JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening and Supplementation for Iron Deficiency and Iron Deficiency Anemia During Pregnancy

US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE Iron deficiency is the leading cause of anemia during pregnancy. According to survey data from 1999 to 2006, overall estimated prevalence of iron deficiency during pregnancy is near 18% and increases across the 3 trimesters of pregnancy (from 6.9% to 14.3% to 28.4%). An estimated 5% of pregnant persons have iron deficiency anemia.

OBJECTIVE The US Preventive Services Task Force (USPSTF) commissioned a systematic review to evaluate the evidence on the benefits and harms of screening and supplementation for iron deficiency with and without anemia on maternal and infant health outcomes in asymptomatic pregnant persons.

POPULATION Asymptomatic pregnant adolescents and adults.

EVIDENCE ASSESSMENT The USPSTF concludes that the current evidence is insufficient, and the balance of benefits and harms of screening for iron deficiency and iron deficiency anemia in asymptomatic pregnant persons on maternal and infant health outcomes cannot be determined. The USPSTF also concludes that the current evidence is insufficient, and the balance of benefits and harms of iron supplementation in asymptomatic pregnant persons on maternal and infant health outcomes cannot be determined.

RECOMMENDATION The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency and iron deficiency anemia in pregnant persons to prevent adverse maternal and infant health outcomes. (I statement) The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of routine supplementation for iron deficiency and iron deficiency anemia in pregnant persons to prevent adverse maternal and infant health outcomes. (I statement)

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Group Information: The US Preventive Services Task Force (USPSTF) members are listed at the end of this article.

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Summary of Recommendations

Population	Recommendation	Grade
Asymptomatic pregnant adolescents and adults	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency and iron deficiency anemia in pregnant persons to prevent adverse maternal and infant health outcomes.	I
Asymptomatic pregnant adolescents and adults	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of routine iron supplementation in pregnant persons to prevent adverse maternal and infant health outcomes.	I

USPSTF indicates US Preventive Services Task Force.

See the Summary of Recommendations figure.

Table 1. Summary of USPSTF Rationale

Rationale	Screening	Supplementation
Detection	The USPSTF found inadequate evidence to assess the effectiveness of risk prediction tools to identify pregnant persons who are at increased risk for iron deficiency or iron deficiency anemia.	
Benefits of early detection and intervention and treatment	• The USPSTF found inadequate evidence on the benefits of screening for iron deficiency and iron deficiency anemia in asymptomatic pregnant persons. • The USPSTF found inadequate evidence on the benefits of treatment for screen-detected iron deficiency and iron deficiency anemia in asymptomatic pregnant persons. • The USPSTF found inadequate evidence on the association between change in iron status because of treatment of screen-detected iron deficiency or iron deficiency anemia and improvement of maternal or infant health outcomes.	• The USPSTF found inadequate evidence on the benefits of routine iron supplementation during pregnancy on maternal or infant health outcomes. • The USPSTF found adequate evidence that routine iron supplementation during pregnancy improves maternal hematologic indices. • The USPSTF found inadequate evidence on the association between change in maternal iron status because of supplementation and improvement in maternal or infant health outcomes.
Harms of early detection and intervention and treatment	• The USPSTF found inadequate evidence on the harms of screening for iron deficiency and iron deficiency anemia in asymptomatic pregnant persons. • The USPSTF found inadequate evidence on the harms of treatment of screen-detected iron deficiency and iron deficiency anemia in pregnant persons.	The USPSTF found adequate evidence to bound the harms of routine iron supplementation during pregnancy as no greater than small, based on studies that reported harms as minimal.
USPSTF assessment	Due to lack of available data, the USPSTF concludes that the current evidence is insufficient, and the balance of benefits and harms of screening for iron deficiency and iron deficiency anemia in asymptomatic pregnant persons on maternal and infant health outcomes cannot be determined.	Due to lack of available data, the USPSTF concludes that the current evidence is insufficient, and the balance of benefits and harms of iron supplementation in asymptomatic pregnant persons on maternal and infant health outcomes cannot be determined.

Abbreviation: USPSTF, US Preventive Services Task Force.

Preamble

The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms to improve the health of people nationwide.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

The USPSTF is committed to mitigating the health inequities that prevent many people from fully benefiting from preventive services. Systemic or structural racism results in policies and practices, including health care delivery, that can lead to inequities in health. The USPSTF recognizes that race, ethnicity, and gender are all social rather than biological constructs. However, they are also often important predictors of health risk. The USPSTF is committed to helping reverse the negative impacts of systemic and structural racism, gender-based discrimination, bias, and other sources of health inequities, and their effects on health, throughout its work.

Importance

The aim of routine screening or iron supplementation for treatment of iron deficiency and iron deficiency anemia during pregnancy is to improve maternal and infant health outcomes. Iron deficiency is the leading cause of anemia during pregnancy.[1] According to National Health and Nutrition Examination Survey (NHANES) data from 1999 to 2006, overall estimated prevalence of iron deficiency during pregnancy is near 18% and increases across the 3 trimesters of pregnancy (from 6.9% to 14.3% to 28.4%).[2] An estimated 5% of pregnant persons have iron deficiency anemia.[1,2] In the US, there are disparities in prevalence of iron deficiency anemia by race, ethnicity, and social factors (eg, socioeconomic status, nutritional status, and food insecurity).[1,2]

USPSTF Assessment of Magnitude of Net Benefit

Due to lack of available data, the USPSTF concludes that the current **evidence is insufficient**, and the balance of benefits and harms of screening for iron deficiency and iron deficiency anemia in asymptomatic pregnant persons on maternal and infant health outcomes cannot be determined (I statement).

Due to lack of available data, the USPSTF concludes that the current **evidence is insufficient**, and the balance of benefits and harms of iron supplementation in asymptomatic pregnant persons on maternal and infant health outcomes cannot be determined (I statement).

See **Table 1** for more information on the USPSTF recommendation rationale and assessment and the eFigure in the Supplement for information on the recommendation grade. See the **Figure** for a summary of the recommendation for clinicians. For more details on the methods the USPSTF uses to determine the net benefit, see the USPSTF Procedure Manual.[3]

Practice Considerations

Patient Population Under Consideration

This recommendation applies to asymptomatic pregnant adolescents and adults. This recommendation does not apply to preg-

Figure. Clinician Summary: Screening and Supplementation for Iron Deficiency and Iron Deficiency Anemia During Pregnancy

What does the USPSTF recommend?	**For asymptomatic pregnant adolescents and adults:** The current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency and iron deficiency anemia in pregnant persons Grade: I statement The current evidence is insufficient to assess the balance of benefits and harms of routine iron supplementation in pregnant persons. Grade: I statement
To whom does this recommendation apply?	• This recommendation applies to asymptomatic pregnant adolescents and adults. • This recommendation does not apply to pregnant persons who are severely malnourished, have symptoms of iron deficiency or iron deficiency anemia, or have specific hematologic conditions (eg, sickle cell disease) or nutritional deficiencies that may increase their need for iron.
What's new?	This recommendation is consistent with the 2015 recommendation statement on screening and supplementation for iron deficiency anemia during pregnancy.
How to implement this recommendation?	• There is insufficient evidence to recommend for or against screening or supplementation during pregnancy for iron deficiency with or without anemia. • More research is needed to determine the benefits of screening or supplementation for iron deficiency with or without anemia during pregnancy to prevent adverse maternal and infant health outcomes. • Screening for iron deficiency and iron deficiency anemia often includes measurement of hematologic indices (eg, hemoglobin, hematocrit, and ferritin values as proxies of iron deficiency anemia), and an abnormal screening test result may be followed by treatment with iron therapy. • Supplementation refers to routine provision of low-dose supplemental iron or intake of iron-fortified foods, without specifically measuring hematologic indices. • Other organizations' guidelines on screening and supplementation vary. However, screening and supplementation for iron deficiency with or without anemia during pregnancy are common. • In the absence of evidence, clinicians should use their clinical judgment regarding whether to screen for iron deficiency and iron deficiency anemia and whether to provide routine iron supplementation during pregnancy.
What additional information should clinicians know about this recommendation?	• Based on recent survey data, Black and Mexican American pregnant persons are disproportionately affected by iron deficiency anemia in pregnancy, with social determinants of health as possible contributors to these disparities. • Iron is necessary for production of hemoglobin, an essential protein in blood required to transport oxygen throughout the body. • Iron deficiency refers to depletion of iron stores and may progress to iron deficiency anemia.
Why is this recommendation and topic important?	• The overall prevalence of iron deficiency and iron deficiency anemia is uncertain; however, prevalence increases over the course of pregnancy. • According to National Health and Nutrition Examination Survey data from 1999 to 2006, overall estimated prevalence of iron deficiency during pregnancy is near 18% and increases across the 3 trimesters of pregnancy (from 6.9% to 14.3% to 28.4%). • An estimated 5% of pregnant persons have iron deficiency anemia.
What are other relevant USPSTF recommendations?	The USPSTF has issued separate recommendations on screening for iron deficiency anemia in children aged 6 to 24 months and folic acid supplementation to prevent neural tube defects in persons who plan to or could become pregnant.
What are additional tools and resources?	• The National Institutes of Health's Office of Dietary Supplements provides a fact sheet on iron for consumers in English (https://ods.od.nih.gov/factsheets/Iron-Consumer) and Spanish (https://ods.od.nih.gov/factsheets/Iron-DatosEnEspanol/) and for clinicians (https://ods.od.nih.gov/factsheets/Iron-HealthProfessional/). • The US Department of Health and Human Services' Office on Women's Health provides a fact sheet about iron deficiency anemia for patients (https://www.womenshealth.gov/a-z-topics/iron-deficiency-anemia).
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org/uspstf/) or the *JAMA* website (https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

nant persons who are severely malnourished, have symptoms of iron deficiency or iron deficiency anemia, or have specific hematologic conditions (eg, sickle cell anemia) or nutritional deficiencies that may increase their need for iron.

Definitions

Iron is necessary for production of hemoglobin, an essential protein in blood required to transport oxygen throughout the body. Iron is also necessary for the production of additional proteins that are vital to various metabolic pathways.[4] Iron deficiency refers to depletion of iron stores and may progress to iron deficiency anemia.[1] Increased demands for iron during pregnancy enhances vulnerability to iron deficiency and iron deficiency anemia.[1] While iron deficiency is a leading cause of anemia, other conditions may also cause anemia. Screening for iron deficiency and iron deficiency anemia often includes measurement of hematologic indices (eg, hemoglobin

level or hematocrit as proxies of iron deficiency anemia), and an abnormal screening test result may be followed by treatment with iron therapy.[1] To establish the presence of iron deficiency or iron deficiency anemia, levels of iron biomarkers (eg, ferritin) may be measured, although there is no consensus on the exact ferritin level that is indicative of iron deficiency.[1] Supplementation refers to routine provision of low-dose supplemental iron or intake of iron-fortified foods without specifically measuring hematologic indices.[1]

Suggestions for Practice Regarding the I Statements

In deciding whether to screen or supplement for iron deficiency with or without anemia during pregnancy, clinicians caring for pregnant persons should consider the following.

Potential Preventable Burden

The overall prevalence of iron deficiency anemia is uncertain due to the absence of universally accepted cutoffs in surveillance systems, older data, and use of hematologic indices as proxies rather than iron biomarkers to assess iron deficiency.[2,5] It is known, however, that the prevalence increases through pregnancy.[1] Based on recent survey data, Black and Mexican American pregnant persons are disproportionately affected by iron deficiency anemia in pregnancy, with social determinants of health as possible contributors to these disparities.[1,2] However, factors such as nutritional status, food insecurity, or access to health care were not reported in the survey data.[1,2]

The USPSTF found limited evidence on current methods, including questionnaires and risk prediction tools, to identify pregnant persons at increased risk for iron deficiency with or without anemia. Commonly cited risk factors include a diet low in iron-rich foods (eg, vegan diet with inadequate sources of iron), gastrointestinal conditions or medications that can decrease iron absorption (eg, antacids), or a short interval between pregnancies.[1] Tobacco use and living at a high altitude may affect hematologic indices and interpretation of test results due to increases in hematocrit and hemoglobin values.[1] The evidence review identified 3 studies reporting strategies to predict iron deficiency or iron deficiency anemia during pregnancy.[1] Generally, in all 3 studies,[6-8] evidence was insufficient to evaluate the accuracy of risk prediction tools.[1]

Potential Harms

Potential screening approaches to identify asymptomatic pregnant persons with iron deficiency or iron deficiency anemia are unlikely to cause serious harms, but evidence is limited. For example, reviewed evidence did not report risk of iron overload.[1] Common adverse effects of iron supplementation or treatment include gastrointestinal tract symptoms such as nausea, constipation, abdominal pain, and vomiting.[1]

Current Practice

The USPSTF found limited evidence on current practices of screening and supplementation to prevent adverse maternal or infant health outcomes from iron deficiency or iron deficiency anemia. Clinical practice guidelines on screening and supplementation vary (see the Recommendations of Others section for additional information).[1,9] However, screening and supplementation are common. For screening, a surveillance report among Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) participants reported that more than one-half of enrolled pregnant persons (53%) underwent hemoglobin testing during their first trimester in 2018.[1,10] There may be other reasons that clinicians measure hematologic indices, such as to prepare for cesarean delivery or anticipated blood loss during delivery. There is evidence for racial and ethnic disparities in screening rates. In a US study[11] (n = 268 594) of Medicaid recipients across 4 states, Asian/Pacific Islander, Black, and Hispanic participants were less likely to receive a complete blood cell count in 3 of 4 states surveyed compared with White participants (raw odds ratios [ORs], 0.51 to 0.92).[1] For supplementation, according to NHANES data from 1996 to 2006, many pregnant persons (77%) reported using a supplement, often containing iron, within the previous 30 days.[1,12] Use of iron supplements may differ by race, geography, and social factors.[1] For example, in a study using NHANES survey data from 1999 to 2010, pregnant persons who were food insecure had lower mean iron intake from supplements compared with pregnant persons who were food secure.[1,13] Pregnant persons may be screened (eg, with measurement of hematologic indices in the first trimester) and supplemented (eg, with prenatal vitamins) concurrently.

Additional Tools and Resources

The Centers for Disease Control and Prevention includes resources on perinatal quality collaboratives (https://www.cdc.gov/maternal-infant-health/pqc/index.html), including state collaborative toolkits, such as the California Maternal Quality Care Collaborative toolkit on improving the health care response to obstetric hemorrhage (https://www.cmqcc.org/resources-tool-kits/toolkits/ob-hemorrhage-toolkit).

The National Institutes of Health's Office of Dietary Supplements provides a fact sheet on iron for consumers in English (https://ods.od.nih.gov/factsheets/Iron-Consumer/) and Spanish (https://ods.od.nih.gov/factsheets/Iron-DatosEnEspanol/) and for clinicians (https://ods.od.nih.gov/factsheets/Iron-HealthProfessional/).

The US Department of Health and Human Services' Office on Women's Health provides a fact sheet about iron deficiency anemia for patients (https://www.womenshealth.gov/a-z-topics/iron-deficiency-anemia).

Other Related USPSTF Recommendations

The USPSTF has issued separate recommendations on screening for iron deficiency anemia in children aged 6 to 24 months[14] and folic acid supplementation to prevent neural tube defects in persons who plan to or could become pregnant.[15]

Update of Previous USPSTF Recommendation

This recommendation is consistent with the 2015 recommendation statement on screening and supplementation for iron deficiency anemia in pregnancy. In 2015, the USPSTF concluded that the current evidence was insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in pregnant women to prevent adverse maternal health and birth outcomes (I statement).[16] The USPSTF also concluded that the current evidence was insufficient to assess the balance of benefits and harms of routine iron supplementation for iron deficiency anemia in pregnant women to prevent adverse maternal health and birth outcomes (I statement).[16]

Supporting Evidence

Scope of Review

The USPSTF commissioned a systematic review[1,17] to update its 2015 recommendation on screening and supplementation for iron deficiency anemia during pregnancy. In this current recommendation, the USPSTF broadened its review to include iron deficiency *without* anemia; it reviewed evidence on the benefits and harms of screening and supplementation for iron deficiency with and without anemia on maternal and infant health outcomes in asymptomatic pregnant persons. To assist with efforts to generalize the evidence to an asymptomatic US pregnant population, the USPSTF considered studies conducted in settings similar to the US (ie, categorized as "high" or "very high" on the United Nations Human Development Index). In addition, to address critical gaps in the evidence identified in 2015,[18] the USPSTF sought evidence on the association between change in maternal iron status and improvement in infant and maternal outcomes in pregnant persons with iron deficiency with or without anemia. Eligible study designs for the review included randomized clinical trials (RCTs), controlled observational studies, and large uncontrolled observational studies on harms.[1,17]

Benefits of Screening (Early Detection) and Treatment

The review found no evidence on the benefits of screening and treatment for screen-detected iron deficiency and iron deficiency anemia during pregnancy on maternal and infant health outcomes.[1,17] A single observational study addressed the association between change in maternal iron status in pregnant persons with iron deficiency with or without anemia and clinical outcomes.[1,17] In the study[19] (n = 20 690) in pregnant persons responding to treatment (defined as persons with a normal hemoglobin value at delivery who reported taking iron supplementation), therapy was associated with reduction in the odds of preeclampsia (adjusted odds ratio [OR], 0.75 [95% CI, 0.61-0.91]) and preterm birth (adjusted OR, 0.59 [95% CI, 0.47-0.72]) compared with persons without anemia.[1,17,19] Nonresponse to therapy or untreated anemia was also associated with increased risk of preterm birth and preeclampsia (adjusted OR, 1.44 [95% CI, 1.16-1.76] and 1.45 [95% CI, 1.26-1.67], respectively) compared with no anemia.[1,17,19] Comparison on these outcomes between pregnant persons taking iron therapy (whether or not successfully treated) with persons not taking iron therapy was not reported, limiting assessment of the association between iron therapy and improvement in health outcomes.[1,17] Additional limitations to generalizing the study's findings included the definition of anemia (based on reported iron intake) and unclear or unreported iron dose, timing, and therapy duration.[1,17]

Benefits of Supplementation

Maternal Health Outcomes

The review identified 16 studies comparing the effects of routine iron supplementation with no supplementation during pregnancy.[1,17] Timing of starting supplementation varied across studies, from the first prenatal visit to 20 weeks' gestation, and continued to delivery.[1,17] Across the 16 studies, evidence on the effects of iron supplementation during pregnancy on maternal or infant health outcomes was limited, inconsistent, or without clear benefit.[1,17] One trial (n = 430) reported no differences in maternal quality of life (across 8 health concepts) with iron supplementation compared with placebo.[1,17,20] Five trials[21-25] (n = 13 610) found no statistically significant differences on rates of hypertensive disorders of pregnancy with iron supplementation compared with placebo or no iron (4.7% vs 3.1% [pooled, weighted rates]; relative risk [RR], 1.24 [95% CI, 0.75-2.06]; I^2 = 48.0%).[1,17] Based on a pooled analysis, 8 trials[20,21,24-29] (n = 4919) found no statistically significant differences in rates of cesarean delivery (42.8% vs 41.5%; RR, 1.01 [95% CI, 0.90-1.14]; I^2 = 42.7%).[1,17] Generally, studies of cesarean delivery did not report procedure indications, which could reflect practice variability, limiting interpretation of this evidence.[1,17] In 4 trials reporting maternal gestational diabetes and maternal hemorrhage, results were imprecise and uncertain.[1,17] Two trials[24,26] (n = 2214) found no differences in rates of maternal gestational diabetes in pregnant persons receiving iron supplementation vs placebo, and 2 trials[21,29] (n = 341) found no statistically significant differences in rates of maternal hemorrhage.[1,17]

Infant Health Outcomes

Across 6 supplementation trials (n = 17 863)[20,21,23,25,27,30] reporting infant health outcomes, evidence was limited or demonstrated no benefit.[1,17] Five trials reported no association between supplementation and infant mortality.[1,17] In post hoc analysis, 1 trial (n = 3929) reported a statistically significant difference in rates of neonatal deaths in the supplementation group compared with the control group (1.1% vs 2.0%; RR, 0.53 [95% CI, 0.29-0.97]).[1,17] Five trials[22,24,26,30,31] (n = 16 827) of maternal iron supplementation reported no statistically significant differences in risk of preterm birth (5.5% vs 6.0%; RR, 0.92 [95% CI, 0.81-1.04]; I^2 = 0.0%).[1,17] Pooled analysis of 6 trials[20-22,27,30,31] (n = 15 591) of maternal iron supplementation reported no statistically significant differences in infants with low birth weight (2.7% vs 2.9%; RR, 0.95 [95% CI, 0.79-1.14]; I^2 = 0.0%).[1,17] Across 4 trials[24-26,30] (n = 5386) reporting infants small for gestational age, evidence was inconsistent and imprecise, with most studies reporting no differences (15.3% vs 15.2%; RR, 0.94 [95% CI, 0.67-1.31]; I^2 = 75.5%).[1,17] A pooled analysis reported few differences between supplementation compared with placebo.[1,17] Low birth weight was defined as less than 2500 g and small for gestational age or intrauterine growth restriction was defined as birth weight less than 10th percentile for gestational age.[1,17]

Maternal Hematologic Outcomes

Although the USPSTF found inconsistent evidence on maternal iron supplementation during pregnancy to improve maternal and infant health outcomes, there was, across 16 trials,[20-42] evidence of an association between supplementation and improved maternal hematologic indices (eg, hemoglobin and ferritin values) and decreased risk of maternal iron deficiency anemia, iron deficiency, and anemia compared with placebo or no therapy.[1,17] Studies included persons at average risk of anemia with baseline hemoglobin levels ranging from 11.9 to 14.3 g/dL. Studies excluded pregnant persons with low hematologic indices at baseline (<8 to 11 g/dL). Seven trials[20,22,27,28,32,38,41] (n = 4045) reported on maternal iron deficiency anemia with supplementation; iron supplementation was associated with decreased risk of maternal iron deficiency anemia during the third trimester (3 trials; n = 330; 9.1% vs 13.8%; RR, 0.63 [95%

CI, 0.41-0.97]; I^2 = 0%; absolute risk difference [ARD], −4% [95% CI, −8% to 0%]) and at term (4 trials; n = 2230; 8.6% vs 19.8%; RR, 0.40 [95% CI, 0.26-0.61]; I^2 = 20.5%; ARD, −10% [95% CI, −16% to −3%]).[1,17] Studies defined iron deficiency anemia as hemoglobin values less than 11.0 g/dL and serum ferritin levels less than 12 or 20 µg/L.[1,17] Nine trials[20,22,28,31-33,36,39,41] (n = 16 556) reported on maternal iron deficiency with supplementation; iron supplementation was associated with decreased risk of maternal iron deficiency during the third trimester (4 trials; n = 1220; 40.3% vs 57.1%; RR, 0.70 [95% CI, 0.53-0.92]; I^2 = 77.4%; ARD, −17% [95% CI, −24% to −10%]) and at term (6 trials; n = 2361; 46% vs 70%; RR, 0.47 [95% CI, 0.33-0.67]; I^2 = 81.9%; ARD, −34% [95% CI, −46% to −22%]).[1,17] Studies defined iron deficiency as serum ferritin values less than 12 or 20 µg/L.[1,17] Nine trials[20,28,30-33,36,39,41] (n = 20 330) reported on maternal anemia; iron supplementation was associated with decreased risk of maternal anemia during the third trimester (7 trials; n = 2148; 18.1% vs 26.0%; RR, 0.71 [95% CI, 0.51-0.97]; I^2 = 64.2%; ARD, −7.97% [95% CI, −15.28% to −0.66%]) and at term (4 trials; n = 2261; 10.9% vs 22.5%; RR, 0.43 [95% CI, 0.26-0.72]; I^2 = 43.7%; ARD, −11.73% [95% CI, −14.87% to −8.60%]).[1,17] Studies defined anemia as hemoglobin values less than 10.0 or 11.0 g/dL in the third trimester and at term and less than 12.0 or 12.1 g/dL postpartum.[1,17] Fifteen trials[21,22,24-30,32,39,41] (n = 20 069) reported maternal hemoglobin values and 13 trials[20-22,24,26-29,31,32,39,41] (n = 19 075) reported maternal ferritin values compared with placebo; most studies found higher hemoglobin and serum ferritin values at term compared with placebo, with inconsistent findings at other time points.[1,17]

Infant Hematologic Outcomes

Evidence of intermediate outcomes in infants was limited to 2 trials[20,31] (n = 12 943) reporting no differences in infant hematologic indices at 6 months or 1 year.[1,17]

Maternal and Infant Hematologic Outcomes

Evidence on the association between maternal supplementation and change in maternal iron status on improvement in infant and maternal outcomes was limited to the same single study (n = 20 690)[19] of pregnant persons discussed in the screening section.

Harms of Screening and Supplementation

No trials reported on harms of screening. Twelve trials[20,24,26-28,30-33,39,41,43] (n = 22 716) reported evidence on the harms of routine supplementation during pregnancy.[1,17] Most trials reported transient gastrointestinal effects such as nausea, constipation, and diarrhea, with 5 trials reporting no difference in transient gastrointestinal effects in comparison groups.[1,20,27,28,30,43] A single trial (n = 12 513) reported that iron supplementation starting in the second trimester was associated with increased risk of gastrointestinal symptoms vs placebo (3.6% vs 2.3%; RR, 1.59 [95% CI, 1.28-1.97]).[1,17,31] Using medication adherence as a proxy for harms, 9 studies reported no statistically significant differences in adherence to supplementation between comparison groups.[1,17] In a separate trial (n = 111), nonadherence to iron therapy was lower in adults taking supplementation compared with those taking placebo (2.2% vs 16.1%; P = .036) and not statistically significant in adolescents (4.5% vs 12.6%; P = .320).[1,17,27] Infant harms were not reported in any studies.[1,17]

Response to Public Comments

A draft version of this recommendation statement was posted for public comment on the USPSTF website from February 27 to March 25, 2024. Some comments agreed with the draft recommendation. In response to comments, the USPSTF added language on iron-rich foods for supplementation, limitations of interpreting prevalence of iron deficiency and iron deficiency anemia, and additional information on screening and supplementation in the Recommendation of Others section. Some comments requested tools to identify potential risk factors for iron deficiency, such as food insecurity and social instability, to assist clinicians in determining which pregnant persons could benefit from screening. Despite careful review, the USPSTF found limited evidence on approaches (such as questionnaires or risk prediction tools) to identify pregnant persons at increased risk for iron deficiency with or without anemia.

Some comments expressed that the current I statements could be misinterpreted as recommendations against screening and supplementation. Others noted that the evidence was limited to RCTs and did not include clinically relevant health outcomes. In response, the USPSTF would like to reiterate that it is not making a recommendation for or against screening or supplementation during pregnancy for iron deficiency without or without anemia. Rather, the I statement is a call for more research on the benefits and harms of screening and supplementation. Further, the USPSTF carefully considers benefits and harms and makes recommendations when supported by sufficient evidence. The USPSTF cast a broad net, as outlined in the final research plan, including evidence from RCTs, controlled cohort studies, and other controlled observational studies. Some key questions also considered large uncontrolled observational studies and association studies. Clinically relevant potential outcomes included, but were not limited to, maternal health-related quality of life, postpartum hemorrhage, blood transfusions, and postpartum depression. The USPSTF continues to call for high-quality research, particularly on the critical gap of the association between changes in maternal iron status and improvement in infant and maternal outcomes in pregnant persons.

Research Needs and Gaps

See **Table 2** for research needs and gaps related to screening and supplementation for iron deficiency and iron deficiency anemia during pregnancy.

Recommendations of Others

For screening, recommendations generally focus on screening for anemia, rather than iron deficiency, and use variable cutoffs to define anemia. The American College of Obstetricians and Gynecologists (ACOG), American Academy of Family Physicians, and Centers for Disease Control and Prevention recommend that all pregnant persons be screened for anemia at their first prenatal visit, preferably during the first trimester of pregnancy.[44-46] ACOG recommends repeat screening at 24 to 28 weeks of gestation.[44]

The Centers for Disease Control and Prevention recommends universal supplementation for all pregnant persons with an oral low-dose iron supplement (30 mg/d).[46] ACOG recommends uni-

Table 2. Research Needs and Gaps for Screening and Supplementation for Iron Deficiency and Iron Deficiency Anemia During Pregnancy

To fulfill its mission to improve health by making evidence-based recommendations for preventive services, the USPSTF routinely highlights the most critical evidence gaps for making actionable preventive services recommendations. For each evidence gap below, research should focus on settings similar to those in the US to assist in generalizability to a US primary care population. This table summarizes the key bodies of evidence needed for the USPSTF to make a recommendation for screening and supplementation for iron deficiency and iron deficiency anemia during pregnancy. For additional information on research needed to address these evidence gaps, see the Research Gaps Taxonomy table on the USPSTF website (https://www.uspreventiveservicestaskforce.org/home/getfilebytoken/aRJ-3-AWuVvmC_kmoGCVHp).
Screening and Supplementation for Iron Deficiency and Iron Deficiency Anemia During Pregnancy
Research is needed in pregnant persons with iron deficiency and iron deficiency anemia to assess whether changes in maternal iron status (eg, because of supplementation or treatment for screen-detected populations) improves maternal and infant health outcomes in settings relevant to US primary care clinical practice.
Research is needed to assess the benefits and harms of screening (eg, with hemoglobin, hematocrit, or ferritin values) for iron deficiency and iron deficiency anemia during pregnancy on maternal (eg, quality of life or need for transfusion) and infant (eg, low birth weight or preterm birth) health outcomes.
Research is needed to assess the benefits and harms of treatment (eg, oral or intravenous iron) in asymptomatic, screen-detected populations with iron deficiency and iron deficiency anemia during pregnancy on maternal and infant health outcomes in settings relevant to US primary care clinical practice.
Research is needed to assess the benefits and harms of routine iron supplementation in asymptomatic pregnant persons without known iron deficiency or iron deficiency anemia on maternal and infant health outcomes.

Abbreviation: USPSTF, US Preventive Services Task Force.

versal supplementation with low-dose iron during pregnancy except in the setting of certain conditions such as hemochromatosis.[44] It recommends evaluation for pregnant women who meet criteria for anemia to determine the cause, followed by treatment with low-dose supplemental iron for those with iron deficiency anemia along with prenatal vitamins.[44] The US Department of Agriculture and US Department of Health and Human Services' "Dietary Guidelines for Americans, 2020-2025" recommends that pregnant women or women planning to become pregnant take a supplement with iron when recommended by a clinician.[47] In addition, women following a vegetarian or vegan dietary pattern should discuss with a clinician whether supplementation of iron, vitamin B_{12}, other nutrients, or some combination thereof is needed.[47]

ARTICLE INFORMATION

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