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Low-Dose Aspirin Use During Pregnancy

ABSTRACT: Low-dose aspirin has been used during pregnancy, most commonly to prevent or delay the onset of preeclampsia. The American College of Obstetricians and Gynecologists issued the *Hypertension in Pregnancy Task Force Report* recommending daily low-dose aspirin beginning in the late first trimester for women with a history of early-onset preeclampsia and preterm delivery at less than 34 0/7 weeks of gestation, or for women with more than one prior pregnancy complicated by preeclampsia. The U.S. Preventive Services Task Force published a similar guideline, although the list of indications for low-dose aspirin use was more expansive. Daily low-dose aspirin use in pregnancy is considered safe and is associated with a low likelihood of serious maternal, or fetal complications, or both, related to use. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine support the U.S. Preventive Services Task Force guideline criteria for prevention of preeclampsia. Low-dose aspirin (81 mg/day) prophylaxis is recommended in women at high risk of preeclampsia and should be initiated between 12 weeks and 28 weeks of gestation (optimally before 16 weeks) and continued daily until delivery. Low-dose aspirin prophylaxis should be considered for women with more than one of several moderate risk factors for preeclampsia. Women at risk of preeclampsia are defined based on the presence of one or more high-risk factors (history of preeclampsia, multifetal gestation, renal disease, autoimmune disease, type 1 or type 2 diabetes, and chronic hypertension) or more than one of several moderate-risk factors (first pregnancy, maternal age of 35 years or older, a body mass index greater than 30, family history of preeclampsia, sociodemographic characteristics, and personal history factors). In the absence of high risk factors for preeclampsia, current evidence does not support the use of prophylactic low-dose aspirin for the prevention of early pregnancy loss, fetal growth restriction, stillbirth, or preterm birth.

Recommendations

The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine make the following recommendations:

- Low-dose aspirin (81 mg/day) prophylaxis is recommended in women at high risk of preeclampsia and should be initiated between 12 weeks and 28 weeks of gestation (optimally before 16 weeks) and continued daily until delivery.
- Low-dose aspirin prophylaxis should be considered for women with more than one of several moderate risk factors for preeclampsia.
- Low-dose aspirin prophylaxis is not recommended solely for the indication of prior unexplained stillbirth, in the absence of risk factors for preeclampsia.
- Low-dose aspirin prophylaxis is not recommended for prevention of fetal growth restriction, in the absence of risk factors for preeclampsia.
- Low-dose aspirin prophylaxis is not recommended for the prevention of spontaneous preterm birth, in the absence of risk factors for preeclampsia.
- Low-dose aspirin prophylaxis is not recommended for the prevention of early pregnancy loss.



Introduction

Aspirin is a cyclooxygenase inhibitor with antiinflammatory and antiplatelet properties. Low-dose aspirin has been used during pregnancy most commonly to prevent or delay the onset of preeclampsia. Other suggested indications for low-dose aspirin have included prevention of stillbirth, fetal growth restriction, preterm birth, and early pregnancy loss. Recent systematic reviews of low-dose aspirin use during pregnancy have improved our understanding of the role of low-dose aspirin in each of these clinical situations. Despite this, the use of low-dose aspirin in clinical obstetrics practice remains varied. The purpose of this document is to summarize the evidence and provide current recommendations regarding the use of low-dose aspirin in pregnancy. It should be noted that although systematic reviews and consensus statements have used different doses of low-dose aspirin, this document will consider only the low-dose aspirin available in the United States (81 mg).

Background

In November 2013, ACOG issued the *Hypertension in Pregnancy Task Force Report* recommending daily low-dose aspirin beginning in the late first trimester for women with a history of early-onset preeclampsia and preterm delivery at less than 34 0/7 weeks of gestation, or for women with more than one prior pregnancy complicated by preeclampsia (1). The following year, the U.S. Preventive Services Task Force (USPSTF) published a similar guideline, although the list of indications for low-dose aspirin use was more expansive (Table 1) (2). The USPSTF guideline also suggested that low-dose aspirin be considered in women with “several” moderate risk factors for preeclampsia (Table 1).

Other health care organizations also have published guidelines for preeclampsia prevention using low-dose aspirin based on risk factors. Published in 2011, the World Health Organization guideline recommended that low-dose aspirin (75 mg/day) be initiated before 20 weeks of gestation for women at high risk of preeclampsia; eg, women with a history of preeclampsia, diabetes, chronic hypertension, renal disease, autoimmune disease, and multiple gestations (3). The National Institute of Health and Care Excellence published a quality statement, *Antenatal Assessment of Pre-eclampsia Risk*, in July 2013 that asked health care providers to prescribe low-dose aspirin (75 mg/day) to pregnant women at increased risk of preeclampsia at the first prenatal visit, to be taken daily from 12 weeks of gestation until birth (4). The degree of risk of preeclampsia was based on the presence of one or more high-risk factors (hypertensive disease in previous pregnancy, chronic kidney disease autoimmune disease, type 1 or type 2 diabetes, and chronic hypertension) or more than one moderate-risk factor (first pregnancy, maternal age of 40 years or older, a body mass index greater than 35, family history of preeclampsia, and multiple pregnancy) (4).

Pathophysiology

Aspirin (acetylsalicylic acid) is a nonsteroidal antiinflammatory drug (NSAID) that works primarily through its inhibition of two cyclooxygenase isoenzymes (COX-1 and COX-2), which are necessary for prostaglandin biosynthesis. The COX-1 isoform is present in the vascular endothelium and regulates the production of prostacyclin and thromboxane A₂, prostaglandins with opposing regulatory effects on vascular homeostasis and platelet function. Prostacyclin is a potent vasodilator and inhibitor of platelet aggregation, whereas thromboxane A₂ (TXA₂) is a potent vasoconstrictor and promotes platelet aggregation. The COX-2 isoform is inducible and expressed almost exclusively following exposure to cytokines or other inflammatory mediators. The effect of aspirin on COX-dependent prostaglandin synthesis is dose dependent. At lower dosages (60–150 mg/day) aspirin irreversibly acetylates COX-1, resulting in decreased platelet synthesis of TXA₂ without affecting vascular wall production of prostacyclin (5, 6). At higher doses, aspirin inhibits both COX-1 and COX-2, effectively blocking all prostaglandin production.

Evidence suggesting that an imbalance in prostacyclin and TXA₂ metabolism was involved in the development of preeclampsia prompted the initial studies of aspirin for preeclampsia prevention because of its preferential inhibition of TXA₂ at lower doses (7, 8). However, it is likely that preeclampsia is a result of poor placentation from a variety of causes, including ischemia, reperfusion, or dysfunctional maternal inflammatory response towards the trophoblast (1, 9). Whether low-dose aspirin improves early placental perfusion is unknown, and likewise, the precise mechanism by which low-dose aspirin prevents preeclampsia in some women is also uncertain (10, 11).

Risks of Aspirin Use in Pregnancy

Maternal Risks

The majority of systematic reviews of randomized controlled trials (RCTs) have found no increase in hemorrhagic complications associated with low-dose aspirin during pregnancy (12–14). A USPSTF report on low-dose aspirin for prevention of preeclampsia identified no increased risk of placental abruption (11 trials [23,332 women]; relative risk [RR], 1.17; CI, 0.93–1.48), postpartum hemorrhage (nine trials [22,760 participants]; RR, 1.02; CI, 0.96–1.09), or mean blood loss (five trials, [2,478 women]; RR not reported) (14). Long-term daily aspirin use in non-pregnant adults (less than 300 mg/day for more than 5 years) has been associated with an increased risk of major gastrointestinal and cerebral bleeding episodes (15). In one RCT of low-dose aspirin during pregnancy for the prevention of preeclampsia, transfusion risk was slightly greater in treated patients, (4.0% versus 3.2%) (16).



Table 1. Clinical Risk Assessment for Preeclampsia*

Risk Level	Risk Factors	Recommendation
High [†]	- History of preeclampsia, especially when accompanied by an adverse outcome - Multifetal gestation - Chronic hypertension - Type 1 or 2 diabetes - Renal disease - Autoimmune disease (systemic lupus erythematosus, antiphospholipid syndrome)	Recommend low-dose aspirin if the patient has one or more of these high-risk factors
Moderate [‡]	- Nulliparity - Obesity (body mass index greater than 30) - Family history of preeclampsia (mother or sister) - Sociodemographic characteristics (African American race, low socioeconomic status) - Age 35 years or older - Personal history factors (eg, low birthweight or small for gestational age, previous adverse pregnancy outcome, more than 10-year pregnancy interval)	Consider low-dose aspirin if the patient has more than one of these moderate-risk factors [§]
Low	Previous uncomplicated full-term delivery	Do not recommend low-dose aspirin

*Includes only risk factors that can be obtained from the patient's medical history. Clinical measures, such as uterine artery Doppler ultrasonography, are not included.

[†]Single risk factors that are consistently associated with the greatest risk of preeclampsia. The preeclampsia incidence rate would be approximately 8% or more in a pregnant woman with one or more of these risk factors.

[‡]A combination of multiple moderate-risk factors may be used by clinicians to identify women at high risk of preeclampsia. These risk factors are independently associated with moderate risk of preeclampsia, some more consistently than others.

[§]Moderate-risk factors vary in their association with increased risk of preeclampsia.

Modified from LeFevre, ML. U.S. Preventive Services Task Force. Low-dose aspirin use for the prevention of morbidity and mortality from preeclampsia: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med* 2014;161:819–26.

Fetal Risks

Several systematic reviews of trials using low-dose aspirin for prevention of preeclampsia have shown no increased risk of congenital anomalies (12–14). Moreover, a recent RCT of 1,228 women, 615 of whom received low-dose aspirin beginning before pregnancy and continuing throughout pregnancy, found no increased risk of adverse fetal or neonatal effects associated with low-dose aspirin exposure (17). The number of congenital malformations also was not found to be increased among a cohort of nearly 15,000 women who reported aspirin use during the first trimester (18). Still, concern has been raised about a possible association between aspirin use during pregnancy and gastroschisis (19–21). A meta-analysis that included five case-control studies suggested that a history of aspirin use was twice as common in women with infants with gastroschisis compared with matched controls without gastroschisis (22). However, these data should be interpreted with extreme caution. In this meta-analysis, the dose of aspirin was not indicated (thus it is not clear whether this applies to the use of low-dose aspirin), the study evaluated women using aspirin in the first trimester only and is subject to recall bias, and there were a number of variables not controlled, including use of other licit and illicit drugs in these trials.

The use of low-dose aspirin (60–150 mg) in the third trimester has not been associated with ductal closure (23, 24). Older animal studies suggested a relationship between in utero exposure to NSAIDs in general and premature closure of the ductus arteriosus resulting in persistent pulmonary hypertension in the neonate (25). However, in contrast to this and other studies that did not differentiate type of dose of NSAID exposure, no increase in perinatal deaths from persistent pulmonary hypertension in the neonate has been reported among more than 30,000 women treated in RCTs involving the study of low-dose aspirin versus placebo for effect on a variety of outcomes (12, 14, 26).

The most recent Cochrane meta-analysis did not find an increased risk of neonatal intracranial hemorrhage (10 trials [26,184 infants]) or other neonatal hemorrhagic complications (eight trials [27,032 infants]) associated with maternal ingestion of low-dose aspirin during the third trimester (12). Analysis of pooled data in the USPSTF systematic review was likewise reassuring, with no increase in intracerebral hemorrhage associated with low-dose aspirin use during pregnancy (10 RCTs [22,158 women]; RR, 0.84; CI, 0.61–1.16) (14).



Contraindications to Aspirin Use During Pregnancy

There are few absolute contraindications to aspirin therapy (27). Patients with a history of aspirin allergy (eg, urticaria) or hypersensitivity to other salicylates are at risk of anaphylaxis and should not receive low-dose aspirin. Because of significant cross-sensitivity between aspirin and other nonsteroidal drugs, low-dose aspirin is also contraindicated in patients with known hypersensitivity to NSAIDs. Exposure to low-dose aspirin in patients with nasal polyps may result in life-threatening bronchoconstriction and should be avoided. The same is true in patients with asthma who have a history of aspirin-induced acute bronchospasm (27). Relative contraindications to low-dose aspirin include a history of gastrointestinal bleeding, active peptic ulcer disease, other sources of gastrointestinal or genitourinary bleeding, and severe hepatic dysfunction. Reye syndrome has been reported rarely (less than 1%) in children younger than 18 years who are given aspirin while recovering from viral illnesses, particularly influenza and chickenpox. The decision to continue low-dose aspirin in the presence of obstetric bleeding or risk factors for obstetric bleeding should be considered on a case-by-case basis.

Timing of Use During Pregnancy

With the exception of studies of low-dose aspirin for prevention of early pregnancy loss, the majority of trials using low-dose aspirin during pregnancy have initiated treatment between 12 weeks and 28 weeks of gestation. Some investigators have reported optimal results only when treatment is started before 16 weeks (28–31). A recent meta-analysis of aggregate data from 45 randomized trials reported only a modest reduction in preeclampsia when low-dose aspirin was started after 16 weeks (RR, 0.81; CI, 0.66–0.99) but significant reductions in severe preeclampsia (RR, 0.47; CI, 0.26–0.83) and fetal growth restriction (RR, 0.56; CI, 0.44–0.70) were demonstrated when low-dose aspirin was started before 16 weeks (31). In another meta-analysis, which included data from the recent Combined Multimarker Screening and Randomized Patient Treatment with Aspirin for Evidence-Based Preeclampsia Prevention trial, the authors reported a reduction in preterm preeclampsia only in the subgroup of patients in which aspirin was initiated before 16 weeks of gestation at a daily dose of 100 mg or more (RR, 0.33; 95% CI, 0.19–0.57) (30). In contrast, another study pooled individual data from 31 high-quality randomized trials and found that the beneficial effects of low-dose aspirin were consistent, whether treatment was started before or after 16 weeks of gestation (32).

There is no apparent benefit to stopping low-dose aspirin before delivery. Study protocols specific to pregnancy have varied, with some discontinuing low-dose aspirin at 36 weeks of gestation and others continuing low-dose aspirin until delivery (14, 33–35).

Discontinuation timing has not been related to excessive maternal or fetal bleeding. Likewise, low-dose aspirin use in the absence of other anticoagulants is not a contraindication to neuraxial blockade (36). Some patients present to care in the first trimester on low-dose aspirin. Whether first-trimester exposure is associated with adverse fetal effects or maternal benefit is not known.

Indications for Low-Dose Aspirin During Pregnancy

Prevention of Preeclampsia

The hypothesis that preeclampsia might be associated with vascular disturbances and coagulation defects resulting from an imbalance in prostacyclin and TXA2 led to the initial studies of aspirin for preeclampsia prevention. The results of several small trials suggested that low-dose aspirin may be beneficial for women at high risk of preeclampsia (8, 37). However, until recently, this finding was not confirmed in larger RCTs (16, 33, 38), including a multicenter trial sponsored by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, which included more than 5,000 women (33). The 2017 Aspirin for Evidence-Based Preeclampsia Prevention trial randomized 1,776 women at high risk of preeclampsia based on a first-trimester screening algorithm to 150-mg aspirin or placebo (39). The authors found a significant decrease in the rate of preterm preeclampsia (4.3% versus 1.6%; odds ratio, 0.38; 95% CI, 0.20–0.74). Although the 150-mg dose was used in this study, there are no available studies comparing 60–80 mg versus 150 mg. Further, the screening algorithm used includes first-trimester serum markers, including placental growth factor and pregnancy-associated plasma protein-A, as well as uterine artery dopplers, which limits the generalizability to a U.S. population. Therefore, a higher dose or doubling of the available 81-mg dose cannot be recommended at this time.

A meta-analysis pooling individual patient data from 31 RCTs showed a modest effect of low-dose aspirin prophylaxis on prevention of preeclampsia in groups of women with various risk profiles (RR, 0.90; 95% CI, 0.84–0.97) (13). A subsequent Cochrane review, which pooled aggregate data from 59 trials, reported a 17% relative reduction in preeclampsia with low-dose aspirin use (12). However, this large risk reduction may reflect publication bias (a small, early positive trial is more likely to be published) or chance findings because the largest trials in the analysis showed no significant protective effect.

The 2014 USPSTF guideline on low-dose aspirin for prevention of morbidity and mortality from preeclampsia is based on the findings of their systematic review, which pooled data from 15 high-quality RCTs, 13 of which reported preeclampsia incidence among women considered at highest risk of disease (Table 1) (2). A 24% reduction in preeclampsia (RR, 0.76; CI, 0.62–0.95) with low-dose



aspirin prophylaxis (60–150 mg/day) was demonstrated (14). However, the authors suggested this dramatic reduction in relative risk might be closer to 10% because of “small study effects” of most of the included trials. Depending on baseline preeclampsia risk, the relative risk reduction with low-dose aspirin was associated with a small decrease in an absolute risk reduction of 2–5%.

Based on the findings from the USPSTF and others, low-dose aspirin prophylaxis (81 mg/day) after 12 weeks of gestation modestly reduces the risk of preeclampsia in women at increased risk, without resulting in adverse fetal effects, increased maternal bleeding, or placental abruption. The recommendation to give low-dose aspirin prophylaxis to high-risk women is based on the number needed to treat in individual risk groups, which in turn is based on disease prevalence and treatment effect. In low-risk groups (disease prevalence of 2%), the number needed to treat is approximately 500, compared with a number needed to treat of 50 women in a high-risk group with a disease prevalence of 20%. The USPSTF guideline recommends giving low-dose aspirin after 12 weeks of gestation to women with an absolute risk of preeclampsia of at least 8%, the lowest incidence of preeclampsia in control groups of studies included in their review (2). Based on historic and demographic risk factors, the USPSTF guideline recommends that women with any of the high-risk factors for preeclampsia should receive low-dose aspirin prophylaxis. Low-dose aspirin prophylaxis should be considered in women with more than one of several moderate risk factors for preeclampsia (Table 1).

The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine support the USPSTF guideline criteria for prevention of preeclampsia. Low-dose aspirin (81 mg/day) prophylaxis is recommended in women at high risk of preeclampsia and should be initiated between 12 weeks and 28 weeks of gestation (optimally before 16 weeks) and continued daily until delivery. Women who were receiving medically-indicated low-dose aspirin for other established medical indications before 12–28 weeks may continue with low-dose aspirin treatment.

Insufficient Evidence for Low-Dose Aspirin

Stillbirth

Low-dose aspirin prophylaxis is not recommended for women with a history of stillbirth in the absence of risk factors for preeclampsia. Stillbirth and preeclampsia share many of the same risk factors, and when stillbirth is related to placental dysfunction, the underlying mechanisms are also likely similar. Few studies have focused solely on the effect of low-dose aspirin prophylaxis on stillbirth. In one early nonrandomized trial, investigators reported a nearly twofold increase in live births when low-dose aspirin was given to women with at least one prior pregnancy loss at more than 13 weeks of gestation and a negative result on antiphospholipid

antibody testing (40). Findings were similar in a retrospective cohort study of 230 women with prior fetal loss at more than 10 weeks of gestation (41). However, the results of prospectively collected stillbirth data from RCTs and meta-analyses designed to study the use of low-dose aspirin for preeclampsia prevention are inconclusive (12–14). Until additional supportive evidence becomes available, low-dose aspirin prophylaxis is not recommended solely for the indication of prior unexplained stillbirth in the absence of risk factors for preeclampsia.

Fetal Growth Restriction

Low-dose aspirin prophylaxis for prevention of recurrent fetal growth restriction is similarly not currently recommended in women without other risk factors for preeclampsia because of insufficient evidence in women with an isolated history of fetal growth restriction. However, in women at risk of preeclampsia, prophylaxis with low-dose aspirin (particularly when initiated less than 16 weeks of gestation) may reduce the risk of fetal growth restriction. Abnormal placentation resulting in poor placental perfusion (ie, placental insufficiency) is the most common pathology associated with fetal growth restriction (42). Some investigators have suggested that low-dose aspirin, initiated early in the first trimester, may prevent fetal growth restriction through its inhibitory action on platelet aggregation and improvement in placental development (43, 44). One study first reported that low-dose aspirin, in combination with dipyridamole, significantly reduced the incidence of recurrent fetal growth restriction (45). Although this outcome was confirmed in a subsequent meta-analysis, the study did not identify which women were most likely to benefit from low-dose aspirin (46). There are currently no well-powered RCTs evaluating the role of low-dose aspirin in the prevention of recurrent fetal growth restriction in otherwise low-risk women. Systematic reviews of low-dose aspirin when used in the setting of preeclampsia prevention have consistently reported a 10–20% reduction in fetal growth restriction or infants who were small for gestational age (12–14, 29–32). Evidence as to whether starting low-dose aspirin before 16 weeks of gestation influences the degree to which low-dose aspirin is beneficial in reducing fetal growth restriction is inconclusive, though some meta-analyses have suggested improved benefit with earlier initiation (29–32). Currently, because the majority of evidence supporting a reduction of fetal growth restriction from low-dose aspirin prophylaxis comes from studies of women who were also at risk of preeclampsia—not with histories of fetal growth restriction alone—there is insufficient evidence to support the use of low-dose aspirin for fetal growth restriction prophylaxis in the absence of other risk factors for preeclampsia.



Preterm Birth

The effect of low-dose aspirin on preterm birth as a primary outcome remains understudied. However, until evidence from high-quality studies directed towards prevention of spontaneous preterm birth become available, low-dose aspirin prophylaxis for prevention of spontaneous preterm birth, in the absence of risk factors for preeclampsia, is not recommended.

Aspirin has been shown to decrease uterine contractility by inhibiting COX-dependent prostaglandin synthesis (47). High doses of aspirin have been studied to treat preterm labor, but the irreversible binding to COX-2 and adverse maternal and fetal effects of high-dose aspirin prohibit its use in the clinical setting. Low-dose aspirin has been reported to reduce preterm birth (at less than 37 weeks of gestation) in 8–14% of women at risk of preeclampsia (12–14, 32). However, whether this reflects a reduction in medically indicated or spontaneous preterm births is not clear in most studies. A recent systematic review and meta-analysis (48) analyzed individual patient data from 17 trials of preeclampsia prevention (28,797 participants) that supplied sufficient detail regarding whether delivery was spontaneous or medically indicated. In that study, treatment with low-dose aspirin resulted in a 7% reduction in the risk of spontaneous preterm birth at fewer than 37 weeks (RR, 0.93; 95% CI, 0.86–0.996) and a 14% reduction in spontaneous preterm birth at fewer than 34 weeks (RR, 0.86; 95% CI, 0.76–0.99) compared with controls. Spontaneous preterm birth at fewer than 28 weeks was reduced by 19%, but the difference was not statistically significant (RR, 0.81; 95% CI, 0.59–1.1) (48). Another study using data from a randomized controlled trial of low-dose aspirin versus placebo given to women with a history of pregnancy loss reported that low-dose aspirin, started before pregnancy and continued through pregnancy, was not associated with a reduction in overall preterm births (RR, 0.72; 95% CI, 0.42–1.23), spontaneous preterm birth (RR, 0.51; 95% CI, 0.19–1.34), or medically indicated preterm birth (RR, 0.89; 95% CI, 0.44–1.80) (49).

Indications for Which There Is No Benefit for Low-Dose Aspirin

Early Pregnancy Loss

The combination of low-dose aspirin and unfractionated or low-molecular-weight heparin has been shown to reduce the risk of early pregnancy loss in women with antiphospholipid syndrome (50). However, low-dose aspirin has not been shown to prevent unexplained early pregnancy loss in women who do not have antiphospholipid syndrome. Pooling data from two trials (256 participants), one study reported no increase in live births among women treated with low-dose aspirin compared with placebo (RR: 0.94, CI, 0.80–1.11) (51). A 2014 study also reported no difference in live births when 1,078 women with one or two prior pregnancy losses were

given low-dose aspirin or placebo before pregnancy (58% versus 53%, $P=.0984$). Pregnancy loss occurred in 13% of 535 women given low-dose aspirin compared with 12% of 543 women in the placebo group ($P=.7812$) (35). Based on the available evidence, the use of low-dose aspirin prophylaxis is not recommended for the prevention of early pregnancy loss.

Conclusions

Daily low-dose aspirin use in pregnancy is considered safe and is associated with a low likelihood of serious maternal, or fetal complications, or both, related to use. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine support the USPSTF guideline criteria for prevention of preeclampsia. Low-dose aspirin (81 mg/d) prophylaxis is recommended in women at high risk of preeclampsia and should be initiated between 12 weeks and 28 weeks of gestation (optimally before 16 weeks) and continued daily until delivery. Low-dose aspirin prophylaxis should be considered for women with more than one of several moderate risk factors for preeclampsia. Women at risk of preeclampsia are defined based on the presence of one or more high-risk factors (history of preeclampsia, multifetal gestation, renal disease, autoimmune disease, type 1 or type 2 diabetes, and chronic hypertension) or more than one moderate-risk factor (first pregnancy, maternal age of 35 years or older, a body mass index greater than 30, family history of preeclampsia, sociodemographic characteristics, and personal history factors) (Table 1). In the absence of high-risk factors for preeclampsia, current evidence does not support the use of prophylactic low-dose aspirin for the prevention of early pregnancy loss, fetal growth restriction, stillbirth, or preterm birth.

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