | RCT | Italy | 33 | HTN or previous obstetrical history (fetal death due to placental insufficiency, severe IUGR, early-onset PE [<32 weeks]) | 60 mg daily  12 weeks; delivery | No |
| Caspi, 199461  Good | RCT | Israel | 47 | Twin pregnancies | 100 mg daily  15 to 23 weeks (mean, 17.7 weeks); delivery | Yes |
| CLASP, 199458  Good | RCT | Argentina, Australia, Belgium, Canada, Germany, Hong Kong, Israel, Malaysia, New Zealand, Russia, Spain, Sweden, Netherlands, United Arab Emirates, UK, USA | 9,364 | Population at risk of PE or IUGR as determined by a clinician (women were considered for prophylactic entry or therapeutic entry)  *Prophylactic entry:* Pregnant women with history of PE or IUGR in a previous pregnancy, chronic HTN, renal disease, or other risk factors, such as maternal age, family history, or multiple pregnancy  *Therapeutic entry:* Pregnant women with signs  or symptoms of PE or IUGR in the current pregnancy | 60 mg daily  12 to 32 weeks; delivery | Yes |
| Davies, 199576†  Fair | RCT | UK | 122 | Population not at elevated risk, healthy nulliparous women (study included for KQ3 only) | 75 mg daily  18 weeks; delivery | Yes |
| Gallery, 199762  Fair | RCT | Australia | 108 | Preexisting chronic HTN, renal disease, or history of PE as determined by patient interview at 16 weeks’ gestation | 100 mg daily  17 to 19 weeks; 2 weeks prior to planned delivery | No |
| Grab, 200063  Fair | RCT | Germany | 43 | Current IUGR, impaired uteroplacental blood flow, chronic HTN, or prior history of PE, stillbirth, or growth restriction | 100 mg daily  18 weeks; 38 weeks | Yes |
| Hauth, 199373†  Good | RCT | US | 606 | Population not at elevated risk, healthy nulliparous women (study included for KQ3 only) | 60 mg daily  23 weeks; delivery | Yes |
| Hermida, 199764  Good | RCT | Spain | 100 | Being treated at the HR unit of the hospital (reasons include family or personal history of gestational HTN, PE, or chronic HTN; cardiovascular, endocrine, bleeding, or metabolic disease; and a personal history of spontaneous abortion, multiple pregnancy, obesity; adolescent or middle-aged nulliparous pregnancy [<18 or >35 years]) | 100 mg daily  12 to 16 weeks; delivery | Yes |
| Jensen, 201077†  Good | Cohort | Denmark | 47,400 | Population not at elevated risk, all children born to women who were pregnant between 1996 and 2002 were enrolled (study included for KQ3 only) | NR  Anytime throughout pregnancy | No |
| Keim, 200678†  Good | Case- control | US | 3,129 | Early fetal loss in a previous pregnancy (study included for KQ3 only) | NR  Anytime throughout pregnancy | No |
| McParland, 199065  Fair | RCT | UK | 106 | Persistent abnormal Doppler flow-velocity waveforms at 24 weeks’ gestation (measured twice) | 75 mg daily  24 weeks; delivery | Yes |
| MFMU, 199857  Good | RCT | US | 2,539 | Medical history that places women in 1 of 4 high- risk groups: women with DM, women with chronic HTN, women with multifetal gestations, women with previous PE. Women with DM could also have HTN (but analyzed with DM group), but women with multifetal gestations were excluded  if they also had DM or HTN. | 60 mg daily  13 to 26 weeks; delivery or if PE develops | Yes |
| Newnham, 199579†  Good | RCT | Australia | 51 | Population not at risk for PE, population at risk for IUGR (study included for KQ3 only) | 100 mg  28 to 36 weeks; delivery | No |
| Rotchell, 199875†  Good | RCT | Barbados | 3,647 | Population not at elevated risk, healthy women without contraindication for aspirin therapy (study included for KQ3 only) | 75 mg daily  12 to 32 weeks; delivery | Yes |
| Schiff, 198966  Good | RCT | Israel | 65 | At least 1 of the following: nulliparity, twin gestation, history of PE, and positive rollover test result | 100 mg daily  28 or 29 weeks; 38 weeks | Yes |
| Sibai, 199372†  Good | RCT | US | 3,135 | Population not at elevated risk, healthy nulliparous women (study included for KQ3 only) | 60 mg daily  13 to 25 weeks; delivery | Yes |
| Subtil, 200374†  Good | RCT | France and Belgium | 3,294 | Population not at elevated risk, healthy nulliparous women (study included for KQ3 only) | 100 mg daily  14 to 20 weeks; 34 weeks | Yes |
| Vainio, 200267  Fair | RCT | Finland | 90 | Bilateral diastolic notch identified by transvaginal Doppler ultrasound and risk of PE or IUGR as determined by medical history | 0.5 mg/kg daily  12 to 14 weeks; not clearly specified | Yes |
| Viinikka, 199368  Fair | RCT | Finland | 208 | Diagnosis of arterial HTN (BP without treatment >140/90 mm Hg before pregnancy), or history of severe PE | 50 mg daily  15 to 16 weeks; delivery | Yes |
| Villa, 201269  Fair | RCT | Finland | 152 | Age, BMI >30 kg/m2, chronic HTN, Sjorgren’s syndrome or lupus, a history of gestational diabetes, PE, small for gestational age, fetus mortus, and 2nd-degree diastolic notch present at 12+0 weeks through 13+6 weeks’ gestation | 100 mg daily  Initiated at 12 to 13 weeks’ gestation; stopping at 35 weeks or delivery | Yes |
| Wallenburg, 198670  Good | RCT | The Netherlands | 46 | Angiotensin-II sensitivity determined by blood test | 60 mg daily  26 weeks; delivery | Yes |
| Yu, 200371  Good | RCT | Brazil, Chile, South Africa, UK | 560 | Women with a mean PI >1.6 and early diastolic notching of uterine arteries identified by transvaginal color Doppler ultrasound | 150 mg daily  22 to 24 weeks; 35 weeks\* | Yes |

\* Estimated.

† Study is included for analysis of KQ3 (harms only) and is not in a high-risk population.

**Abbreviations:** BMI = body mass index; BP = blood pressure; CVD = cardiovascular disease; DM = diabetes mellitus; HTN = hypertension; IUGR = intrauterine growth restriction; NR = not reported; PE = preeclampsia; RCT = randomized; controlled trial.