

Screening for Iron Deficiency Anemia in Young Children: USPSTF Recommendation Statement

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abstract

DESCRIPTION: Update of the US Preventive Services Task Force (USPSTF) 2006 recommendation on screening for iron deficiency anemia.

METHODS: The USPSTF reviewed the evidence on the association between change in iron status as a result of intervention and improvement in child health outcomes, as well as screening for and treatment of iron deficiency anemia with oral iron formulations, in children ages 6 to 24 months.

POPULATION: This recommendation applies to children ages 6 to 24 months living in the United States who are asymptomatic for iron deficiency anemia. It does not apply to children younger than age 6 months or older than 24 months, children who are severely malnourished, children who were born prematurely or with low birth weight, or children who have symptoms of iron deficiency anemia.

RECOMMENDATION: The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in children ages 6 to 24 months. (I statement)

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

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.

SUMMARY OF RECOMMENDATION AND EVIDENCE

The US Preventive Services Task Force (USPSTF) concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in children ages 6 to 24 months. (I statement)

Go to the Clinical Considerations section for suggestions for practice regarding the I statement.

RATIONALE

Importance

The estimated prevalence of iron deficiency anemia in children ages 1 to 5 years in the United States is ~1% to 2%.^{1,2}

Detection

There is convincing (older) evidence that hemoglobin measurement has

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high sensitivity but low specificity for detecting iron deficiency anemia because the majority of cases of childhood anemia are not caused by iron deficiency.

Benefits of Early Detection and Treatment

The USPSTF found inadequate evidence on the effect of routine screening for iron deficiency anemia in asymptomatic children ages 6 to 24 months on growth or child cognitive, psychomotor, or neurodevelopmental outcomes. The USPSTF found no studies that evaluated the direct effect of routine screening programs on child health outcomes. The USPSTF found inadequate evidence (ie, no recent studies that are generalizable to the current US population) on the effects of treatment of iron deficiency anemia in children ages 6 to 24 months on growth or child cognitive or neurodevelopmental outcomes. No studies directly assessed the association between change in iron status as a result of intervention and improvement in child health outcomes. This represents a critical gap in the evidence.

Harms of Early Detection and Treatment

The USPSTF found inadequate evidence on the harms of routine screening for iron deficiency anemia in asymptomatic children ages 6 to 24 months. The USPSTF identified no studies that evaluated the direct harms of routine screening on child health outcomes. The USPSTF found inadequate evidence on the harms of treatment of iron deficiency anemia in children ages 6 to 24 months. The USPSTF found no recent studies that are generalizable to the current US population and reported on the harms of treatment of iron deficiency anemia with iron.

USPSTF Assessment

The USPSTF concludes that the evidence on screening for iron deficiency anemia in asymptomatic

children ages 6 to 24 months to prevent adverse growth, cognitive, or neurodevelopmental outcomes is lacking, and that the balance of benefits and harms cannot be determined.

CLINICAL CONSIDERATIONS

Patient Population Under Consideration

This recommendation applies to children ages 6 to 24 months living in the United States who are asymptomatic for iron deficiency anemia (Fig 1). It does not apply to children younger than age 6 months or older than 24 months, children who are severely malnourished, children who were born prematurely or with low birth weight, or children who have symptoms of iron deficiency anemia. Recommendations regarding screening for iron deficiency anemia in pregnant women and iron supplementation during pregnancy are addressed in a separate recommendation statement (available at www.uspreventiveservicestaskforce.org).

Suggestions for Practice Regarding the I Statement

Potential Preventable Burden

Estimates of the prevalence of iron deficiency in children ages 1 to 3 years in the United States range from 8% to 14%, and approximately one-third of these children also have anemia.³ Based on 1999 to 2002 National Health and Nutrition Examination Survey (NHANES) data, the estimated prevalence of iron deficiency anemia in children ages 12 to 35 months is 2.1%.¹ Several factors have been identified that may increase a child's risk for iron deficiency anemia, including prematurity or low birth weight, use of non-iron-fortified formula or introduction to cow's milk in the first year of life, and exclusive breastfeeding without regular intake of iron-fortified food after age 6 months. Demographic factors

associated with increased risk for iron deficiency anemia include low socioeconomic status and having parents who are migrant workers or recent immigrants. Additional factors that may be associated with increased risk for iron deficiency in children include weight and height in the 95th percentile or greater, bottle feeding beyond the first year of life, having a mother who is currently pregnant, or living in an urban area. Evidence on whether Hispanic ethnicity increases children's risk for iron deficiency has been mixed, with some studies showing an increased risk and others showing no increased risk. Older data from NHANES (1988–1994) showed that Mexican American children were nearly 3 times more likely than white children to have iron deficiency, whereas more recent NHANES data from 1999 to 2002 found no increased risk in Hispanic children.³ The USPSTF found no studies that assessed the performance of risk assessment tools to identify children who are at increased risk for iron deficiency anemia.

Some observational studies suggest that iron deficiency anemia in early childhood may be associated with neurodevelopmental and behavioral delays and poorer performance on cognitive tests. However, concluding that there is a direct causal link between iron deficiency anemia and these outcomes is difficult because of the methodological flaws in these studies and potential confounding due to underlying nutritional and socioeconomic differences between groups.³ The aim of screening for iron deficiency anemia in young children is to identify and treat anemia before it leads to poor child health outcomes.

Potential Harms

The harms of screening for iron deficiency anemia have not been well studied. Potential harms of screening include false-positive results, anxiety, and cost. Reported adverse events of treatment with iron include limited gastrointestinal symptoms, darkening color of stool, staining of teeth and



Screening for Iron Deficiency Anemia in Young Children: Clinical Summary

Population	Asymptomatic U.S. children ages 6 to 24 months
Recommendation	<p>No recommendation.</p> <p>Grade: I statement (insufficient evidence)</p>

Risk Assessment	No studies assessed the performance of risk assessment tools to identify children who are at increased risk for iron deficiency anemia.
Screening Tests	Although the evidence is insufficient to recommend specific tests for screening, measurement of serum hemoglobin or hematocrit is often the first step.
Treatment and Interventions	Iron deficiency anemia in children is usually treated with oral iron; the usual dose in infants and young children is 3 to 6 mg/kg of elemental iron per day in 2 to 3 divided doses.
Balance of Benefits and Harms	The current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in young children.
Other Relevant USPSTF Recommendations	The USPSTF addresses screening for iron deficiency anemia in pregnant women and iron supplementation during pregnancy in a separate recommendation statement (available at www.uspreventiveservicestaskforce.org).

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.uspreventiveservicestaskforce.org.

FIGURE 1
Screening for iron deficiency anemia in children: clinical summary.

gums, and drug interactions with other medications. The previous USPSTF recommendation also noted that accidental iron overdose can occur in children receiving treatment or supplementation with iron.

Current Practice

No recent nationally representative data on the current rate of screening are available.

Screening Tests

Although the evidence is insufficient to recommend specific tests for screening, measurement of serum hemoglobin or hematocrit is often the first step.

Treatment and Interventions

In the United States, iron deficiency anemia in children is usually treated with oral iron. The usual dose in infants and young children is 3 to 6

mg/kg of elemental iron per day in 2 to 3 divided doses.³

Other Approaches to Prevention

According to the Institute of Medicine, the Recommended Dietary Allowance for iron in infants ages 7 to 12 months is 11 mg per day. In children ages 1 to 3 years, the Recommended Dietary Allowance is 7 mg per day. Natural food sources of iron include certain fruits, vegetables, meat, and poultry. The Institute of Medicine also notes that nonheme iron, which is found in vegetarian diets, may be less well absorbed than heme iron, which is found in diets containing meat; therefore, the iron requirement may be almost twice as much in children who eat a purely vegetarian diet.⁴ Fortified breads and grain products (such as cereal) are also good sources of iron for young children eating solid foods.⁵

Iron-fortified formula is another source of iron for infants. Federally regulated iron fortification of food products in the United States began in 1941, and the iron content in enriched grain products has increased over the years.⁶ More than 50% of the iron in the US food supply comes from iron-fortified cereal grain products.⁵

Useful Resources

The USPSTF has published a separate recommendation statement on screening for iron deficiency anemia and iron supplementation in pregnant women (available at www.uspreventiveservicestaskforce.org).

OTHER CONSIDERATIONS

Research Needs and Gaps

Although iron deficiency anemia has been associated with

neurodevelopmental and cognitive impairments and behavioral delays based on observational data, studies that show an improvement in these health outcomes through treatment are lacking. Studies that evaluate the effects (short- and long-term) of change in iron status on health outcomes in settings similar to the United States with respect to nutrition, hemoparasite burden, and socioeconomic status are needed. Similarly, well-designed long-term, controlled studies that evaluate the benefits and harms of screening for and early treatment of asymptomatic iron deficiency anemia on health outcomes (diagnosis of neurodevelopmental, cognitive, or behavioral disease rather than hematologic indexes) are needed.

DISCUSSION

Burden of Disease

Iron is necessary for the production of hemoglobin, an essential protein found in red blood cells. Iron deficiency occurs when body stores of iron become depleted. Iron deficiency can occur when there is an increased need for iron (eg, during rapid growth in infants and toddlers) or when there is decreased iron intake and absorption (eg, lack of iron sources in the diet). Iron deficiency anemia results when iron stores become so low that hemoglobin synthesis is impaired.

Iron deficiency is the most common nutrient deficiency worldwide⁷ and in the United States.^{8,9} It represents ~40% of cases of anemia in the United States.¹ The estimated overall prevalence of iron deficiency anemia in the United States is 1% to 2% in children ages 1 to 5 years³ and 2.1% in children ages 12 to 35 months.¹ Depending on the type of study used to estimate rates, the prevalence of iron deficiency in children ages 1 to 3 years in the United States ranges from 8% to 14%.³

The major concern about iron deficiency anemia in infants and

young children is whether it causes neurodevelopmental or behavioral delays or cognitive impairment. Few well-designed long-term studies on the effects of iron deficiency anemia in infancy and childhood on these health outcomes are available. Based primarily on observational data, studies have found an association between iron deficiency (with or without anemia) in infancy and childhood and impaired neurodevelopment in older children. Cognitive and behavioral delays in children have also been found to be associated with iron deficiency anemia. However, these observational studies have limitations due to the types of measures reported and confounding with nutritional and socioeconomic factors, making causation difficult to determine.³

Scope of Review

The USPSTF commissioned a systematic review of the evidence to update its 2006 recommendation on screening for iron deficiency anemia. The current review assessed the evidence on young children ages 6 to 24 months. The USPSTF focused on reviewing the evidence on the association between change in iron status as a result of intervention and improvement in child health outcomes, as well as treatment of iron deficiency anemia with oral iron formulations. The USPSTF considered studies conducted in settings similar to the United States in rates of malnutrition, hemoparasite burden, and general socioeconomic status. The focus of the current recommendation is on screening and prevention of iron deficiency anemia; however, findings on iron deficiency, as reported by individual studies, also are provided for a better understanding of the potential burden in the US population.

Accuracy of Screening Tests

Serum hemoglobin or hematocrit is the primary screening test for iron deficiency anemia. Hemoglobin is

sensitive for detecting iron deficiency anemia; however, it is not sensitive for detecting iron deficiency because mild deficiency states may not affect hemoglobin levels.³ Hemoglobin is also nonspecific, as ~60% of cases of anemia result from causes other than iron deficiency.¹ The positive predictive value of low hemoglobin for iron deficiency in children age 12 months ranges from 10% to 40%.¹⁰ In infants, particularly before age 12 months, iron deficiency and iron deficiency anemia often resolve spontaneously, reducing the positive predictive value of any screening test. The sensitivity and specificity of other single tests (eg, serum ferritin, transferrin saturation, and erythrocyte protoporphyrin) as primary screening tools for iron deficiency anemia have not been well studied.¹¹ Serum ferritin, often used to measure iron status, acts as an acute-phase reactant, so it should ideally be measured in the absence of infection or inflammation.³

Effectiveness of Early Detection and Treatment

No studies directly evaluated the effectiveness of screening for iron deficiency anemia in asymptomatic children ages 6 to 24 months and reported on health outcomes. In addition, no new studies of oral iron treatment of iron deficiency anemia in this age group were found. The 2006 evidence review reported on older treatment trials that were not included in this update because they were found to be of poor quality or were conducted in settings not applicable to the current US population. In 2006, the USPSTF concluded that there was poor evidence (conflicting studies) of the effectiveness of interventions that demonstrate improved health outcomes, such as developmental status, in asymptomatic children.

No studies applicable to the current US population demonstrated an association between change in iron status as a result of intervention and

improvement in child health outcomes. Indirect evidence from 2 studies of iron supplementation in iron-sufficient children found no difference in growth or developmental scale scores with changes in iron status.³

Potential Harms of Screening and Treatment

The USPSTF found no new studies that reported on the harms of iron treatment in children ages 6 to 24 months. The 2006 review concluded that there was no evidence on the harms of treatment but noted that accidental iron overdose can occur in children receiving treatment or supplementation with iron. One older trial from 1991 that was not included in the previous review found no difference in overall or specific adverse events, including gastrointestinal events.¹²

Estimate of Magnitude of Net Benefit

Overall, the USPSTF found insufficient evidence on screening for iron deficiency anemia in asymptomatic children ages 6 to 24 months. The USPSTF identified no studies that evaluated the benefits or harms of screening in this age group. Studies on the benefits and harms of treatment were generally older, conducted in settings not considered applicable to the current US population, or of poor quality. The USPSTF did not find sufficient evidence to determine the balance of benefits and harms of screening for iron deficiency anemia and thus cannot make a recommendation in favor of or against screening.

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from March 31 to April 27, 2015. A few comments requested more information on which populations are at increased risk for iron deficiency anemia and to which population the recommendation

applies. Existing language describing risk factors for iron deficiency anemia and the target population for this recommendation was inserted earlier in the statement to make this information clearer. Some comments also requested separate analyses of certain high-risk populations. Although the USPSTF sought this information, limitations in the evidence prevented it from performing separate analyses. A few comments noted that there was ambiguity in how the terms “iron deficiency” and “iron deficiency anemia” were used. The recommendation was reviewed to ensure consistent use of each term and language was added to better explain that the focus of the recommendation is on iron deficiency anemia.

How Does Evidence Fit With Biological Understanding?

Although associations have been reported between iron deficiency and iron deficiency anemia and poorer neurodevelopmental measures, such as lower scores on intelligence or cognitive functioning tests, as well as behavioral delays, trials showing that treatment improves these outcomes are lacking. One oft-cited study conducted in Costa Rica reported on long-term developmental outcomes and found that compared with children who had good iron status as infants, children with chronic iron deficiency at ages 12 to 23 months who received treatment and had their anemia resolve within 3 months still scored lower on reading, writing, arithmetic, and motor tests at ages 11 to 14 years, as well as tests of cognitive function at age 19 years.^{13,14} This suggests that preventing iron deficiency anemia may be preferable to treating it once it develops, or that perhaps other nutrients or factors may be mediating the association between iron deficiency anemia and cognitive function and may need to be addressed in addition to iron.

UPDATE OF PREVIOUS USPSTF RECOMMENDATION

This recommendation is consistent with the 2006 recommendation statement on screening for iron deficiency anemia in children ages 6 to 12 months; however, this recommendation has been expanded to include children up to age 24 months. Both the 2006 and the current recommendation statement found insufficient evidence to determine the balance of benefits and harms of screening in young children. Although the 2006 recommendation included a statement on supplementation in young children, the USPSTF has now determined that given the current widespread use of iron-fortified foods in the United States, including infant formulas and cereals, the impact of making a recommendation on physician-prescribed supplementation is likely limited. For this reason, the USPSTF decided to focus the current recommendation on screening only.

RECOMMENDATIONS OF OTHERS

The Centers for Disease Control and Prevention recommends screening for iron deficiency anemia at ages 9 to 12 months, 6 months later, and then annually from ages 2 to 5 years in infants and preschool-age children who are at high risk for iron deficiency anemia.¹⁵ The Institute of Medicine recommends screening at age 9 months in full-term infants who are breastfed or not receiving iron-fortified formula. It recommends screening by age 3 months in preterm infants who are not receiving iron-fortified formula. Only infants who are found to have anemia at one of these earlier screenings should be rescreened routinely at ages 15 to 18 months.¹⁶ The American Academy of Pediatrics recommends universal screening for anemia at age 12 months and selective screening at any age in children who are at increased risk for iron deficiency or iron deficiency anemia.¹⁷ Consistent with

the USPSTF, the American Academy of Family Physicians concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in children ages 6 to 24 months.¹⁸

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ABBREVIATIONS

NHANES: National Health and Nutrition Examination Survey

USPSTF: US Preventive Services Task Force

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