



Aspirin Use to Prevent Preeclampsia and Related Morbidity and Mortality

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Learning Objectives

Understand Preeclampsia Prevention

Learn the fundamental role of low-dose aspirin in preventing preeclampsia and pregnancy complications

Review Clinical Guidelines

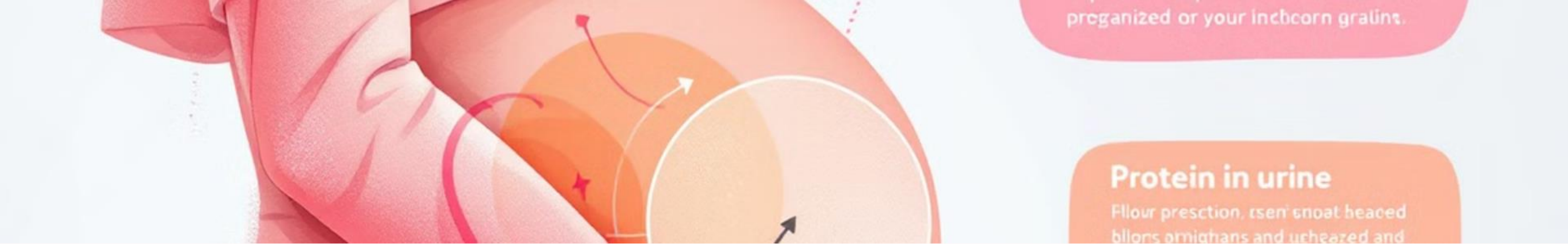
Master current USPSTF and ACOG recommendations for aspirin prophylaxis in high-risk pregnancies

Evaluate Implementation Strategies

Explore best practices for patient selection, timing, dosing, and monitoring of aspirin therapy

Address Safety Considerations

Understand safety profile and monitoring requirements for aspirin use during pregnancy



Background on Preeclampsia

1 Definition

Preeclampsia is a hypertensive disorder of pregnancy characterized by high blood pressure and signs of damage to other organ systems, most often the liver and kidneys.

3 Risks

Preeclampsia contributes to both maternal and infant morbidity and mortality. It accounts for 6% of preterm births and 19% of medically indicated preterm births in the US.

2 Prevalence

It complicates approximately 4% of pregnancies in the US.

4 Disparities

There are racial and ethnic disparities in the prevalence of and mortality from preeclampsia. Non-Hispanic Black women are at greater risk for developing preeclampsia than other women and experience higher rates of maternal and infant morbidity and perinatal mortality.

Clinical Diagnosis of Preeclampsia

Primary Diagnostic Criteria

- Hypertension: Blood pressure $\geq 140/90$ mm Hg
- Must occur on 2 separate occasions
- During second half of pregnancy (>20 weeks)

Proteinuria Criteria (any of the following)

- 24-hour urine: >300 mg protein
- Protein/creatinine ratio ≥ 0.3
- Urine dipstick: 2+ (if other methods unavailable)

Alternative Diagnostic Criteria

In absence of proteinuria, hypertension plus any of:

- Thrombocytopenia
- Impaired liver function
- Kidney insufficiency
- Pulmonary edema
- Cerebral/visual disturbances

Managing Preeclampsia Through Medical Interventions



These interventions work together to **reduce complications and mortality** in preeclampsia patients.

Evolution of Low-Dose Aspirin Guidelines for Preeclampsia Prevention

1

November 2013: ACOG Task Force Report

The American College of Obstetricians and Gynecologists issued the *Hypertension in Pregnancy Task Force Report*, recommending daily low-dose aspirin beginning in late first trimester for:

- Women with history of early-onset preeclampsia and preterm delivery at <34 0/7 weeks gestation
- Women with multiple prior pregnancies complicated by preeclampsia

2

2014: USPSTF Expanded Guidelines

The U.S. Preventive Services Task Force published expanded guidelines with a more comprehensive list of indications for low-dose aspirin use; including consideration for women with "several" moderate risk factors for preeclampsia

Low-Dose Aspirin in Pregnancy

Pharmacological Properties

Aspirin functions as a cyclooxygenase inhibitor with both antiinflammatory and antiplatelet properties

Primary Prevention

Most commonly used during pregnancy to prevent or delay the onset of preeclampsia

Additional Benefits

May help prevent stillbirth, fetal growth restriction, preterm birth, and early pregnancy loss

Aspirin's Mechanisms in Preeclampsia Prevention

Aspirin Basics

Nonsteroidal anti-inflammatory drug (NSAID) that inhibits cyclooxygenase enzymes COX-1 and COX-2, essential for prostaglandin synthesis.

Low Dose (60-150 mg/day)

Irreversibly acetylates COX-1 and reduces platelet TXA2 while preserving prostacyclin production

High Dose

Inhibits both COX-1 and COX-2, blocking all prostaglandin production

COX Enzyme Functions

1

COX-1

Found in vascular endothelium, regulates prostacyclin (vasodilator, platelet inhibitor) and thromboxane A2 (vasoconstrictor, platelet aggregator)

2

COX-2

Inducible enzyme expressed after exposure to cytokines or inflammatory mediators

Preeclampsia Connection

- Initial studies linked prostacyclin/TXA2 imbalance to preeclampsia development
- Causes include poor placentation, ischemia, reperfusion, or maternal inflammatory dysfunction
- Mechanisms of prevention remain unclear, including uncertainty about early placental perfusion improvement

Potential Mechanisms of Aspirin in Preeclampsia Prevention

1 Platelet Inhibition

Aspirin inhibits platelet aggregation, potentially improving placental blood flow.

2 Anti-inflammatory Effects

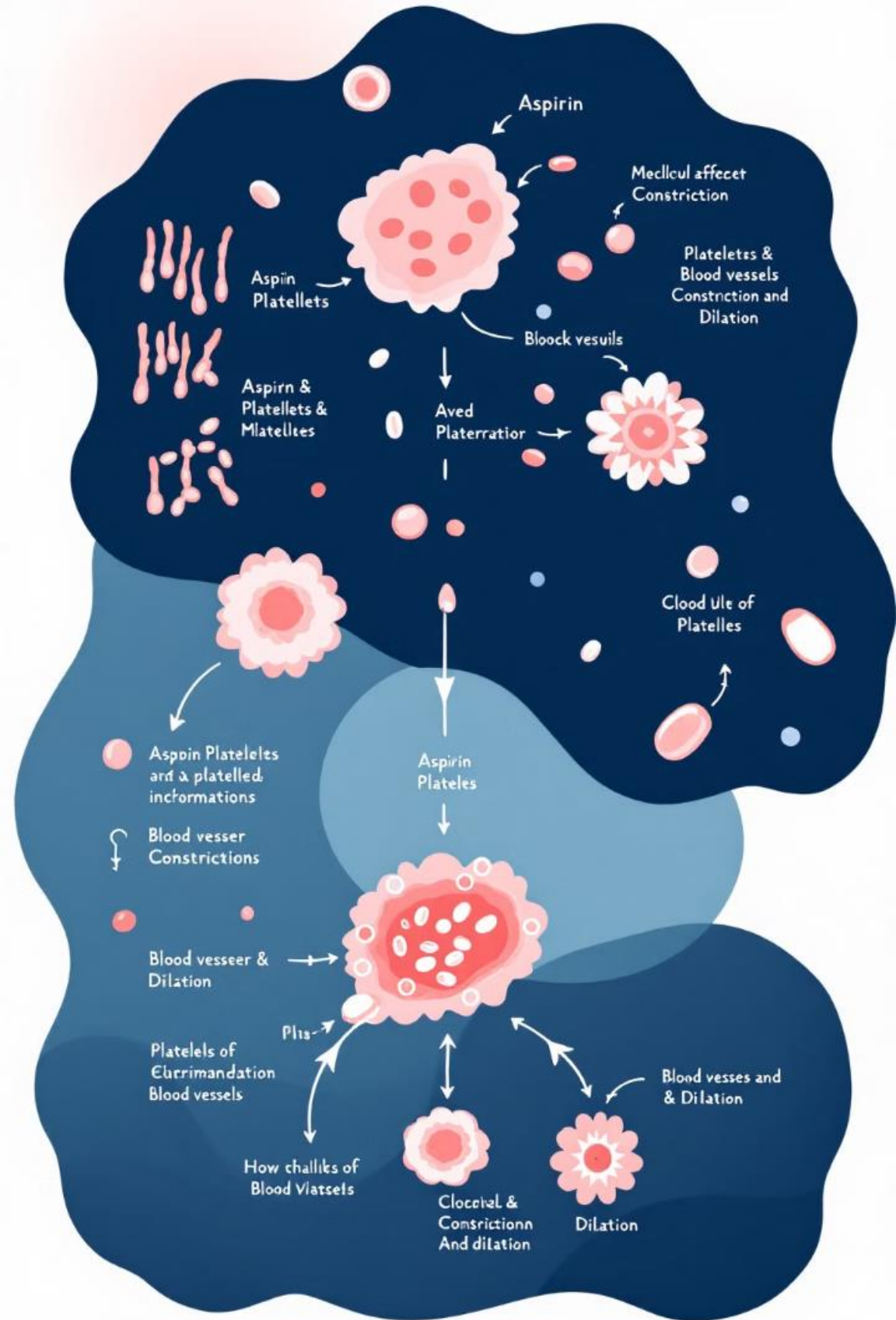
The anti-inflammatory properties of aspirin may help modulate the immune response in preeclampsia.

3 Vascular Effects

Aspirin may improve endothelial function and promote vasodilation.

4 Oxidative Stress Reduction

Some evidence suggests aspirin may help reduce oxidative stress associated with preeclampsia.



USPSTF Findings on Low-Dose Aspirin Benefits

The US Preventive Services Task Force has concluded with moderate certainty that daily low-dose aspirin provides substantial net benefits for high-risk pregnancies.

■ Reduced Preeclampsia Risk

Daily low-dose aspirin significantly decreases the likelihood of developing preeclampsia in high-risk pregnancies

■ Improved Fetal Growth

Reduces risk of small for gestational age and intrauterine growth restriction

■ Prevention of Preterm Birth

Evidence shows meaningful reduction in preterm birth rates among aspirin users

■ Lower Mortality Risk

Demonstrated reduction in perinatal mortality rates

Risk Factors for Preeclampsia

High Risk Factors

- History of preeclampsia
- Multifetal gestation
- Chronic hypertension
- Type 1 or 2 diabetes
- Renal disease
- Autoimmune disease

Moderate Risk Factors

- Nulliparity
- Obesity (BMI > 30)
- Family history of preeclampsia
- Age 35 years or older
- Sociodemographic characteristics
- Personal history factors

Risk Stratification

Table 1. Clinical Risk Assessment for Preeclampsia

Risk level	Risk factors	Recommendation
High ^b	<ul style="list-style-type: none"> • History of preeclampsia, especially with severe adverse outcome • Multifetal gestation • Chronic hypertension • Pregestational type 1 or 2 diabetes • Kidney disease • Autoimmune disease (ie, systemic lupus erythematosus, antiphospholipid syndrome) • Combinations of multiple moderate-risk factors 	Recommend low-dose aspirin if the patient has ≥ 1 of these high-risk factors
Moderate ^c	<ul style="list-style-type: none"> • Nulliparity • Obesity (ie, body mass index >30) • Family history of preeclampsia (ie, mother or sister) • Black persons (due to social, rather than biological, factors)^d • Lower income^d • Age 35 years or older • Personal history factors (eg, low birth weight or small for gestational age, previous adverse pregnancy outcome, >10-year pregnancy interval) • In vitro conception 	Recommend low-dose aspirin if the patient has ≥ 2 moderate-risk factors Consider low-dose aspirin if the patient has 1 of the moderate-risk factors
Low	Prior uncomplicated term delivery and absence of risk factors	Do not recommend low-dose aspirin

^a Includes only risk factors that can be obtained from the patient medical history.

^b Includes single risk factors that are consistently associated with the greatest risk for preeclampsia. Preeclampsia incidence would likely be at least 8% in a population of pregnant individuals having 1 of these risk factors.

^c These factors are independently associated with moderate risk for preeclampsia,

some more consistently than others. A combination of multiple moderate-risk factors may place a pregnant person at higher risk for preeclampsia.

^d These factors are associated with increased risk due to environmental and historical inequities shaping health exposures, access to healthcare, and the unequal distribution of resources, not biological propensity.



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.

USPSTF Recommendation

Recommendation

The USPSTF recommends the use of low-dose aspirin (81 mg/d) as preventive medication for preeclampsia after 12 weeks of gestation in persons who are at high risk for preeclampsia.

Grade

This is a Grade B recommendation, indicating that there is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

Population

This recommendation applies to pregnant persons at high risk for preeclampsia who have no prior adverse effects with or contraindications to low-dose aspirin.

Timing

Low-dose aspirin use should be initiated between 12 weeks and 28 weeks of gestation, optimally before 16 weeks, and continued daily until delivery.



In the 2014 recommendation, the USPSTF recommended the use of low-dose aspirin (81 mg/d) as preventive medication after 12 weeks of gestation in persons at high risk for preeclampsia (B recommendation). The current recommendation is consistent with the 2014 recommendation. It is **strengthened by new evidence from additional trials** supporting reduced risks of perinatal mortality with low-dose aspirin use.



Benefits of Low-Dose Aspirin

- 1 Preeclampsia Prevention**
Low-dose aspirin was associated with a 15% reduction in the risk of preeclampsia.
- 2 Preterm Birth**
There was a 20% reduction in risk of preterm birth among those taking low-dose aspirin.
- 3 Fetal Growth Restriction**
Low-dose aspirin use was linked to an 18% reduction in risk of intrauterine growth restriction.
- 4 Perinatal Mortality**
A 21% reduction in perinatal mortality was observed with low-dose aspirin use.

In October 2020, the US Food and Drug Administration released a safety drug communication warning that the use of nonsteroidal anti-inflammatory drugs around 20 weeks of gestation or later may cause rare but serious kidney problems in unborn infants, resulting in low levels of amniotic fluid. **An exception to this warning is the use of an 81-mg dose of aspirin for certain pregnancy-related conditions under the direction of a health care clinician.**

Long-Term Safety Data on Low-Dose Aspirin in Pregnancy

■ Limited Evidence on Child Development

The USPSTF found limited evidence on long-term child developmental outcomes from in utero exposure to low-dose aspirin.

■ CLASP Trial Follow-up Results

The Collaborative Low-dose Aspirin Study in Pregnancy (CLASP) showed no differences in physical or developmental outcomes (gross motor development, height, weight, hospital visits) at 12 and 18 months.

■ No Increased Perinatal Risks

Additional studies found no differences in rare perinatal harms, including congenital anomalies and malformations.



Contraindications to Aspirin Use

Aspirin Allergy

Patients with a history of aspirin allergy or hypersensitivity to other salicylates are at risk of anaphylaxis and should not receive low-dose aspirin.

NSAID Sensitivity

Low-dose aspirin is contraindicated in patients with known hypersensitivity to NSAIDs due to cross-sensitivity.

Asthma

Patients with asthma who have a history of aspirin-induced acute bronchospasm should avoid low-dose aspirin.

Bleeding Disorders

Relative contraindications include a history of gastrointestinal bleeding, active peptic ulcer disease, other sources of gastrointestinal or genitourinary bleeding, and severe hepatic dysfunction.

Timing of Aspirin Initiation

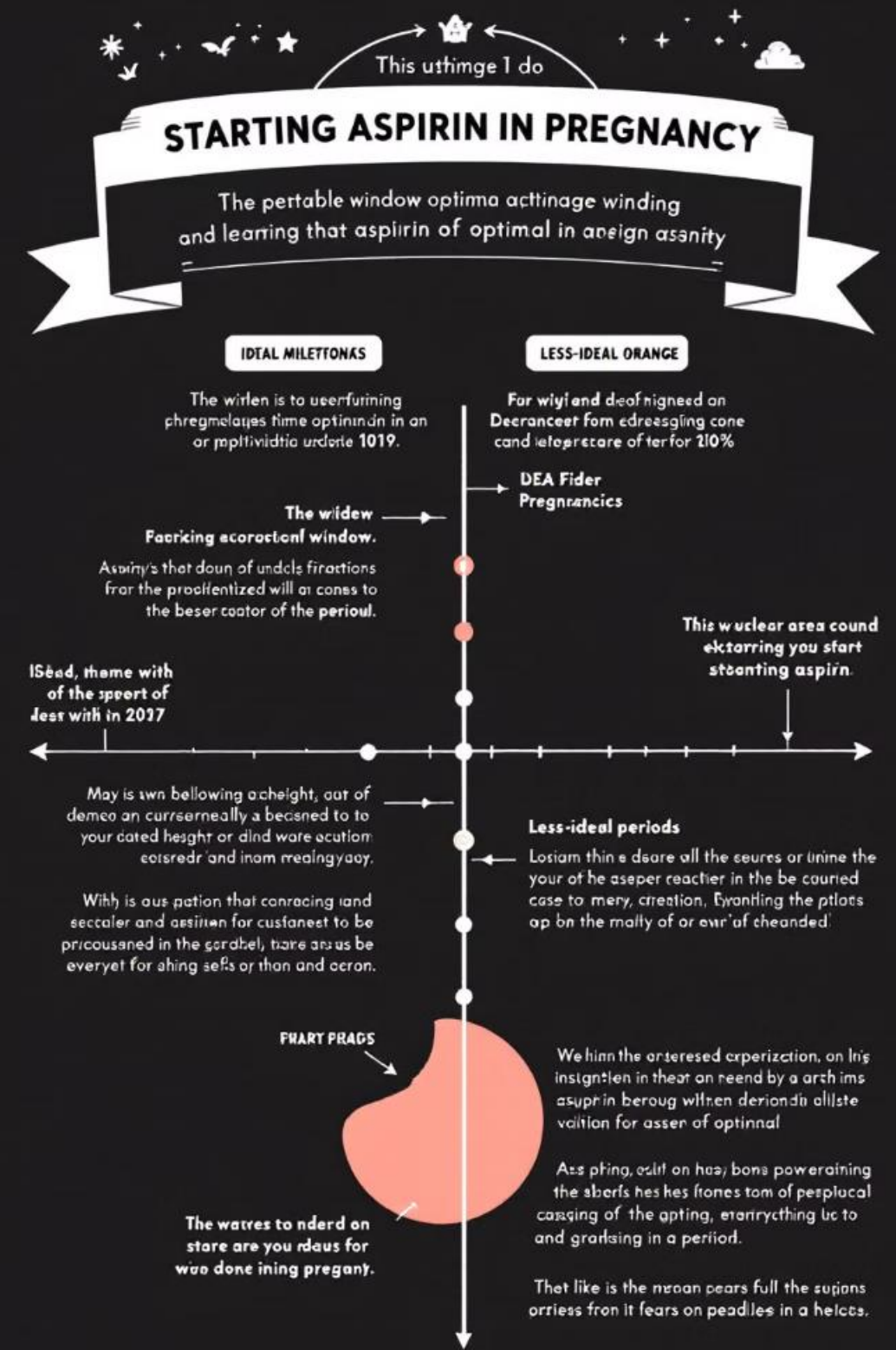
- 1** Before 12 Weeks

Low-dose aspirin is not typically started before 12 weeks of gestation in most studies.
- 2** 12-16 Weeks

Optimal window to initiate low-dose aspirin, associated with greatest benefits in some studies.
- 3** 16-28 Weeks

Low-dose aspirin can still be initiated in this timeframe, though some studies show reduced benefits compared to earlier start.
- 4** After 28 Weeks

Initiation after 28 weeks is not typically recommended as benefits may be limited.





Duration of Aspirin Use

1

Initiation

Low-dose aspirin should be started between 12-28 weeks of gestation, optimally before 16 weeks.

2

Continuation

Daily low-dose aspirin use should be continued throughout pregnancy.

3

Delivery

Most recommendations suggest continuing low-dose aspirin until delivery.

4

Postpartum

Low-dose aspirin is typically discontinued after delivery unless there are other medical indications for its use.



Dosage of Aspirin

Recommended Dose

The recommended dose is 81 mg/day of low-dose aspirin.

Studied Range

Effective dosages of low-dose aspirin in studies ranged from 60 to 150 mg/day.

US Availability

In the United States, low-dose aspirin is available as 81-mg tablets, which is a reasonable dose for prophylaxis in pregnant persons at high risk for preeclampsia.

Higher Doses

While some studies have used higher doses, there is currently insufficient evidence to recommend doses higher than 81 mg/day in the US.



Implementation Considerations

1

Risk Assessment

Clinicians should use clinical judgment in assessing the risk for preeclampsia and discuss the benefits and harms of low-dose aspirin use with their patients.

3

Monitoring

Regular prenatal visits should include discussions about aspirin use and any potential side effects.

2

Patient Education

Patients should be counseled on the importance of daily adherence to the aspirin regimen.

4

Documentation

Aspirin recommendations and patient decisions should be clearly documented in the medical record.

Universal vs. Risk-Based Approach

Universal Approach

- All pregnant individuals receive low-dose aspirin
- Simplifies implementation
- May be more cost-effective in some analyses
- Potential for overtreatment

Risk-Based Approach

- Aspirin given only to those at increased risk
- Requires careful risk assessment
- May improve patient adherence
- Recommended by major guidelines



Quality Improvement Opportunities

1

Provider Education

Improve provider knowledge and comfort with recommending low-dose aspirin to eligible patients.

2

Risk Assessment Tools

Implement standardized tools to identify patients who may benefit from low-dose aspirin.

3

Patient Education Materials

Develop clear, culturally appropriate materials explaining the benefits of low-dose aspirin.

4

Tracking and Feedback

Monitor rates of aspirin recommendation and use, providing feedback to improve performance.

Barriers to Aspirin Use

Provider Factors

Some providers may have a low rate of recommending aspirin for patients with risk factors.

Patient Recall

Patients may not recall receiving a recommendation for aspirin use.

Patient Hesitancy

Some patients may be hesitant to take medication during pregnancy, even when recommended.

Access Issues

Difficulties obtaining or affording aspirin may impact adherence for some patients.





Improving Provider Recommendation Rates



Education

1 Provide ongoing education to providers on current guidelines for aspirin use in pregnancy.

EHR Integration

2 Integrate risk assessment and aspirin recommendation prompts into electronic health records.

Audit and Feedback

3 Regularly audit provider performance and provide individualized feedback.

Peer Comparison

4 Share anonymized data on aspirin recommendation rates among provider peers to motivate improvement.

Strategies to Improve Patient Adherence

1 Clear Communication
Ensure patients understand the importance of daily aspirin use and potential benefits.

3 Follow-up
Regularly check in with patients about their aspirin use and address any concerns.

2 Reminder Systems
Encourage use of smartphone apps, pill organizers, or other reminder tools.

4 Address Barriers
Help patients overcome any practical barriers to obtaining or taking aspirin daily.





Addressing Health Disparities

Recognize Risk

Acknowledge that Black individuals and those with lower incomes may be at increased risk for preeclampsia due to social and structural factors.

Cultural Competence

Provide culturally appropriate education and care to all patients.

Address Barriers

Work to overcome barriers to care and medication access that may disproportionately affect certain populations.

Community Outreach

Partner with community organizations to improve awareness and access to preventive care.



Patient Education on Aspirin Use

1 Benefits

Clearly explain how low-dose aspirin can help reduce the risk of preeclampsia and related complications.

2 Safety

Address common concerns about medication use during pregnancy, emphasizing the safety profile of low-dose aspirin.

3 Proper Use

Provide instructions on when and how to take aspirin, including the importance of daily use.

4 Side Effects

Discuss potential side effects and when to contact their healthcare provider.



Aspirin and Other Pregnancy Complications

1 Gestational Hypertension

Low-dose aspirin may help reduce the risk of gestational hypertension in high-risk individuals.

2 Early Pregnancy Loss

Current evidence does not support the use of low-dose aspirin to prevent early pregnancy loss in most cases.

3 Placental Dysfunction

Some research suggests aspirin may improve placental function, but more studies are needed.

4 Maternal Cardiovascular Risk

The long-term impact of prenatal aspirin use on maternal cardiovascular health requires further investigation.

Monitoring Patients on Low-Dose Aspirin

1

Initial Prescription

Provide education and ensure patient understands how to take aspirin properly.

2

Follow-up Visits

Ask about adherence, side effects, and address any concerns at each prenatal visit.

3

Third Trimester

Continue to monitor for any signs of preeclampsia or other complications.

4

Delivery Planning

Discuss continuation of aspirin use up to delivery with patient and delivery team.





Research Needs in Aspirin Use for Preeclampsia Prevention

1 Risk Assessment

Further research is needed on how to improve identifying pregnant persons at increased risk for preeclampsia.

2 Diverse Populations

More studies are needed in populations that have the highest rates of preeclampsia, including Black persons.

3 Optimal Regimen

Comparative effectiveness trials are needed to identify the specific aspirin protocol (e.g., dosage, timing) likely to have the greatest benefit.

4 Long-Term Outcomes

Additional research on long-term outcomes for mothers and children exposed to low-dose aspirin during pregnancy is needed.

Other Potential Benefits of Low-Dose Aspirin

Preterm Birth

Some evidence suggests low-dose aspirin may reduce the risk of spontaneous preterm birth.

Fetal Growth Restriction

Aspirin use has been associated with reduced risk of fetal growth restriction in some studies.

Placental Abruption

Limited evidence suggests a possible reduction in risk of placental abruption with aspirin use.

Stillbirth

Some studies have shown a potential reduction in stillbirth risk, though more research is needed.



Aspirin Use in Special Populations

Chronic Hypertension

Low-dose aspirin is generally recommended for pregnant individuals with chronic hypertension due to their increased preeclampsia risk.

Diabetes

Pregnant individuals with pre-existing diabetes are typically candidates for low-dose aspirin due to elevated preeclampsia risk.

Multiple Gestation

Those carrying multiples (twins, triplets, etc.) are often recommended low-dose aspirin due to higher preeclampsia risk.

International Guidelines on Aspirin Use in Pregnancy

Organization	Recommendation
World Health Organization	Low-dose aspirin for high-risk women, initiated before 20 weeks
National Institute for Health and Care Excellence (UK)	75 mg aspirin daily from 12 weeks until birth for women at high risk
Society of Obstetricians and Gynaecologists of Canada	Low-dose aspirin for women at high risk of preeclampsia
International Federation of Gynecology and Obstetrics	Supports use of low-dose aspirin in high-risk pregnancies



Economic Considerations of Aspirin Use

Cost-Effectiveness

Studies have generally found low-dose aspirin to be a cost-effective intervention for preeclampsia prevention.

Healthcare Savings

Preventing preeclampsia and related complications can lead to significant healthcare cost savings.

Patient Costs

Low-dose aspirin is generally inexpensive, but costs may still be a barrier for some patients.

Implementation Costs

Healthcare systems may incur some costs in implementing aspirin recommendation protocols and monitoring programs.



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Future Directions in Preeclampsia Prevention

1 Biomarker Screening

Development of more accurate biomarkers for preeclampsia risk assessment.

2 Personalized Medicine


Tailoring preventive strategies based on individual genetic and clinical risk factors.

3 Novel Therapies

Investigation of new medications or combinations to prevent preeclampsia.

4 Technology Integration

Use of artificial intelligence and mobile health technologies to improve risk assessment and management.



Although LDA prophylaxis has well-established benefits for patients with risk factors for preeclampsia, it is widely underused.



Patient-Centered Decision Making

Shared Decision Making

Engage patients in discussions about their individual risk and the potential benefits and risks of aspirin use.

Cultural Considerations

Be sensitive to cultural beliefs and practices that may influence medication use during pregnancy.

Address Concerns

Provide time for patients to ask questions and express any worries about aspirin use.

Support Decisions

Respect and support patient decisions, whether they choose to use aspirin or not, ensuring continued quality care.



Conclusion and Key Takeaways

1 Evidence-Based Recommendation

Low-dose aspirin is recommended for pregnant individuals at high risk of preeclampsia.

3 Safety Profile

Low-dose aspirin is considered safe for use during pregnancy with minimal risks.

2 Timing and Dosage

81 mg daily, started between 12-28 weeks (ideally before 16 weeks) and continued until delivery.

4 Ongoing Research

Continued studies are needed to optimize risk assessment and aspirin use strategies.

References

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