



American Society of Hematology
2021 L Street NW, Suite 900,
Washington, DC 20036
Phone: 202-776-0544 | Fax 202-776-0545
bloodadvances@hematology.org

American Society of Hematology 2026 guidelines for diagnosis of iron deficiency

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Jacquelyn Powers (Baylor College of Medicine, United States) Ming Lim (University of Utah, United States) Maureen Achebe (Brigham and Women's Hospital, United States) Imo Akpan (Columbia University Irving Medical Center, United States) Michael Auerbach (Georgetown School of Medicine, United States) Megan Brown (Penn State Milton S. Hershey Medical Center, United States) Maria Cardenas (Hospital Italiano de Buenos Aires, Argentina) Caroline Cromwell (Weill Cornell Medicine, United States) Thomas DeLoughery (Oregon Health & Science University, United States) Robert Fleming (Saint Louis University, United States) Martina Fraga (University of Michigan Health System, United States) George Goshua (Yale University School of Medicine, United States) Paula James (Queen's University, Canada) Adam Lewkowitz (Women & Infants Hospital of Rhode Island, United States) Jori May (University of Alabama at Birmingham, United States) Grace Nnadozie (MetroHealth Hospitals, United States) Frances Ogunnaya (Rutgers Health Newark Beth Israel Medical Center, United States) Guillermo Ruiz-Arguelles (Clinica Ruiz de Puebla, Mexico) Michelle Sholzberg (St. Michael's Hospital, Li Ka Shing Knowledge Institute, Canada) Layla Van Doren (Yale School of Medicine, United States) Angela Weyand (University of Michigan Medical School, United States) Michelle Zeller (McMaster University, Canada) Muayad Azzam (University of Kansas Medical Center, United States) Ali Choaib (KUMC, United States) Qais Hamarsha (The University of Kansas Medical Center, United States) Hassan Kawtharany (Saint Louis University School of Medicine, United States) Jana Khawandi (The University of Kansas Medical Center, United States) Reem Mustafa (University of Kansas Medical Center, United States)

Abstract:

Background: Iron deficiency is the most common micronutrient deficiency, and when untreated progresses to anemia. Existing guidance on the diagnostic criteria for iron deficiency is limited and not evidence based. **Objective:** These evidence-based guidelines of the American Society of Hematology (ASH) are intended to support patients, clinicians, and other health care professionals in their decisions about the diagnosis of iron deficiency taking a global perspective in all settings. **Methods:** ASH established a multi-disciplinary guideline panel that included one patient representative and was balanced to minimize potential bias from conflicts of interest. The University of Kansas Health System supported the guideline-development process, including performing systematic evidence reviews on the prevalence of iron deficiency across populations and studies to inform diagnostic thresholds up to July 2025. The panel prioritized clinical questions according to clinical impact and high-risk populations. The panel used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, including GRADE Evidence-to-Decision frameworks, to assess evidence and make recommendations, which were subsequently open for public comment. **Results:** The panel agreed on 5 recommendations. **Conclusions:** Key recommendations of these guidelines include serum ferritin thresholds for specific populations with the goal to prioritize the diagnosis of iron deficiency, irrespective of the presence of anemia, remarks for considerations of other diagnostic thresholds, and guidance on the diagnosis of iron deficiency in persons with inflammation. Gaps in the literature and research priorities were also identified.

Conflict of interest: COI declared - see note

COI notes: All authors were members of the guideline panel or members of the systematic review team or both. As such, they completed a disclosure of interest form, which was reviewed by ASH and is available as supplements 2 and 3.

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Agreement to Share Publication-Related Data and Data Sharing Statement:

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Jacquelyn M. Powers¹, Ming Y. Lim², Maureen Okam Achebe³, Imo J. Akpan⁴, Michael Auerbach⁵, Megan C. Brown⁶, Maria Paula Cardenas⁷, Caroline Cromwell⁸, Thomas DeLoughery⁹, Robert E. Fleming¹⁰, Martina Fraga¹¹, George Goshua¹², Paula James¹³, Adam Lewkowitz¹⁴, Jori May¹⁵, Grace Nnadozie¹⁶, Frances Ogunnaya¹⁷, Guillermo J. Ruiz-Arguelles¹⁸, Michelle Sholzberg¹⁹, Layla Van Doren²⁰, Angela C. Weyand²¹, Michelle P. Zeller²², Muayad Azzam²³, Ali Choaib²⁴, Qais Hamarsha²⁵, Hassan Kawatharany²⁶, Jana Khawandi²⁷, Reem A. Mustafa²⁸

Correspondence

Jacquelyn M. Powers
6701 Fannin Street, Suite 1580
Houston, TX 77030
Jacquelyn.Powers@bcm.edu

1. Baylor College of Medicine, Department of Pediatrics, Houston, Texas, 0009-0001-4141-984X
2. University of Utah, Division of Hematology and Hematologic Malignancies, Department of Internal Medicine, Salt Lake City, Utah, 0000-0001-5208-3387
3. Brigham and Women's Hospital, MGB Cancer Institute, Harvard Medical School, Division of Hematology, Boston, Massachusetts, 0000-0002-1514-2357
4. Columbia University Irving Medical Center, Department of Medicine, Division of Hematology-Oncology, New York, New York, 0000-0002-6793-599X
5. Georgetown University School of Medicine, Department of Medicine, Washington, D.C., 0000-0003-0707-8647
6. Emory University, Department of Pediatrics, Atlanta, Georgia, 0000-0001-8117-1239
7. Hospital Italiano de Buenos Aires, Department of Internal Medicine, Hematology, Buenos Aires, Argentina, 0009-0004-7647-5341
8. Weill Cornell Medicine, Department of Medicine, Hematology, New York, New York, 0009-0006-2686-1185
9. Oregon Health and Science University, Department of Hematology & Medical Oncology, Portland, Oregon, 0000-0002-5790-4700
10. Saint Louis University School of Medicine, Department of Pediatrics, St. Louis, Missouri, 0000-0003-0154-4483
11. University of Michigan Medicine, Department of Pharmacy, Ann Arbor, Michigan, 0009-0003-2769-3951

12. Yale University School of Medicine & Yale Cancer Center, Section of Medical Oncology and Hematology; Center for Outcomes Research & Evaluation, Yale-New Haven Hospital, New Haven, Connecticut, 0000-0002-1624-4427
13. Queen's University, Department of Medicine, Kingston, Ontario, 0000-0003-4649-9014
14. Warren Alpert Medical School of Brown University, Department of Obstetrics & Gynecology, Providence, Rhode Island, 0000-0002-8706-1409
15. University of Alabama at Birmingham, Department of Medicine, Birmingham, Alabama, 0000-0001-7744-5700
16. MetroHealth Hospitals, Case Western Reserve University, Department of Medicine/Department of Pediatrics, Cleveland, Ohio, 0000-0002-1673-4151
17. Rutgers Health Newark Beth Israel Medical Center, Department of Internal Medicine, Newark, New Jersey, 0009-0007-2369-1157
18. Clinica Ruiz, Centro de Hematología y Medicina Interna, Puebla, Mexico, 0000-0002-9335-0653
19. Departments of Medicine, and Laboratory Medicine and Pathobiology, St. Michael's Hospital, Li Ka Shing Knowledge Institute, University of Toronto, Toronto, Ontario, 0000-0003-1220-0301
20. Yale School of Medicine, Medicine, Section of Medical Oncology & Hematology, New Haven, Connecticut, 0009-0008-9513-2298
21. University of Michigan Medical School, Department of Pediatrics, Ann Arbor, Michigan, 0000-0003-2595-8541
22. Division of Hematology and Thromboembolism and Michael G. DeGroote Centre for Transfusion Research, Department of Medicine, McMaster University, Hamilton, Ontario, Medical Services, Canadian Blood Services, Ottawa, Ontario, 0000-0002-6489-6980
23. Evidence-based Practice and Impact Center, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, Kansas, 0000-0002-2046-8343
24. Evidence-based Practice and Impact Center, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, Kansas, 0009-0005-3132-394X
25. Evidence-based Practice and Impact Center, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, Kansas, 0000-0001-9711-4650
26. Evidence-based Practice and Impact Center, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, Kansas, 0009-0007-3725-8485
27. Evidence-based Practice and Impact Center, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, Kansas, 0000-0001-7581-4787
28. Evidence-based Practice and Impact Center, Department of Internal Medicine/Division of Nephrology, University of Kansas Medical Center, Kansas City, Kansas, 0000-0002-2091-0875

Abstract

Background: Iron deficiency is the most common micronutrient deficiency, and when untreated progresses to anemia. Existing guidance on the diagnostic criteria for iron deficiency is limited and not evidence based.

Objective: These evidence-based guidelines of the American Society of Hematology (ASH) are intended to support patients, clinicians, and other health care professionals in their decisions about the diagnosis of iron deficiency taking a global perspective in all settings.

Methods: ASH established a multi-disciplinary guideline panel that included one patient representative and was balanced to minimize potential bias from conflicts of interest. The University of Kansas Health System supported the guideline-development process, including performing systematic evidence reviews on the prevalence of iron deficiency across populations and studies to inform diagnostic thresholds up to July 2025. The panel prioritized clinical questions according to clinical impact and high-risk populations. The panel used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, including GRADE Evidence-to-Decision frameworks, to assess evidence and make recommendations, which were subsequently open for public comment.

Results: The panel agreed on 5 recommendations.

Conclusions: Key recommendations of these guidelines include serum ferritin thresholds for specific populations with the goal to prioritize the diagnosis of iron deficiency, irrespective of the presence of anemia, remarks for considerations of other diagnostic thresholds, and guidance on the diagnosis of iron deficiency in persons with inflammation. Gaps in the literature and research priorities were also identified.

Summary of recommendations

These guidelines are based on updated and original systematic reviews of evidence conducted under the direction of the University of Kansas Health System. The panel followed best practices for guideline development.^{1,2} The panel used the GRADE approach to assess the certainty of the evidence and formulate recommendations.³

Iron deficiency is a common micronutrient deficiency and may occur with or without anemia. Individuals with iron deficiency experience symptoms including but not limited to fatigue, pica, irritability, poor concentration, headaches, and restless legs syndrome. Highest risk individuals include young children and individuals who are menstruating or pregnant, with prevalence being highest in women; persons of lower socioeconomic status are disproportionately affected. Individuals with gastrointestinal conditions (e.g. celiac disease, inflammatory bowel disease, and those who have undergone bariatric surgery), dietary restrictions, blood loss or other chronic conditions (e.g. heart failure, rheumatologic disease, chronic kidney disease) are also at risk. Management includes administration of oral or intravenous iron replacement therapy as well as steps to address the underlying etiology, which may include dietary modifications and/or therapy to control or minimize blood loss. Iron deficiency is an under-recognized condition due to lack of screening in high-risk populations as well as variability in laboratory reference ranges, which often include values within the deficient range, leading to underdiagnosis and undertreatment.

Interpretation of strong and conditional recommendations

The strength of a recommendation is expressed as either strong ("the guideline panel recommends..."), or conditional ("the guideline panel suggests...") and should be interpreted as described in Figure 1.

Interpretation of good practice statements

Good practice statements endorse interventions or practices that the guideline panel agreed have unequivocal net benefit yet may not be widely recognized or used.⁴ Good practice statements in these guidelines are not based on a systematic review of available evidence. Nevertheless, they may be interpreted as strong recommendations.

Recommendations

Diagnosis of iron deficiency in children

Recommendation 1. In children aged 9 months to 4 years, the ASH Guideline Panel **suggests** using a serum ferritin threshold of ≤ 20 ng/mL instead of a threshold of ≤ 12 ng/mL for the diagnosis of iron deficiency (conditional recommendation based on low certainty in the evidence about effects $\oplus\oplus\bigcirc\bigcirc$).

Remark:

- This threshold is for *children without* known or suspected inflammation, and a higher serum ferritin threshold may be required for children with inflammation.
- Due to a lack of direct evidence, specific recommendations for children aged >4 years until adolescence (defined as age ≥ 11 years⁵ as per the American Academy of Pediatrics) and non-menstruating adolescents were not developed. For children aged >4 years until adolescence, a serum ferritin threshold of ≤ 20 ng/mL is appropriate for the diagnosis of iron deficiency by indirectly applying evidence for young children. For non-menstruating adolescents, a serum ferritin threshold of ≤ 30 ng/mL is appropriate for the diagnosis of iron deficiency by indirectly applying evidence from menstruating adolescents and adult populations.
- For menstruating adolescents, please see Recommendation 3.

Diagnosis of iron deficiency in adults (excluding menstruating and pregnant individuals)

Recommendation 2. In the adult population (excluding menstruating or pregnant individuals), the ASH Guideline Panel **suggests** using a serum ferritin threshold of ≤ 30 ng/mL instead of ≤ 15 ng/mL for the diagnosis of iron deficiency (conditional recommendation based on low certainty in the evidence about effects $\oplus\oplus\bigcirc\bigcirc$).

Remark:

- For people with signs or symptoms associated with iron deficiency or ongoing iron deficiency risk factors (Table 1), a serum ferritin threshold of ≤ 50 ng/mL is appropriate to diagnose iron deficiency and guide management decisions.
- This threshold is for *adults without* known or suspected inflammation. A separate recommendation was made for adults with inflammation (See Recommendation 5).

Diagnosis of iron deficiency in menstruating individuals

Recommendation 3. In menstruating individuals, the ASH Guideline Panel **suggests** using a serum ferritin threshold of ≤ 30 ng/mL and **suggests against** using a serum ferritin threshold of ≤ 15 ng/mL for the diagnosis of iron deficiency (conditional recommendation based on low certainty in the evidence about effects $\oplus\oplus\bigcirc\bigcirc$).

Remark: For people with heavy menstrual bleeding (HMB) or other forms of abnormal uterine bleeding (AUB) resulting in excessive blood loss, symptoms associated with iron deficiency, additional risk factors for iron deficiency (Table 1), upcoming surgery, or planning pregnancy, a serum ferritin threshold of ≤ 50 ng/mL is appropriate to diagnose iron deficiency and guide management decisions.

Good Practice Statement: A detailed menstrual history is necessary to facilitate the diagnosis of AUB, particularly HMB. It would be essential to address abnormal and/or HMB, if identified.

Diagnosis of iron deficiency in pregnant individuals

Recommendation 4. In pregnant individuals, the ASH Guideline Panel **suggests** using a serum ferritin threshold of ≤ 30 ng/mL (conditional recommendation based on low certainty in the evidence about effects $\oplus\oplus\bigcirc\bigcirc$) and **recommends against** using a serum ferritin threshold of ≤ 15 ng/mL for the diagnosis of iron deficiency (strong recommendation based on low certainty in the evidence about effects $\oplus\oplus\bigcirc\bigcirc$).

Remark: For pregnant individuals with anemia, with or without other iron deficiency risk factors and/or symptoms associated with iron deficiency (Table 2), a serum ferritin

threshold of ≤ 50 ng/mL may be appropriate to diagnose iron deficiency and guide management decisions.

Diagnosis of iron deficiency in adults with inflammation

Recommendation 5. For adults with anemia of inflammation, the ASH Guideline Panel **suggests** performing both serum ferritin and transferrin saturation (TSAT) rather than serum ferritin alone to evaluate for iron deficiency (conditional recommendation based on very low certainty in the evidence about effects $\oplus\bigcirc\bigcirc\bigcirc$)

Remarks:

- Inflammation is on a continuum, and establishing a serum ferritin threshold for the diagnosis of iron deficiency is challenging. However, in adults with anemia of inflammation, the diagnosis of iron deficiency may be considered when (A) TSAT $< 20\%$ or (B) serum ferritin < 100 ng/mL.
- TSAT should be drawn in a fasting state (5-9 hours⁶, including fasting from multivitamin/iron supplements), as the test is susceptible to recent dietary intake.
- Anemia of inflammation may occur in individuals with inflammatory bowel disease, infectious diseases, cancer, chronic kidney disease, heart failure, rheumatologic disorders, and other inflammatory disorders.
- Due to a lack of data on the diagnosis of iron deficiency in children with inflammation, no recommendations were made for this population (see Recommendation 1).

Good practice statement: Anemia of inflammation may be present concurrently with other causes of anemia. Thus, in individuals with inflammation, the serum ferritin and TSAT should be analyzed in context of the full clinical picture including consideration of the history, physical exam, underlying disease process, and other existing management guidelines^{7,8} for chronic diseases. Such guidelines may consider higher serum ferritin and/or TSAT thresholds for the diagnosis of iron deficiency.

These recommendations place the highest value on identifying individuals with iron deficiency to promote access to care and timely interventions. Outcomes affected by the timely diagnosis of iron deficiency (Table 3) were considered important by the panel for clinical decision-making across questions. Recommendations also take into consideration values and preferences of affected populations, cost and cost-effectiveness, resource requirements, impact on health equity, acceptability, and feasibility. Figure 2 illustrates all 5 diagnostic recommendations and associated remarks.

Introduction

Aims of these guidelines and specific objectives

The purpose of these guidelines is to provide evidence-based recommendations on the diagnosis of iron deficiency that will improve the accurate identification of affected individuals while minimizing harms of overdiagnosis. Through improved provider and patient education using the available evidence and evidence-based recommendations, these guidelines aim to provide clinical decision support for shared decision-making that will result in better recognition of iron deficiency, which will lead to identification and management of underlying etiology where applicable, improved counseling of affected individuals, and early initiation of iron therapy to improve iron status.

The target audience includes hematologists, family physicians, pediatricians, obstetricians and gynecologists, internists, other clinicians and healthcare providers including advanced practice providers, decision-makers, and patients. These guidelines may be relevant to policy makers engaged in developing local, national, or international initiatives that seek to enhance guidance on screening at-risk populations for iron deficiency and to implement standardized clinical decision limits in laboratory reporting. This document may also serve as the basis for adaptation by local, regional, or national guideline panels.

Description of the health problem

Iron is a critical micronutrient that serves key functions throughout the body including erythropoiesis, DNA replication, mitochondrial energy production, and neurotransmitter synthesis. Despite its countless physiologic roles, iron deficiency is common and affects individuals across the lifespan in a variety of settings. Iron deficiency is associated with fatigue and poorer health-related quality of life, among other important patient-reported outcomes. When underrecognized and untreated, iron deficiency progresses to iron deficiency anemia, the most common hematologic condition worldwide. Iron deficiency with or without anemia occurs when there is a net negative balance between iron intake and absorption and iron demands and losses. This imbalance may occur in the setting of insufficient dietary iron, increased iron needs (rapid growth or pregnancy), blood loss including menstrual blood loss or losses within the

gastrointestinal tract, and decreased iron absorption (e.g. inflammatory states). The most affected populations include young children and menstruating individuals, largely adolescent girls and adult women, especially during pregnancy. Individuals with underlying gastrointestinal disorders, bleeding disorders, and other chronic comorbid conditions are commonly affected by iron deficiency as well. Due to non-medical drivers of health, individuals of economically disadvantaged backgrounds and/or within certain racial and ethnic minority groups are disproportionately affected. Despite its commonality, there is wide variation in the iron parameters used to diagnose iron deficiency. The lack of standardization as well as laboratory reference ranges that include values within a deficient range lead to underdiagnosis of iron deficiency with subsequent delay in the receipt of readily available and effective iron therapies.

Methods

The guideline panel developed and graded the recommendations and assessed the certainty of the supporting evidence following the GRADE approach.³ The overall guideline development process, including funding of the work, panel formation, management of conflicts of interest, internal and external review, and organizational approval, was guided by the American Society of Hematology (ASH) policies and procedures intended to meet recommendations for trustworthy guidelines by the Institute of Medicine and the Guidelines International Network.^{1,9,10}

Organization, panel composition, planning and coordination

The work of this panel was coordinated by ASH and the University of Kansas Health System (funded by ASH under a paid agreement). Project oversight was provided by the ASH Guideline Oversight Subcommittee, which reports to the ASH Committee on Quality. ASH vetted and appointed individuals to the guideline panel. The University of Kansas Health System vetted and retained researchers to conduct systematic reviews of evidence and coordinate the guideline development process including the use of the GRADE approach. The membership of the panel and the systematic review team is described in Supplement 1.

The panel included adult and pediatric hematologists, one maternal fetal medicine specialist, one neonatologist, and one pharmacist, who all had clinical and research expertise on the guideline topic, as well as one patient representative. Several panel members had additional expertise and skills including implementation science, cost-effectiveness, transfusion medicine, and laboratory medicine. One co-

chair was a content expert; the other co-chair was an expert in guideline development methodology. Excluding the methodology team, all panelists were full and equal voting members for all recommendations.

In addition to synthesizing evidence systematically, the University of Kansas Health System supported the guideline development process, including determining methods, preparing meeting materials, and facilitating panel discussions. The panel's work was performed using web-based tools (www.surveymonkey.com and www.gradeapro.org) and face-to-face and online meetings.

Guideline funding and management of conflicts of interest

Development of these guidelines was wholly funded by ASH, a nonprofit medical specialty society that represents hematologists. Most members of the guideline panel were members of ASH. ASH staff supported panel appointments and coordinated meetings but had no role in choosing the guideline questions or determining the recommendations.

Members of the guideline panel received travel reimbursement for attendance at in-person meetings. Through the University of Kansas Health System, some researchers who contributed to the systematic evidence reviews received salary or grant support. Other researchers participated to fulfill the requirements of an academic degree or program.

Conflicts of interest of all panel members were managed according to ASH policies based on recommendations of the Institute of Medicine (IOM 2011) and the Guidelines International Network.¹⁰ Panel members disclosed all financial and nonfinancial interests relevant to the guideline topic. ASH staff and the ASH Guideline Oversight Subcommittee reviewed the disclosures and composed the guideline panel to include a diversity of expertise and perspectives and avoid a majority of the panel having the same or similar conflicts. Greatest attention was given to direct financial conflicts with for-profit healthcare companies that could be directly affected by the guidelines. A majority of the guideline panel, including the co-chairs, had no such conflicts. None of the University of Kansas Health System researchers who contributed to the systematic evidence reviews or who supported the guideline development process had any such conflicts. Many panelists had relevant nonfinancial interests, such as published opinions on the guideline topic.

Supplement 2 provides the complete disclosure-of-interests forms of all panel members. In part A of the forms, individuals disclosed direct financial interests for 2 years prior to appointment; in part B, indirect

financial interests; and in part C, relevant other interests that are not mainly financial. Part D describes new interests disclosed by individuals after appointment. Part E summarizes ASH decisions about which interests were judged to be conflicts and how they were managed, including through recusal.

Supplement 3 provides the complete disclosure of interest forms of researchers who contributed to these guidelines.

Formulating specific clinical questions and determining outcomes of interest

The panel used the GRADEpro Guideline Development Tool (www.grade-pro.org)¹¹ to brainstorm and then prioritize questions with the final selected questions listed here.

- 1. Should a serum ferritin threshold of ≤ 12 ng/mL or ≤ 20 ng/mL be used to diagnose iron deficiency, with or without anemia, in children aged 9 months to 4 years of age?**
- 2. Should a serum ferritin threshold of ≤ 15 ng/mL, ≤ 30 ng/mL, or ≤ 50 ng/mL be used to diagnose iron deficiency, with or without anemia, in the adult population (excluding menstruating and pregnant individuals)?**
- 3. Should serum ferritin threshold of ≤ 15 ng/mL, ≤ 30 ng/mL, or ≤ 50 ng/mL be used to diagnose iron deficiency, with or without anemia, in menstruating individuals?**
- 4. Should a serum ferritin threshold of ≤ 15 ng/mL, ≤ 30 ng/mL, or ≤ 50 ng/mL be used to diagnose iron deficiency, with or without anemia, in pregnant individuals?**
- 5. Should a serum ferritin alone versus serum ferritin with TSAT be used to diagnose iron deficiency, with or without anemia, in the general population (including pediatrics and adults of all age groups) with inflammation?**

The panel selected outcomes of interest for each question a priori, following the approach described in detail elsewhere.³ In brief, the panel first brainstormed all possible outcomes before rating their relative importance for decision-making following the GRADE approach.³

Given the lack of direct evidence assessing the impact of using different serum ferritin diagnostic thresholds on patient-important outcomes, the panel relied primarily on test accuracy data. The panel believed that the accuracy of different serum ferritin thresholds would not differ for the adult population, menstruating individuals, and pregnant individuals. Hence, the same systematic review data

for test accuracy informed all three of these populations. Separate diagnostic test accuracy data was used to inform guidance on infants and young children. Separate test accuracy data was also captured to inform the population with inflammation.

In contrast to diagnostic test accuracy, the panel believed that the prevalence of iron deficiency would vary considerably among the different populations. For that reason, the methods team conducted separate systematic reviews on the prevalence of iron deficiency for young children, adults (non-menstruating, non-pregnant), menstruating individuals (adolescent and adult), and pregnant individuals. Targeted searches were also performed to inform the potential impact of the diagnosis (and anticipated treatment of) iron deficiency on different patient-important outcomes. For pregnant individuals, this included data on the potential impact on both the pregnant individual and the fetus.

Serum ferritin as a diagnostic test

In considering diagnostic tests for iron deficiency, the panel weighed many available measures of iron status. Given that serum ferritin is widely available, commonly assessed, and considered the best indirect measure of total body iron stores, the panel prioritized this test in considering diagnostic questions. Serum ferritin is an acute phase reactant and is ideally tested during an individual's baseline state of health. In healthy individuals without evidence of acute infection or chronic disease, serum ferritin is an accurate marker of iron status, and when low is diagnostic of iron deficiency. Existing laboratory serum ferritin reference intervals in both pediatric and adult populations are biased toward lower values, however. This issue occurred because the studies that informed such reference ranges included "apparently healthy individuals" without considering that a portion of such individuals were iron deficient.¹² As a result, clinical use of methodologically flawed serum ferritin lower limits of normal has contributed to under-diagnosis of iron deficiency and variations in its management. The development of accessible and readily interpretable diagnostic laboratory thresholds facilitates prompt and equitable care. For all these reasons, the panel prioritized the identification of appropriate serum ferritin thresholds for the diagnosis of iron deficiency.

The panel acknowledges several limitations of serum ferritin testing, which include variability across laboratory methods for testing serum ferritin and lack of harmonization across platforms. Testing methods have evolved and include nonradiometric immunoassays such as enzyme-linked immunoassay (ELISA), chemiluminescent microparticle immunoassay (CMIA), chemiluminescent assays (CLIA), and electrochemiluminescence immunoassay (ECLIA) as well as radiometric assays such as radioimmunoassays (RIA) and immunoradiometric assays (IRMA). As a result, different laboratory assays

may obtain and report different serum ferritin values on the same serum sample. This -assay-to-assay variability occurs across the range of serum ferritin values but is most pronounced, and potentially clinically significant, at the higher end of serum ferritin values.¹³⁻¹⁵

A systematic review and meta-analysis on performance and comparability of laboratory methods for measuring serum ferritin concentrations in human serum or plasma found that overall, laboratory methods had comparable accuracy and performance based on linearity between compared methods; however, there were limited studies that reported on the agreement between testing methods.^{13,16} Several studies have found poor agreement (bias from -11.5 to 44 ng/mL and standard deviation higher than 25 ng/mL) between assays in non-pregnant women and children.¹⁴ Another study showed that serum ferritin results were consistently 36% to 44% higher with one type of assay over another in individuals with chronic kidney disease.¹⁵ Quality data from the Institute of Quality Management in Healthcare in Canada assessed 97 laboratories, which included commonly used serum ferritin reagent kits and instruments globally, to understand laboratory management of serum ferritin reference intervals. Post-analytical reporting showed a difference from the all-methods-mean results at the low end of serum ferritin (i.e. <50 ng/mL) of +/- 30-40%, which means that for a serum ferritin of 10 ng/mL, the potential range across laboratories would be 7-14 ng/mL. For a serum ferritin of 30 ng/mL, the range across laboratories would be 21-42 ng/mL. This inter-laboratory variation suggests that an approximation approach to serum ferritin clinical decision limits for the diagnosis of iron deficiency is appropriate, and this was considered by the panel when evaluating different serum ferritin thresholds (Institute for Quality Management in Healthcare. Proficiency Testing Endocrinology Program Data, ENDO-2202-Q).

Need to convert from lower limit of normal to a clinical decision limit for serum ferritin

The panel also noted that for all populations, many community and hospital laboratories across all income settings use a laboratory-defined serum ferritin lower limit of normal (LLN) rather than a clinical decision limit (CDL) for serum ferritin. The use of a LLN results in significant variation in reference ranges between laboratories and the classification of values consistent with iron deficiency as within the reference range, both of which contribute to the under-recognition of iron deficiency by ordering providers. In contrast, use of a CDL would mean that the laboratory would flag results at or below a clinically relevant diagnostic threshold as abnormal, regardless of the reference range. Use of a CDL would allow health care providers to more accurately identify iron deficiency in lieu of currently used population-based reference ranges.

The panel suggested that community and hospital laboratories across all income settings convert from a laboratory-defined lower limit of normal (LLN) to a clinical decision limit (CDL) for the recommended serum ferritin thresholds. Flagging results at or below this threshold as abnormal would facilitate health care providers' ability to diagnosis iron deficiency compared to currently used population-based reference ranges. The panel further suggested that a comment accompany the post-analytical test report to facilitate guideline implementation.

Selection of serum ferritin thresholds for comparison

Regarding the selection of serum ferritin thresholds to compare for the diagnosis of iron deficiency, the panel considered indirect evidence that evaluated the physiological effects of serum ferritin thresholds, recommendations from other organizations, as well as the panel's expert consensus. The threshold of ≤ 15 ng/mL was considered by the panel predominantly based on the World Health Organization (WHO) recommended serum ferritin threshold of < 15 ng/mL for the diagnosis of iron deficiency in apparently healthy individuals.¹⁷ The serum ferritin threshold of ≤ 30 ng/mL was assessed based on a systematic review of guideline recommendations on numerous populations¹⁸ and a cross-sectional study from the US National Health and Nutrition Examination Surveys (NHANES) estimating the serum ferritin concentration at which the hemoglobin concentration plateaus and soluble transferrin receptor (sTfR) concentration begins to increase (sTfR minimum point).¹⁹ In this study, among non-pregnant women of reproductive age, a hemoglobin plateau occurred at a serum ferritin of 25.2 ng/mL (95% CI 24.2–26.2) and the sTfR minimum point occurred at a serum ferritin of 24.0 ng/mL (95% CI 23.3–24.6).¹⁹ The serum ferritin threshold of ≤ 50 ng/mL was evaluated based on a systematic review of guideline recommendations¹⁸ as well as physiological data on iron absorption²⁰ and correlation between levels of serum ferritin and hepcidin.²¹

Comparison of different serum ferritin thresholds in young children versus adult populations

The panel considered lower serum ferritin thresholds for young children relative to other populations, specifically considering a serum ferritin threshold of ≤ 12 ng/mL, as this threshold is recommended by WHO¹⁷, to ≤ 20 ng/mL, based on physiologic studies on iron status in children.¹⁹ Assigning a lower diagnostic serum ferritin threshold in children, however, does not imply that iron needs for children are less, or that children are resistant to iron deficiency. In fact, based on body weight (mg/kg), the iron requirements for children are substantially higher than for adults.²² This greater need is due to iron demands for growth and expansion of red cell mass. If sufficient iron is available to meet these needs, the lower iron stores in children are not problematic but does mean that children are vulnerable to

become iron deficient in settings of low dietary iron or blood loss. Compared with children and adolescents, and in the absence of menstruation or pregnancy, adults have greater iron stores relative to iron utilization, which is reflected in higher serum ferritin levels. In such settings of high physiologic demand, iron is mobilized from ferritin stores into the circulation, due at least in part to erythroid signals which modulate the hepcidin-ferroportin axis.²³ Because erythropoietic activity is comparatively lower in adults, relatively more iron is retained as ferritin. Serum ferritin thresholds should be interpreted relative to the specific individual to which they are being applied with an emphasis on ensuring that iron needs are met.

Bone marrow iron staining as the diagnostic reference standard for iron deficiency

To assess the diagnostic test accuracy of serum ferritin, a reference diagnostic gold standard was needed for comparison. The panel considered many available tests that assess iron status to define iron deficiency including assessment of other iron parameters, response to oral iron therapy, and the historical reference standard of bone marrow aspirate iron staining examination. Based on the review of existing literature by the Methodology team, the guideline panel members agreed that bone marrow aspirate iron staining was the primary standard for which sufficient published data for the proposed analysis exists. Most of the diagnostic test accuracy data for serum ferritin in diagnosing iron deficiency (assessed by sensitivity and specificity) was determined using published data as compared to bone marrow aspirate iron staining. One additional study that used a TSAT $\leq 20\%$ as a reference standard for iron deficiency was also reviewed and included in diagnostic test accuracy data.²⁴

While marrow examination for the sole purpose of assessing iron stores is now rarely justifiable, absent or very low stainable marrow iron was historically the most broadly accepted standard to identify iron deficiency.²⁵ The panel acknowledges its limitations, such as bone marrow specimen sampling bias, subjectivity in grading, and unclear correlation with functionally available total body iron stores.²⁶⁻²⁹

The reliability of marrow iron assessment by Perls' Prussian blue staining depends on the adequacy of the specimen, including the presence of bone spicules, and may be limited in many samples.²⁶ Iron assessment is semi-quantitative, utilizing ordinal scales with subjectivity in distinguishing between iron deficiency (either absent or grade 1 staining) versus iron sufficiency (grade 2 or higher).^{27,30} In infants and young children, stainable iron can be absent from shortly after birth until the first year, and very low thereafter through the fourth year of life.³¹ In addition, iron stored in marrow reticular cells and macrophages might not necessarily reflect iron available to developing erythroblasts.^{25,28} Finally, The relationship between marrow iron and the iron status of other tissues vulnerable to deficiency has not

been systematically investigated, and using the bone marrow as a reference standard places emphasis on iron's role in erythropoiesis without fully appreciating the effects of iron status on other critical cellular processes throughout the body. Functional iron deficiency or iron-restricted erythropoiesis, for example, occurs when there is iron present in the body, but it is unavailable for utilization due to systemic inflammatory effects. In such individuals, bone marrow iron may not be an adequate reflection of iron status. In persons with inflammation, the panel considered separate diagnostic test accuracy data to inform the diagnostic recommendation for iron deficiency.

Recognizing these limitations, our analyses provided a means of comparing preselected serum ferritin thresholds for the best combination of sensitivity and specificity to identify iron deficiency, at least as defined by bone marrow iron staining. The caveats with this definition were among many considerations in ultimately assigning recommended serum ferritin thresholds for clinical use.

Evidence review and development of recommendations

For each guideline question, the University of Kansas Health System prepared a GRADE "Evidence-to-Decision" (EtD) framework, using the GRADEpro Guideline Development Tool (www.grade-pro.org).³²⁻³⁴ The EtD table summarized the results of systematic reviews of the literature that were performed for this guideline. The EtD table addressed desirable and undesirable effects of testing options (different serum ferritin thresholds), values and preferences (relative importance of outcomes), certainty of evidence, resource utilization (cost-effectiveness), equity, acceptability, and feasibility. The guideline panel reviewed draft EtD tables during the guideline panel meeting and made suggestions for corrections. The panel also identified missing indirect evidence to inform the impact and consequences of using different serum ferritin thresholds as they relate to patient-important outcomes. To ensure that recent studies were not missed, searches (presented in Supplement 4) were updated in July 2025. Panel members were asked to suggest any studies that fulfilled the inclusion criteria for the individual questions that may have been missed in the searches.

Under the direction of the University of Kansas Health System, researchers followed the general methods outlined in the Cochrane Handbook for Systematic Reviews of diagnostic test accuracy ([Handbook for Systematic Reviews of Diagnostic Test Accuracy | Cochrane](#)). Risk of bias was assessed at the health outcome level using the quality assessment of diagnostic accuracy studies, QUADAS-2 and QUADAS-C. In addition to conducting systematic reviews of diagnostic test accuracy, the researchers

searched for evidence related to prevalence and baseline risks, values, preferences and costs, and summarized findings within the EtD frameworks.³²⁻³⁴ Subsequently, certainty of the body of evidence (also known as quality of the evidence or confidence in the estimated effects) was assessed for outcomes of interest following the GRADE approach based on the following domains: risk of bias, precision, consistency and magnitude of the estimates of effects, directness of the evidence, and risk of publication bias. Certainty was categorized into four levels ranging from very low to high.³ Within this report, these categories are represented by symbols, as described in Figure 3.

Interested readers may find more explanation about the GRADE approach to assessing and rating certainty in a body of evidence in other publications.³

During a 2-day in-person meeting followed by online communication and conference calls, the panel developed clinical recommendations based on the evidence summarized in the EtD tables. For each recommendation, the panel took a population perspective and came to consensus on the following: the certainty of the evidence, the balance of benefits and harms of the different testing options (serum ferritin threshold), and the assumptions about the associated values and preferences. The guideline panel also considered the potential for additional investigations as well as resource use (iron therapy, healthcare utilization) associated with a higher number of individuals being diagnosed with iron deficiency. The panel agreed on the recommendations (including direction and strength), remarks, and qualifications by consensus or, in rare instances, by voting (an 80% majority was required for a strong recommendation), based on the balance of all desirable and undesirable consequences. The specific wording for each recommendation was intentional. The final guidelines, including recommendations, were reviewed and approved by all members of the panel.

Document review

Draft recommendations were reviewed by all members of the panel, revised, and then made available online on September 29, 2025 for external review by stakeholders including allied organizations, other medical professionals, patients, and the public. 39 individuals or organizations submitted comments. The document was revised to address pertinent comments and modify remarks for clarity, but no changes were made to recommendations. On April 22, 2026, the ASH Guideline Oversight Subcommittee and the ASH Committee on Quality approved that the defined guideline development process was followed, and on April 28, 2026, the officers of the ASH Executive Committee approved

submission of the guidelines for publication under the imprimatur of ASH. The guidelines were then subjected to peer review by *Blood Advances*.

How to use these guidelines

ASH guidelines are primarily intended to help clinicians and patients make shared decisions about diagnostic and treatment alternatives, with the goal of improving quality of patient care. Other purposes are to inform policy, education and advocacy, and to state future research needs. These guidelines are not intended to serve or be construed as a standard of care. Clinicians must make decisions based on the clinical presentation of each individual patient, ideally through a shared process that considers the patient's values and preferences with respect to the anticipated outcomes of the chosen option.

Decisions may be constrained by the realities of a specific clinical setting and local resources, including but not limited to institutional policies, time limitations, or availability of treatments.

Policymakers, including payers, may use guidelines to inform decisions about allocation of healthcare resources, e.g., coverage decisions. Such decisions should be consistent with the intended interpretation of strong and conditional recommendations (Figure 1). For example, it would be a misinterpretation of these guidelines to deny or restrict access to an intervention based on the direction or strength of a recommendation or based on the certainty of evidence supporting the recommendation. It is the position of ASH that patients should have access to all safe and effective treatment options recommended by the individual patient's physician.^{35,36}

These guidelines may not include all appropriate methods of care for the clinical scenarios described. As science advances and new evidence becomes available, recommendations may become outdated. Following these guidelines cannot guarantee successful outcomes. ASH does not warrant or guarantee any products described in these guidelines.

Statements about the underlying values and preferences as well as qualifying remarks accompanying each recommendation are its integral parts and serve to facilitate more accurate interpretation. They should never be omitted when quoting or translating recommendations from these guidelines. The use of these guidelines is also facilitated by the links to the EtD frameworks and interactive summary of findings tables in each section.

Recommendations

Diagnosis of iron deficiency in children

Should a serum ferritin threshold of ≤ 12 ng/mL or ≤ 20 ng/mL be used to diagnose iron deficiency, with or without anemia, in children aged 9 months to 4 years of age?

Recommendation 1. In children aged 9 months to 4 years, the ASH Guideline Panel **suggests** using a serum ferritin threshold of ≤ 20 ng/mL instead of a threshold of ≤ 12 ng/mL for the diagnosis of iron deficiency (conditional recommendation based on low certainty in the evidence about effects $\oplus\oplus\bigcirc\bigcirc$).

Remark:

- This threshold is for *children without* known or suspected inflammation, and a higher serum ferritin threshold may be required for children with inflammation.
- Due to a lack of direct evidence, specific recommendations for children aged >4 years until adolescence (defined as age ≥ 11 years⁵ as per the American Academy of Pediatrics) and non-menstruating adolescents were not developed. For children aged >4 years until adolescence, a serum ferritin threshold of ≤ 20 ng/mL is appropriate for the diagnosis of iron deficiency by indirectly applying evidence for young children. For non-menstruating adolescents, a serum ferritin threshold of ≤ 30 ng/mL is appropriate for the diagnosis of iron deficiency by indirectly applying evidence from menstruating adolescents and adult populations.
- For menstruating adolescents, please see recommendation 3.

Summary of the evidence

Evidence for the diagnostic test accuracy included one observational study ($n=87$) with a median age of 36.5 months (IQR 17.1 months). The study compared a serum ferritin threshold of <12 ng/mL versus <18 ng/mL (which was utilized to inform the threshold of 20 ng/mL).³⁷ For a serum ferritin threshold ≤ 12

ng/mL, the pooled sensitivity and specificity were 0.44 and 0.90, respectively, and for serum ferritin threshold ≤ 20 ng/mL, it was 0.74 and 0.77, respectively.

The systematic review on the prevalence of iron deficiency included 56 studies (n=121,394). The pooled estimate for the global prevalence of iron deficiency in this population was 30% (L.L. and R.A.M., manuscript in preparation).

Four observational studies also provided indirect evidence through estimation of physiologically based serum ferritin thresholds for this age group.^{19,38-40} Supplement 5 provides the evidence profile and EtD framework for Recommendation 1.

Benefits

The accurate diagnosis of iron deficiency in children allows for prompt intervention (dietary counseling, iron supplementation) to prevent the progression of iron deficiency to iron deficiency anemia or, in individuals with iron deficiency anemia, progression to more severe anemia. The benefits of identifying and treating iron deficiency in children are particularly significant due to the high iron demands in development and the demonstrated improvement in hematologic parameters⁴¹, cognition, and neurodevelopment^{42,43} with supplementation.

The panel prioritized a serum ferritin threshold that maximized true positives and minimized false negatives based on the expected benefit of identification of a great number of patients with iron deficiency who may benefit from treatment. The panel suggests the serum ferritin threshold of ≤ 20 ng/mL independent of concomitant signs or symptoms of iron deficiency.

Harms and burdens

The panel placed greater value on not missing the diagnosis of iron deficiency in children (false negatives) over incorrectly identifying children as iron deficient (false positives) given that a missed diagnosis may lead to adverse health consequences including poor neurodevelopment, worse cognition^{44,45} as well as increased fatigue and decreased physical performance in older children and adolescents.^{46,47} The panel determined that the undesirable effects of a lower serum ferritin threshold of ≤ 12 ng/mL were greater than ≤ 20 ng/mL due to a higher number of false negatives, given missed diagnosis of iron deficiency may result in a prolongation of unaddressed negative health issues. In contrast, those incorrectly identified as iron deficient may experience adverse effects from unnecessary iron supplementation (most commonly gastrointestinal side effects) with limited benefits. Intravenous

iron, though less commonly used in this age group, poses a small risk of infusion reactions (see *Harms and burdens* in Recommendation 2 for additional discussion of the undesirable effects of iron supplementation). The harms related to administration of iron therapy and follow-up laboratory evaluation in false positives may be more significant in young children compared to other populations. The panel recognized that children in malaria endemic areas may be more vulnerable to harm with unnecessary iron supplementation, specifically in settings in which malaria prevention or management services are unavailable.⁴⁸

Other EtD criteria and considerations

With the implementation of a higher ferritin threshold, more children will be diagnosed with iron deficiency. The panel considered that this could have effects on public health and health equity, discussed in detail in *Other EtD criteria and considerations* for Recommendation 2. The panel recognized that some stakeholders may be concerned about the challenges of treating more children; however, at least one acceptability survey of healthcare providers (n=155) found that the majority (81%) did not have concerns about increasing diagnostic threshold.⁴⁹ The panel also recognized that a higher diagnostic threshold would likely lead to additional laboratory testing and subsequent follow-up appointments, which may not be consistently accessible for all children.

Conclusions and research needs for this recommendation

The guideline panel suggests using ***a serum ferritin threshold of ≤ 20 ng/mL instead of a serum ferritin threshold of ≤ 12 ng/mL to diagnose iron deficiency in children between 9 months and 4 years of age*** despite a low certainty of evidence. This conditional recommendation was developed based on the body of available direct and indirect evidence with consideration of net health benefits and harms, cost-effectiveness, acceptability, feasibility, and health equity.

This higher threshold will result in a higher proportion of children with iron deficiency receiving a diagnosis and potentially benefitting from appropriate evaluation and management. The panel preferred the higher threshold (≤ 20 ng/mL) for the higher sensitivity (better ability to correctly identify children with iron deficiency) despite a lower specificity because of the potential negative consequences of missing a diagnosis of iron deficiency in this age group. Consideration of the undesirable effects of false positives included the potential harms of iron therapy as well as the potential harms of follow-up testing.

Based on available data, there is a low certainty of evidence regarding the effects of the use of a higher diagnostic threshold on children's health outcomes. However, this lack of certainty is likely due in part to a lack of research into the impact of therapy on such outcomes and does not imply that such effects do not exist.

The panel identified the following additional research needs and questions for children:

1. Prevalence of iron deficiency in children aged >4 years until adolescence and in non-menstruating adolescents
2. Assessment of changes in serum ferritin and TSAT values across all pediatric age groups from birth to adulthood
3. Evaluation of outcomes related to screening at various serum ferritin thresholds for iron deficiency in young children and impact of treatment on such outcomes
4. Stakeholder engagement to evaluate the acceptability, feasibility, and health state utility values of different serum ferritin thresholds. Stakeholders include patients, caregivers, physicians, and other pediatric healthcare providers
5. Randomized clinical trials comparing health outcomes in children when treated based on different serum ferritin thresholds
6. Cost effectiveness studies comparing the diagnosis and downstream implications of testing and treatment at different serum ferritin thresholds
7. Exploration of the health equity implications of different serum ferritin thresholds for pediatric individuals, including those living in malaria endemic areas

Diagnosis of iron deficiency in adults (excluding menstruating or pregnant individuals)

Should a serum ferritin threshold of ≤ 15 ng/mL, ≤ 30 ng/mL, or ≤ 50 ng/mL be used to diagnose iron deficiency, with or without anemia, in the adult population (excluding menstruating and pregnant individuals)?

Recommendation 2. In the adult population (excluding menstruating or pregnant individuals), the ASH Guideline Panel **suggests** using a serum ferritin threshold of ≤ 30 ng/mL instead of ≤ 15 ng/mL for the diagnosis of iron deficiency (conditional recommendation based on low certainty in the evidence about effects $\oplus\oplus\bigcirc\bigcirc$).

Remark:

- For people with signs or symptoms associated with iron deficiency, or ongoing iron deficiency risk factors (Table 1), a serum ferritin threshold of ≤ 50 ng/mL is appropriate to diagnose iron deficiency and guide management decisions.
- This threshold is for *adults without* known or suspected inflammation. A separate recommendation was made for adults with inflammation (See Recommendation 5).

Summary of the evidence

Evidence for the diagnostic test accuracy included a total of 17 cross-sectional studies^{24,50-65} (5,327 individuals); 13 studies included both male and female adults, one study included only menstruating individuals, and three studies included only pregnant individuals. All but one of the included studies used serum ferritin (at thresholds of 15, 30, or 50 ng/mL) as the index test and bone marrow examination (absent or reduced Perl's Prussian blue staining) as a reference standard to confirm the diagnosis of iron deficiency. One additional study used TSAT ($\leq 21\%$) as a reference standard for the diagnosis of iron deficiency.²⁴ For serum ferritin cut-off ≤ 15 ng/mL, the pooled sensitivity and specificity was 0.41 and 0.99, respectively. For a serum ferritin threshold of ≤ 30 ng/mL, the pooled sensitivity and specificity were 0.67 and 0.96, respectively; for a serum ferritin threshold of ≤ 50 ng/mL, the pooled sensitivity and specificity it was 0.89 and 0.86, respectively.

The systematic review on the prevalence of iron deficiency in adults (non-menstruating, non-pregnant) included 52 studies (n=154,819 individuals). The pooled estimate for the global prevalence of iron deficiency in this population was 16% (Q.H. and R.A.M., manuscript in preparation). Supplement 6 provides the evidence profile and EtD framework for Recommendation 2.

Benefits

The accurate diagnosis of iron deficiency in adults allows for prompt iron supplementation to prevent the progression of iron deficiency to iron deficiency anemia or, in individuals with iron deficiency anemia, progression to more severe anemia. The benefits of identifying and treating iron deficiency in adults⁶⁶⁻⁶⁸ include improvement in symptoms such as fatigue, impaired cognition, pica, emotional lability⁶⁶⁻⁶⁹, restless legs, the need for blood transfusion⁷⁰, physical performance, and overall health-related quality of life, even if non-anemic.^{71,72}

The panel prioritized a serum ferritin threshold that maximized true positives and minimized false negatives based on the expected benefit of identification of a great number of patients with iron deficiency who may benefit from treatment.

Harms and burden

The panel placed greater value on not missing the diagnosis of iron deficiency (false negatives) over incorrectly identifying individuals as iron deficient (false positives) given that a missed diagnosis may lead to adverse health consequences including symptoms of fatigue, impaired cognition, decreased physical performance, which negatively impact overall quality of life. The panel determined that the undesirable effects of the lowest serum ferritin threshold of ≤ 15 ng/mL were greater than the higher serum ferritin thresholds given a missed diagnosis of iron deficiency may result in a prolongation of unaddressed negative health issues. The panel determined that the undesirable effects of the highest serum ferritin threshold of ≤ 50 ng/mL were also significant, as those incorrectly identified as iron deficient may experience adverse effects from unnecessary evaluation (i.e., bidirectional endoscopy) and/or iron supplementation with limited benefit. The panel determined that the serum ferritin threshold of ≤ 30 ng/mL best balanced the number of false negatives and false positives, and thus, had the lowest degree of undesirable effects. The panel recognized that different individuals may place greater weight on different types of undesirable effects (unnecessary testing versus failure to be diagnosed and receive treatment). Finally, some panel members emphasized that bidirectional endoscopy may be more critical in the setting of anemia rather than iron deficiency alone.

Regarding the potential undesirable adverse effects of iron therapy, oral iron supplementation may lead to gastrointestinal side effects. Undesirable adverse events of intravenous iron include infusion reactions. A systematic review and meta-analysis of oral iron, intravenous iron, and no iron found that

overall intravenous iron was not associated with an increased risk of serious adverse events or infections.^{73,74} While there is a low certainty in the estimate of the risk of adverse effects due to imprecision and inconsistency, given available evidence, the guideline panel considered the risk of adverse effects from iron therapy to be small.⁷⁵

Other EtD criteria and considerations

The panel acknowledged that there is significant variation between patients with iron deficiency and their associated symptoms at different serum ferritin thresholds, which creates important certainty or variability in patient values.

The feasibility of serum ferritin testing does not differ based on thresholds, and the test is widely available. A 2024 study of healthcare providers from 23 countries found that 100% of respondents reported using serum ferritin testing in clinical practice.⁷⁶ The panel recognized that some stakeholders may be concerned about the challenges of treating more patients with iron deficiency based on new diagnostic thresholds; however, at least one acceptability survey of healthcare providers (n=155) found that the majority (81%) did not have concerns about increasing diagnostic threshold.⁴⁹ For those who were concerned, 32% (n=37) indicated that a cutoff of ≤ 30 ng/mL was too low and would lead to underdiagnosis. The panel recommends early stakeholder engagement and targeted knowledge translation with implementation of new thresholds. Finally, while the direct cost of the serum ferritin test will not differ according to the use of different diagnostic thresholds for iron deficiency, the substantial variability globally in the cost associated with serum ferritin testing was acknowledged.

While there is no direct evidence on the impact of different serum ferritin thresholds on health equity, using a higher threshold will identify more individuals with iron deficiency. Identifying more individuals with iron deficiency with inadequate access to care may indirectly enhance equity by promoting efforts to improve treatment access for marginalized groups (by influencing insurance coverage options, health policy advocacy, or provider willingness to treat). On the other hand, the panel acknowledge that higher thresholds may also have adverse effects on equity by increasing the financial burden on individuals and health systems.

The panel also expressed concerns about using a higher threshold in malaria-endemic regions due to the risk of worsening infection in patients with uncontrolled malaria who are started on iron therapy. In malaria endemic settings, the relationship between iron status and serum ferritin levels is complex, as is also the relationship between iron status and risk for malarial infection. However, the panel

acknowledged that in the context of treatment, iron therapy would be appropriate and beneficial. The impact of different ferritin thresholds in the context of these settings is unknown. Given these considerations, despite the lack of evidence, the panel posited that the overall impact on healthy equity using a higher serum ferritin threshold would be “probably increased.”

Conclusions and research needs for this recommendation

The guideline panel suggests **a serum ferritin threshold of ≤ 30 ng/mL over a serum ferritin threshold of ≤ 15 ng/mL to diagnose iron deficiency in the general adult population (excluding menstruating or pregnant individuals)** despite a low certainty of evidence. This conditional recommendation was developed based on the body of available direct and indirect evidence with consideration of net health benefits and harms, cost-effectiveness, acceptability, feasibility, and health equity.

This higher threshold will result in a higher proportion of adults with iron deficiency receiving a diagnosis and potentially benefitting from appropriate evaluation and management. The panel preferred the higher threshold (≤ 30 ng/mL) for the higher sensitivity (better ability to correctly identify patients with iron deficiency) despite a lower specificity because of the potential negative consequences of missing a diagnosis of iron deficiency. Consideration of the undesirable effects of false positives included the potential harms of iron therapy as well as the potential use of endoscopic evaluation to identify the cause of iron deficiency.

The low certainty of evidence and limited published evidence evaluating the impact of serum ferritin diagnostic thresholds on clinical outcomes influenced the strength of the recommendation. However, this lack of certainty is likely due in part to a lack of research into the impact of therapy on such outcomes and does not imply that such effects do not exist.

The panel identified the following additional research needs and questions for adults:

1. Studies focused on an appropriate reference standard for iron deficiency as well as the harmonization of serum ferritin laboratory testing across platforms and/or reagents
2. Stakeholder engagement to assess perspectives of patients, physicians, and other healthcare providers on the feasibility, acceptability, and health state utility implications, measured directly (time trade-off, standard gamble) or indirectly (EQ-5D questionnaire), of different serum ferritin thresholds (15, 30, and 50 ng/mL), and to evaluate the association between untreated versus treated iron deficiency (with and without anemia) and related health state utilities.

3. Randomized clinical trials comparing patient-important outcomes using different serum ferritin diagnostic thresholds to guide iron therapy in adults with iron deficiency
4. Cost-effectiveness studies comparing diagnosis at different serum ferritin diagnostic thresholds, including the higher threshold of 50 ng/mL, with an assessment of the magnitude and impact of the need for additional evaluations (i.e., colonoscopy) with the higher serum ferritin thresholds
5. Exploration of health equity implications for different serum ferritin diagnostic thresholds in adults
6. Impact of higher serum ferritin thresholds for individuals in malaria endemic regions including approach to prevention, diagnosis, and treatment of iron deficiency in such settings

Diagnosis of iron deficiency in menstruating individuals

Should a serum ferritin threshold of ≤ 15 ng/mL, ≤ 30 ng/mL, or ≤ 50 ng/mL be used to diagnose iron deficiency in menstruating individuals?

Recommendation 3. In menstruating individuals, the ASH Guideline Panel **suggests** using a serum ferritin threshold of ≤ 30 ng/mL and **suggests against** using a serum ferritin threshold of ≤ 15 ng/mL for the diagnosis of iron deficiency (conditional recommendation based on low certainty in the evidence about effects $\oplus\oplus\bigcirc\bigcirc$).

Remark: For people with heavy menstrual bleeding (HMB) or other forms of abnormal uterine bleeding (AUB) resulting in excessive blood loss, symptoms associated with iron deficiency, additional risk factors for iron deficiency (Table 1), upcoming surgery, or planning pregnancy, a serum ferritin threshold of ≤ 50 ng/mL is appropriate to diagnose iron deficiency and guide management decisions.

Good Practice Statement: A detailed menstrual history is necessary to facilitate the diagnosis of AUB, particularly HMB. It would be essential to address abnormal and/or HMB, if identified.

Summary of the evidence

The same diagnostic test accuracy data was used to inform recommendations for adults, menstruating, and pregnant populations, as described in the *Summary of the evidence* under Recommendation 2.

The systematic review on the prevalence of iron deficiency in menstruating individuals included 79 studies (n=264,178 individuals) and were comprised of menstruating individuals between ages 12 and 45 years. The pooled estimate for the global prevalence of iron deficiency in this population was 27% (A.C. and R.A.M., manuscript in preparation).

Additionally, 5 observational studies,⁷⁷⁻⁸¹ 12 randomized controlled trials,⁸²⁻⁹³ 2 meta-analyses,^{68,94} 2 systematic reviews,^{95,96} and 1 Cochrane review⁹⁷ informed an estimation of the effect of different serum ferritin thresholds on treatment decisions and the resultant impact on patient-important outcomes. Supplement 7 provides the evidence profile and EtD framework for Recommendation 3.

Benefits

Defining a diagnostic serum ferritin threshold for iron deficiency is of great importance to guide further diagnostic evaluation and access to treatments, particularly for medically underserved populations at greater risk of iron deficiency.⁹⁸ The accurate diagnosis of iron deficiency in menstruating individuals allows for prompt iron supplementation to prevent the progression of iron deficiency to iron deficiency anemia or, in individuals with iron deficiency anemia, progression to more severe anemia. The benefits of identifying and treating iron deficiency in menstruating individuals were assumed to include those demonstrated in the adult population (see *Benefits* in Recommendation 2), with additional benefits. Iron repletion in menstruating individuals that become pregnant may derive the additional benefit of avoiding iron deficiency in pregnancy. The panel judged that a serum ferritin threshold of ≤ 30 ng/mL was a feasible threshold to implement across all income settings. However, the panel supported the use of a serum ferritin threshold of ≤ 50 ng/mL in subgroups of menstruating people, recognizing those with HMB as a particularly vulnerable subgroup.⁹⁹

The panel prioritized a serum ferritin threshold that maximized true positives and minimized false negatives based on the expected benefit of identification of a great number of patients with iron deficiency who may benefit from treatment.

Harms and burdens

The panel placed greater value on not missing the diagnosis of iron deficiency (false negatives) over incorrectly identifying individuals as iron deficiency (false positives) given that a missed diagnosis may lead to adverse health consequences. In menstruating individuals, these consequences include risk of progressive iron deficiency and anemia, major bleeding at gynecologic surgery, blood transfusion and red cell antigen alloimmunization (potentially complicating future pregnancies), fatigue, impaired cognition, altered mood, poor physical performance, and decreased health-related quality of life. The panel determined that the undesirable effects of a serum ferritin threshold of ≤ 15 ng/mL were highest due to the high proportion of those with HMB in this population as well as the high risk of blood transfusion among those undergoing gynecologic surgeries.¹⁰⁰

The panel further considered indirect evidence demonstrating cost-effectiveness of use of a serum ferritin threshold ≤ 25 ng/mL for women of reproductive age, recognizing that a serum ferritin of 25 vs. 30 ng/mL may be interchangeable due to lab assay variability.¹⁰¹ While a diagnostic threshold of ≤ 50 ng/mL was probably favoured, there was concern regarding the higher number of false positives with this threshold and the potential undesirable effects associated with unnecessary iron supplementation (see *Harms and burdens* in Recommendation 2 for additional discussion of the undesirable effects of iron supplementation). In addition, the panel felt that most people with iron deficiency from menstrual blood loss have a serum ferritin far lower than 50 ng/mL at diagnosis.

Other EtD criteria and considerations

See *Other EtD criteria and considerations* for Recommendation 2, which are also relevant to this recommendation.

Conclusions and research needs for this recommendation

The guideline panel ***suggests using a serum ferritin threshold of ≤ 30 ng/mL and suggests against using a serum ferritin threshold of ≤ 15 ng/mL for the diagnosis of iron deficiency in menstruating individuals*** despite a low certainty of evidence. This conditional recommendation was developed based on the body of available direct and indirect evidence with consideration of net health benefits and harms, cost-effectiveness, acceptability, feasibility, and health equity.

Using a higher serum ferritin threshold of ≤ 30 ng/mL instead of a lower serum ferritin threshold of ≤ 15 ng/mL in menstruating individuals reduces the risk of untreated iron deficiency and progression to iron deficiency anemia. In consideration of the threshold of ≤ 30 ng/mL compared with ≤ 50 ng/mL, the recommendation was influenced heavily by concerns about risk of false positives with ≤ 50 ng/mL given limited data on impact on clinical outcomes. Overall, based on the body of available evidence, it is likely that adoption of a diagnostic serum ferritin threshold of ≤ 30 ng/mL reduces the risk of undiagnosed and untreated iron deficiency among menstruating individuals. As for the highest serum ferritin threshold of ≤ 50 ng/mL, the panel ultimately supported its use in certain subgroups of menstruating individuals given the potential desirable effects of earlier diagnosis, intervention and the potential for symptomatic improvement in some.

The low certainty of evidence and limited published evidence evaluating the impact of serum ferritin diagnostic thresholds on clinical outcomes influenced the strength of the recommendation. However, this lack of certainty is likely due in part to a lack of research into the impact of therapy on such outcomes and does not imply that such effects do not exist.

The panel identified the following areas for additional research in menstruating people:

1. Studies focused on an appropriate reference standard for iron deficiency as well as the harmonization of serum ferritin laboratory testing across platforms and/or reagents
2. Evaluation of outcomes related to various serum ferritin diagnostic thresholds and the impact of treatment on such outcomes (including subgroups listed above)
3. Stakeholder engagement to assess perspectives of patients, physicians, and other healthcare providers on the feasibility, acceptability, and health state utility implications, measured directly (time trade-off, standard gamble) or indirectly (EQ-5D), of different serum ferritin thresholds (15, 30, and 50 ng/mL), and to evaluate the association between untreated versus treated iron deficiency (with and without anemia) and related health state utilities.
4. Randomized clinical trials comparing patient-important outcomes using different serum ferritin diagnostic thresholds to guide iron therapy in menstruating individuals
5. Cost-effectiveness studies comparing diagnosis at different serum ferritin diagnostic thresholds, including the higher threshold of 50 ng/mL, in menstruating individuals (including subgroups listed above)

6. Exploration of health equity implications for different serum ferritin diagnostic thresholds in menstruating individuals

Diagnosis of iron deficiency in pregnant individuals

Should a serum ferritin threshold of ≤ 15 ng/mL, ≤ 30 ng/mL, or ≤ 50 ng/mL be used to diagnose iron deficiency in pregnant individuals?

Recommendation 4. In pregnant individuals, the ASH Guideline Panel **suggests** using a serum ferritin threshold of ≤ 30 ng/mL (conditional recommendation based on low certainty in the evidence about effects $\oplus\oplus\bigcirc\bigcirc$) and **recommends against** using a serum ferritin threshold of ≤ 15 ng/mL for the diagnosis of iron deficiency (strong recommendation based on low certainty in the evidence about effects $\oplus\oplus\bigcirc\bigcirc$).

Remark: For pregnant individuals with anemia, with or without other iron deficiency risk factors and/or symptoms associated with iron deficiency (Table 2), a serum ferritin threshold of ≤ 50 ng/mL may be appropriate to diagnose iron deficiency and guide management decisions.

Summary of the evidence

The same diagnostic test accuracy data was used to inform recommendations for adults, menstruating, and pregnant populations, as described in the *Summary of the evidence* under Recommendation 2.

The systematic review on the prevalence of iron deficiency in pregnant individuals included 31 studies (n=93,782 individuals), which were comprised of pregnant individuals across all trimesters. The panel selected to use the average pooled estimate from all trimesters rather than prevalence data at a specific time point in pregnancy. Thus, the pooled estimate for the global prevalence of iron deficiency in pregnant individuals was 37% (A.C. and R.A.M., manuscript in preparation). Supplement 8 provides the evidence profile and EtD framework for Recommendation 4.

Benefits

The accurate diagnosis of iron deficiency during pregnancy allows for prompt iron supplementation to prevent the progression of iron deficiency to iron deficiency anemia or, in individuals with iron deficiency anemia, progression to more severe anemia. The panel prioritized a serum ferritin threshold that maximized true positives and minimized false negatives based on the expected benefit of identification of a great number of patients with iron deficiency who may benefit from treatment. While relevant to all populations, the benefit of identifying and treating iron deficiency, irrespective of the presence or absence of anemia, is paramount in pregnant individuals due to the high iron demands of pregnancy and delivery¹⁹ and associated improvement in both maternal and neonatal outcomes with iron supplementation.¹⁰²⁻¹⁰⁶ However, the panel also considered the lack of direct data comparing clinical outcomes using a diagnostic serum ferritin threshold of 30 ng/mL versus 50 ng/mL.

Harms and burdens

To determine the undesirable effects at each serum ferritin threshold, the panel weighed the number of false negatives and false positives, the potential adverse effects of iron supplementation, and the paucity of clinical outcome data to justify treatment initiation at the highest serum ferritin threshold of 50 ng/mL. The panel placed greater value not missing the diagnosis of iron deficiency (false negatives) over incorrectly identifying individuals as iron deficiency (false positives) given that a missed diagnosis may lead to adverse health consequences.

The panel determined that the undesirable effects of the lowest serum ferritin threshold of ≤ 15 ng/mL were greater than higher thresholds given a missed diagnosis of iron deficiency may result in a prolongation of unaddressed negative health issues. In contrast, those incorrectly identified as iron deficient may experience adverse effects from unnecessary supplementation (see *Harms and burdens* in Recommendation 2 for additional discussion of the undesirable effects of iron supplementation). The panel noted that side effects of oral iron supplementation may be amplified during pregnancy and acknowledged the time and financial burdens of intravenous iron. The panel considered that data on the potential benefits and harms of iron supplementation at higher serum ferritin thresholds is mixed.¹⁰⁷ Iron supplementation in the setting of maternal hemoglobin >13 g/dL was associated with pre-eclampsia and hypertensive disorders of pregnancy.¹⁰⁸ Data on benefits of iron administration at higher serum ferritin levels on cognitive outcomes in infants has also been mixed.^{109,110}

Thus, the panel determined that the serum ferritin threshold of ≤ 30 ng/mL best balanced the number of false negatives and false positives, and thus, had the lowest degree of undesirable effects. The panel also recognized that different individuals may place greater weight on different types of undesirable effects (unnecessary supplementation versus failure to be diagnosed and receive treatment).

Other EtD criteria and considerations

See *Other EtD criteria and considerations* for Recommendation 2, which are also relevant to this recommendation.

Specific to the pregnant population, the certainty of evidence was judged to be low due to serious risk of bias and serious indirectness of included studies. While data showed poorer maternal, neonatal, and fetal outcomes with lower serum ferritin, the panel acknowledged that there are no data that directly link maternal or neonatal outcomes to specific serum ferritin thresholds during pregnancy, much less in a specific trimester of pregnancy.¹⁰³ The panel also discussed the impact of the serum ferritin diagnostic threshold on equity. Specifically, adopting a higher serum ferritin threshold may benefit individuals with limited healthcare access, enabling them to receive iron supplementation prior to the development of anemia, which may reduce disparities in maternal health in high-risk populations.¹¹¹ Finally, the potential feasibility and implementation challenges of a higher serum ferritin threshold for the diagnosis of iron deficiency in this population was recognized.

Conclusions and research needs for this recommendation

The panel ***suggests using a serum ferritin threshold of ≤ 30 ng/mL and recommends against using a serum ferritin threshold of < 15 ng/mL for the diagnosis of iron deficiency*** in pregnant people despite a low certainty of evidence. This conditional recommendation was developed based on the body of available direct and indirect evidence with consideration of health benefits and harms regarding both maternal and neonatal outcomes, acceptability, feasibility, and health equity.

Using a higher serum ferritin threshold of ≤ 30 ng/mL instead of a lower serum ferritin threshold of ≤ 15 ng/mL, at any gestational age, reduces both the risk of untreated iron deficiency during pregnancy as well as the risk of progression to iron deficiency anemia. In consideration of the threshold of ≤ 30 ng/mL compared with ≤ 50 ng/mL, the recommendation was influenced heavily by concerns about risk of false positives with the highest threshold of 50 ng/mL given limited data on impact on maternal and fetal outcomes. Consideration of the undesirable effects of false positives included the potential harms of

iron therapy and additional follow-up testing. The panel supported the use of this highest threshold of ≤ 50 ng/mL in pregnant individuals with concomitant anemia with the goal of minimizing progression of iron deficiency anemia in later trimesters as well as the reliance of the fetus on maternal iron stores. However, there were concerns about the feasibility of implementing this threshold. There was not unanimous support for the threshold of 50 ng/mL for pregnant individuals without anemia due to uncertain benefits and uncertain potential harms of treatment at this threshold.

The panel identified the following additional research questions on iron status assessment and diagnostic thresholds in pregnancy:

1. Examination of the relationship between serum ferritin and TSAT in pregnant individuals across gestational stages and trimesters.
2. Evaluation of outcomes related to serum ferritin testing in pregnancy, including the optimal timing (gestational age) for screening and treatment
3. Stakeholder engagement to assess perspectives of patients, physicians, and other obstetric healthcare providers on the feasibility, acceptability, and health state utility implications, measured directly (time trade-off, standard gamble) or indirectly (EQ-5D questionnaire), of different serum ferritin thresholds (15, 30, and 50 ng/mL), and to evaluate the association between untreated versus treated iron deficiency (with and without anemia) and related health state utilities
4. Randomized clinical trials and prospective comparison of patient-important outcomes using different serum ferritin diagnostic thresholds to guide iron therapy in pregnancy
5. Cost-effectiveness studies comparing diagnosis at different serum ferritin diagnostic thresholds in pregnancy
6. Exploration of health equity implications for different diagnostic serum ferritin diagnostic thresholds on maternal and fetal outcomes

Diagnosis of iron deficiency in adults with inflammation

Should a serum ferritin alone vs a serum ferritin with TSAT be used to diagnose iron deficiency, with or without anemia, in the general population (including pediatrics and adults of all age groups) with inflammation?

Recommendation 5. For adults with anemia of inflammation, the ASH Guideline Panel **suggests** performing both serum ferritin and transferrin saturation (TSAT) rather than serum ferritin alone to evaluate for iron deficiency (conditional recommendation based on very low certainty in the evidence about effects ⊕○○○).

Remarks:

- Inflammation is on a continuum, and establishing a serum ferritin threshold for the diagnosis of iron deficiency is challenging. However, in adults with anemia of inflammation, the diagnosis of iron deficiency may be considered when (A) TSAT <20% or (B) serum ferritin <100 ng/mL.
- TSAT should be drawn in a fasting state (5-9 hours⁶, including fasting from multivitamin/iron supplements), as the test is susceptible to recent dietary intake.
- Anemia of inflammation may occur in individuals with inflammatory bowel disease, infectious diseases, cancer, chronic kidney disease, heart failure, rheumatologic disorders, and other inflammatory disorders.
- Due to a lack of data on the diagnosis of iron deficiency in children with inflammation, no recommendations were made for this population (see Recommendation 1).

Good practice statement: Anemia of inflammation may be present concurrently with other causes of anemia. Thus, in individuals with inflammation, the serum ferritin and TSAT should be analyzed in context of the full clinical picture including consideration of the history, physical exam, underlying disease process, and other existing management guidelines^{7,8} for chronic diseases. Such guidelines may consider higher serum ferritin and/or TSAT thresholds for the diagnosis of iron deficiency.

Summary of the evidence

Evidence for the diagnostic test accuracy included two comparative cross-sectional studies individuals (n=67),^{112,113} one study included adults with heart failure, and one study included adults with renal failure. Both studies presented data on the sensitivity and specificity comparing serum ferritin alone

versus performing both serum ferritin and TSAT. The pooled sensitivity and specificity for serum ferritin alone (<100 ng/mL) were 0.38 and 0.88, respectively. For serum ferritin threshold <100 ng/mL and/or TSAT <20%, the pooled sensitivity and specificity were 0.91 and 0.70, respectively. Supplement 9 provides the evidence profile and EtD framework for Recommendation 5.

Benefits

The accurate diagnosis of iron deficiency in the setting of inflammation allows for the potential initiation of therapy to mitigate the negative consequences of iron deficiency, which include worsening of anemia and exacerbation of poorer outcomes related to the underlying comorbid condition and primary cause of inflammation. The diagnosis of absolute iron deficiency can be challenging in the presence of inflammation as the serum ferritin may be falsely “normal” or “elevated” due to being an acute-phase reactant. Therefore, panel members considered assessment of a serum ferritin alone as often insufficient to assess iron status in adults with inflammation and supported the use of multiple iron parameters to inform the diagnosis. The TSAT reflects circulating iron and identifies states of iron-restricted erythropoiesis, irrespective of the presence of inflammation, thereby providing additional information to inform the individual’s iron status.

The panel considered serum ferritin <100 ng/mL or transferrin saturation <20% to be accurate for the diagnosis of iron deficiency for many, but not necessarily all individuals in the setting of inflammation. The panel recognized that inflammation is a continuum and that dichotomous thresholds are limited in fully characterizing the spectrum and range of inflammation. Regardless, thresholds for diagnostic and treatment guidance were judged to be of moderate benefit to patients.

Harms and burden

To determine the undesirable effects of using a serum ferritin alone versus serum ferritin or TSAT to make a diagnosis of iron deficiency in adults with inflammation, the panel considered false positive and false negative diagnoses. The panel considered the undesirable effects of unnecessary iron therapy in persons falsely identified to be deficient, and the negative health consequences of missing the diagnosis of iron deficiency, which would include worse fatigue, impaired cognition, poorer health-related quality of life and worse outcomes related to the comorbid illness (false negatives). The panel prioritized the desire to minimize false negatives and considered the undesirable effects of using serum ferritin ≤100 ng/mL alone as moderate and undesirable effects of using serum ferritin ≤100 ng/mL or transferrin

saturation <20% overall likely to be small. Panel members expressed their willingness to give iron treatment when TSAT was $\leq 20\%$ even if anemia might be due to iron restricted erythropoiesis rather than absolute iron deficiency due to the potential for positive health benefits for both conditions.

Other EtD criteria and considerations

Certainty of the evidence of test accuracy was judged to be low due to concerns around the risk of bias and the use of indirect evidence. For instance, in evaluating management effects, the panel considered indirect evidence from four randomized controlled trials in individuals with iron deficiency and heart failure that defined iron deficiency as serum ferritin ≤ 100 ng/mL or TSAT <20%.^{85,114-116} All four trials showed a consistent improvement in symptoms with very few reported side effects. The panel acknowledged that due to the presence of chronic comorbid conditions and inflammation, though individuals may have an improvement in symptoms with intravenous iron, resolution of anemia may not be complete (due to other contributing causes of anemia) even after treatment with intravenous iron. The panel posits that most individuals would value being aware of having absolute or functional iron deficiency, though individuals may vary in their prioritization of receiving treatment for iron deficiency in the setting of other comorbidities. Despite variations in costs and charges of the laboratory tests, the panel considered the difference between a serum ferritin alone and serum ferritin and TSAT to likely be of negligible costs and savings. The panel assessed the testing to likely be acceptable to patients and feasible for providers.

Given the difficulty of diagnosing absolute iron deficiency in individuals with inflammation, and acknowledging that inflammation is a continuum, a variety of tests have been proposed to supplement the diagnosis. These included the use of the soluble transferrin receptor or using markers of inflammation, such as the sedimentation rate or C-reactive protein, to “adjust” serum ferritin threshold for inflammation. In reviewing these potential adjunctive tests, none have sufficient data to recommend their use as standalone tests but may be helpful in the full context of the individual’s clinical condition and other laboratory values.

Conclusions and research needs for this recommendation

The guideline panel ***suggests assessment of both a serum ferritin and TSAT for the diagnosis of iron deficiency in adults with inflammation*** despite a low certainty of evidence for a net health benefit and harm reduction.

Based on available evidence, a serum ferritin of <100 ng/mL or TSAT <20% may identify many individuals with concomitant iron deficiency in the setting of inflammation, thereby reducing untreated iron deficiency and its attendant negative health consequences. Due to a low certainty of evidence and very limited number of prospective trials providing indirect evidence, a recommendation regarding specific thresholds was not made.

The panel identified the following additional research questions in individuals with inflammation:

1. Studies on various iron parameters including diagnostic hepcidin assays to inform diagnose iron deficiency in the setting of anemia of inflammation
2. Evaluation of the relationship between serum ferritin and TSAT in pediatrics, including optimal threshold for diagnosing iron deficiency in children with concomitant inflammation
3. Randomized clinical trials that examine different iron parameters for the diagnosis of iron deficiency in individuals with inflammation to guide treatment and assess patient-important outcomes

What are others saying and what is new in these guidelines?

Guidance from the World Health Organization recommends a serum ferritin threshold of <12 ng/mL for children and a threshold of <15 ng/mL for otherwise healthy adults.¹⁷ These thresholds are considered highly specific but have low sensitivity for the accurate diagnosis of individuals with iron deficiency. Evidence assessed by this guideline panel examined these specific ranges and identified low evidence to suggest the use of these thresholds in any population.

A new joint clinical report on iron deficiency and iron deficiency anemia from the American Academy of Pediatrics (AAP) and the American Society of Pediatric Hematology Oncology (ASPHO) will provide diagnostic guidance for infants, children, and adolescents that are consistent with the serum ferritin thresholds developed in these ASH diagnostic guidelines. The American College of Obstetrics and Gynecology (ACOG) recommends a serum ferritin threshold of <30 ng/mL for the diagnosis of iron deficiency in pregnant people.¹¹⁷ The National Bleeding Disorder Foundation (NBDF) Medical and Scientific Advisory Council (MASAC) 2026 guidelines recommend a ferritin level of <50 ng/mL as the cut-off for diagnosing iron deficiency in males and females with inherited bleeding disorders at all ages.¹¹⁸

Call to action on screening

Recommendations on screening were out of scope of this diagnostic guideline due to the need to prioritize diagnostic thresholds to facilitate accurate diagnosis across populations. Therefore, an evidence-based review focused on screening for iron deficiency was not performed.

Since 2010, the AAP has recommended universal anemia screening in young children at 12 months of age.¹¹⁹ A joint clinical report from the AAP and ASPHO published in 2026 recommends universal screening for both anemia and iron deficiency in all young children as well as all menstruating individuals after the onset of menarche.¹²⁰ The NBDF MASAC 2026 guidelines include recommendations for screening all individuals with inherited bleeding disorders for iron deficiency and anemia.¹¹⁸ ACOG does not currently recommend routine screening for iron deficiency during pregnancy.¹¹⁷ However, a body of evidence demonstrates the pervasiveness of iron deficiency (defined as serum ferritin <30 ng/mL) in pregnancy, irrespective of the presence or absence of anemia.¹²¹ In addition to impacting maternal outcomes, iron deficiency has potential negative impacts on the developing fetus.⁴³ The use of hemoglobin and mean corpuscular volume (MCV) as surrogates for iron sufficiency is inaccurate,¹²² and literature demonstrates positive effects of early iron repletion in non-anemic pregnant individuals.¹²³⁻¹²⁵ Based on the above, the panel believes it is reasonable to screen for iron deficiency by checking serum ferritin in all pregnant individuals as well as other high-risk populations, with or without concomitant anemia.

Limitations of these guidelines

The limitations of these guidelines are inherent in the low or very low certainty of the evidence we identified for many of the questions.

Revision or adaptation of the guidelines

Plans for updating these guidelines

After publication of these guidelines, ASH will maintain them through surveillance for new evidence, ongoing review by experts, and regular revisions.

Updating or adapting recommendations locally

While a global perspective was taken in the development of this guideline, adaptation of these guidelines will be necessary in many circumstances. These adaptations should be based on the associated EtD frameworks.¹²⁶

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Figure 2 created in <https://BioRender.com>.

Authorship contributions

All authors were assigned specific sections of the manuscript and contributed first drafts of their respective recommendation areas. Powers wrote the full draft of manuscript and integrated all authors' section drafts of their recommendations. Powers revised the compiled manuscript based on feedback from all authors. Guideline panel members (Lim, May) critically reviewed the manuscript and provided suggestions for improvement. Guideline panel member May created Figure 2. Members of the knowledge synthesis team (Hamarsha, Choaib, Khawandi, Azzam) contributed evidence summaries to

1122 the guidelines. All authors approved of the content. Powers and Mustafa were the co-chairs of the panel
1123 and led panel meetings.

1124 **Disclosures of conflicts of interest**

1125 All authors were members of the guideline panel or members of the systematic review team or both. As
1126 such, they completed a disclosure of interest form, which was reviewed by ASH and is available as
1127 supplements 2 and 3.

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1480 **Figure 1. Strength of Recommendations**

1481 **Figure 2. Algorithm of diagnostic recommendations**

1482 **Figure 3. Certainty of Evidence**

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Table 1. Signs and symptoms associated with and risk factors for iron deficiency in non-menstruating, non-pregnant adults

Signs	Tachycardia, murmur (in presence of anemia) Tongue depapillation, cheilosis, koilonychia (spoon nails), diffuse nonscarring scalp alopecia
Symptoms	Fatigue, decreased quality of life Decreased cognitive function Restless leg syndrome Pica/Pagophagia (ice craving) Decreased exercise tolerance
Risk factors	Physiological state: Extreme exercise Blood Loss: Inflammatory bowel disease Peptic ulcer disease, gastritis GI malignancies Blood donation, Surgery Hereditary hemorrhagic telangiectasia Hookworm or parasitic infection Low iron intake: Restricted diet (including vegan or vegetarian) Reduced absorption: Gastric bypass surgery Gastroesophageal reflux disease or gastritis <i>Helicobacter pylori</i> infection Long-term use of proton pump inhibitor / antacid Celiac disease Bariatric surgical procedure

1508 **Table 2: Pregnancy-specific risk factors associated with iron deficiency during the perinatal period**

Preceding history of heavy menstrual bleeding
Teenage pregnancy
Hyperemesis gravidarum
Multiple gestation
Vaginal bleeding after the first trimester
Abnormal placentation (placenta previa, placenta accreta spectrum, placental abruption)
Short interpregnancy interval (<18 months between delivery and subsequent conception)
Multiparity

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1511 **Table 3. Outcomes affected by the timely diagnosis of iron deficiency that were considered by the**
 1512 **panel for clinical decision-making across different populations**

Population	Outcomes
All	Symptoms Cognitive function Fatigue Health-related quality of life Mental health, Emotional lability Physical activity, shortness of breath, and/or cardiovascular health Pica Restless leg syndrome and/or periodic limb movement disorder Dermatologic health Treatment Red cell transfusion
Pregnant	Maternal Preterm delivery Postpartum hemorrhage Fetal Fetal cognitive development Fetal iron deficiency Low birth weight Premature birth Treatment-related Oral iron

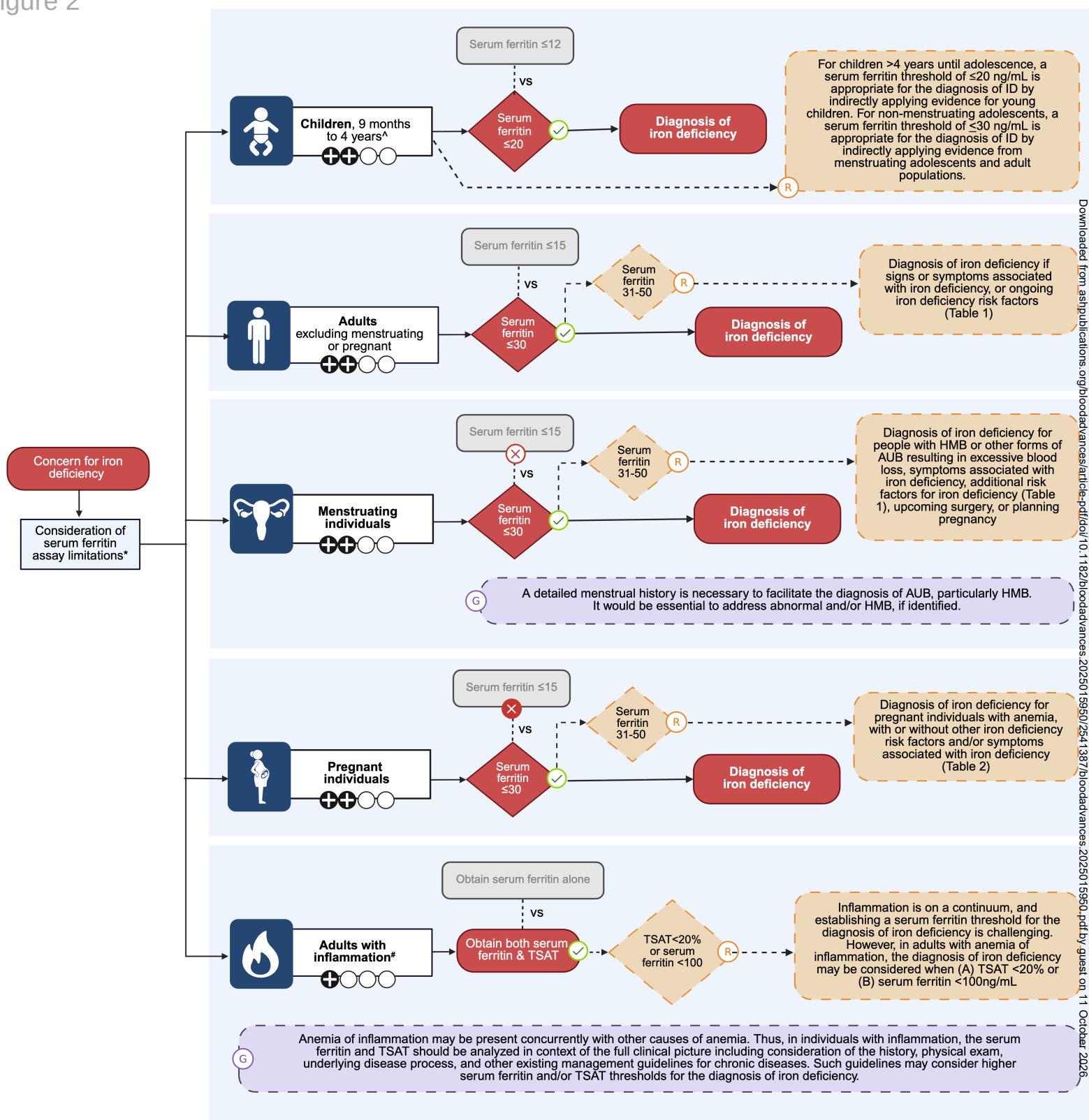
	Gastrointestinal adverse events Intravenous iron Infusion site reactions Infusion reaction, not life-threatening and life threatening Systemic infection
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Figure 1. Strength of Recommendations

Recommendation Strength										
“Recommends...”		“Recommends against...”		“Suggests...”		“Suggests against...”				
										
Interpretation of Strong Recommendations				Interpretation of Conditional Recommendations						
Patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.				Most individuals in this situation would want the suggested course of action, but many would not. Decision aids may be useful in helping patients to make decisions consistent with their individual risks, values, and preferences.					
	Clinicians	Most individuals should follow the recommended course of action. Formal decision aids are not likely to be needed to help individual patients make decisions consistent with their values and preferences.				Different choices will be appropriate for individual patients; clinicians must help each patient arrive at a management decision consistent with the patient’s values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their individual risks, values, and preferences.				
		Policymakers	The recommendation can be adopted as policy in most situations. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.				Policymaking will require substantial debate and involvement of various stakeholders. Performance measures should assess if decision making is appropriate.			
			Researchers	The recommendation is supported by credible research or other convincing judgments that make additional research unlikely to alter the recommendation. On occasion, a strong recommendation is based on low or very low certainty in the evidence. In such instances, further research may provide important information that alters the recommendations.				The recommendation is likely to be strengthened (for future updates or adaptation) by additional research. An evaluation of the conditions and criteria (and the related judgments, research evidence, and additional considerations) that determined the conditional (rather than strong) recommendation will help identify possible research gaps.		

Figure 2



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*Serum ferritin results may vary based on testing platforms used, but variation is low at low serum ferritin values. See *Serum ferritin as a diagnostic test* for additional discussion.

^AThis cutoff is for children *without* known or suspected inflammation, and a higher serum ferritin threshold may be required for patients with inflammation.

[#]Anemia of inflammation may occur in individuals with inflammatory bowel disease, infectious diseases, cancer, chronic kidney disease, heart failure, rheumatologic disorders and other inflammatory disorders.

Abbreviations: AUB, abnormal uterine bleeding; HMB, heavy menstrual bleeding; TSAT, transferrin saturation

✓ Conditional Recommendation X Conditional Recommendation Against X Strong Recommendation Against R Remark G Good Practice Statement

+ ○ ○ ○ Very Low Certainty of Evidence + + ○ ○ Low Certainty of Evidence

Figure 3. Certainty of Evidence

Evidence Certainty	
High Certainty	
	There is high confidence that the true value of the estimate of interest is on one side of a threshold of interest or within a specific range.
Moderate Certainty	
	There is moderately confidence that that the true value of the estimate of interest is on one side of a threshold of interest or within a certain range. The true value of the estimate may deviate slightly from the target of the certainty rating (i.e. may possibly fall in a different range).
Low Certainty	
	There is low confidence that that the true value of the estimate of interest is on one side of a threshold of interest or within a certain range. The true value of the estimate may deviate from the target of the certainty rating (i.e. likely fall in a different range).
Very Low Certainty	
	There is low confidence that that the true value of the estimate of interest is on one side of a threshold of interest or within a certain range. The true value of the estimate may deviate from the target of the certainty rating (i.e. likely fall in a different range).