Iron Deficiency in the United States: Limitations in Guidelines, Data, and Monitoring of Disparities

Maria Elena D. Jefferds, PhD, Zuguo Mei, MD, MPH, Yaw Addo, PhD, MS, Heather C. Hamner, PhD, MS, MPH, Cria G. Perrine, PhD, Rafael Flores-Ayala, DrPH, Christine M. Pfeiffer, PhD, and Andrea J. Sharma, PhD, MPH

Iron deficiency and the more severe sequela, iron deficiency anemia, are public health problems associated with morbidity and mortality, particularly among pregnant women and younger children. The 1998 Centers for Disease Control and Prevention recommendations for prevention and control of iron deficiency in the United States is old and does not reflect recent evidence but is a foundational reference for many federal, clinical, and program guidelines.

Surveillance data for iron deficiency are sparse at all levels, with critical gaps for pregnant women and younger children. Anemia, iron deficiency, and iron deficiency anemia are often conflated but should not be. Clinical guidelines for anemia, iron deficiency, and iron deficiency anemia give inconsistent recommendations, causing nonsystematic assessment of iron deficiency. Screening for iron deficiency typically relies on identifying anemia, despite anemia's low sensitivity for iron deficiency. In the National Health and Nutrition Examination Survey, more than 70% of iron deficiency is missed among pregnant women and children by relying on hemoglobin for iron deficiency screening.

To improve assessment and diagnosis and strengthen surveillance, better and more complete data and updated foundational guidance on iron deficiency and anemia are needed that consider new evidence for measuring and interpreting laboratory results. (*Am J Public Health*. 2022;112(S8):S826–S835. https://doi.org/10.2105/AJPH.2022.306998)

AJPH Supplement 8, 2022, Vol 112, No. S8

Iron deficiency is associated with increased morbidity and mortality among high-risk population groups, particularly pregnant women and younger children.[1–4] US foundational guidance on preventing and controlling iron deficiency is dated or inconclusive,[5–8] and public health surveillance is limited. The US Preventive Services Task Force reports that there are insufficient data to recommend routine screening for iron deficiency in the absence of anemia.[7,8]

We describe the importance of adequate iron status for individuals, limitations in the Centers for Disease Control and Prevention's (CDC's) *Recommendations to Prevent and Control Iron Deficiency in the United States*,[5] evidence gaps, and barriers to improving surveillance. We also provide the prevalence of anemia, iron deficiency, and iron deficiency anemia for pregnant women and younger children based on available data, and we highlight efforts to strengthen surveillance estimates among high-risk groups.

During the first 1000 days of life, from pregnancy to a child's second birthday, iron requirements increase substantially to support blood volume expansion in pregnancy, build iron stores in the infant, and aid growth and brain development. Two thirds of the body's iron is stored in red blood cells as hemoglobin, which is used for oxygen transport, with the remaining one third used as a necessary cofactor for many enzymes affecting metabolism, immunity, and neurotransmitters.[9]

During pregnancy, red blood cell production increases about 40%, with a direct association between blood volume expansion and fetal growth.[10] Furthermore, the majority of child brain growth and development happens before age 2.[11] Iron is a key determinant of neural development, affecting

brain structures, neurotransmitter systems, and myelination of nerve fibers. When iron stores are low, iron is preferentially used for hemoglobin synthesis, leaving the brain at risk for the adverse effects of iron deficiency even in the absence of anemia.[3,12–14] Recent evidence also suggests that iron deficiency may be associated with reduced efficacy of some childhood vaccinations.[15] Among adults, iron deficiency is associated with reduced physical productivity and work capacity.[4]

Serum ferritin is an indicator of iron stores. As ferritin levels decline, hemoglobin concentration is reduced to an anemic level only at the end stage of severe iron deficiency (Figure 1). Recent evidence suggests that many pregnant women may have undiagnosed nonanemic iron deficiency.[17,18] Identifying and treating iron deficiency early may, therefore, prevent the long-term adverse effects associated with unrecognized deficiency[3,13] and stop the progression and more serious consequences associated with severe iron deficiency anemia. Anemia during pregnancy can result in poor fetal growth, preterm birth, and low birth weight for the infant, and risk of death for the mother and baby increases with anemia severity.[1,2,19,20]

Consequently, practices to assess anemia often focus on the prevention of severe shorter-term outcomes, such as risks associated with hemorrhage in childbirth, severe maternal morbidity, and mortality.[21]

Because iron deficiency is a leading, but not the only, cause of anemia,[4,19] iron deficiency, iron deficiency anemia, and anemia are frequently conflated, which is problematic. Furthermore, the criteria to diagnose iron deficiency, iron deficiency anemia, and anemia varies (Table A, available as a supplement to the online version of this article at https://www.ajph.org). Anemia is often used as a proxy for iron deficiency or iron deficiency anemia,[7,8] given the low cost and ease by which hematologic indicators can be measured with a point-of-care test. This practice persists despite more than 2 decades of evidence indicating that hemoglobin is not an efficient predictor of iron deficiency in the United States.[5] Relying on anemia screening leaves early stages of treatable iron deficiency unidentified and untreated; consequently, longer-term adverse outcomes of iron deficiency, such as impaired cognitive and motor development, may go unchecked.

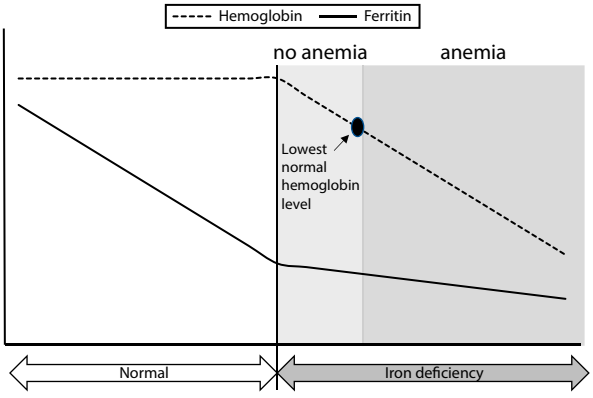

FIGURE 1— Relationship Between Ferritin and Hemoglobin

Source. Adapted from Guthrie and Picciano.[16]

Studies indicate that universal iron deficiency screening using ferritin may be cost effective compared with no screening or targeted screening.[22,23] The US Preventive Services Task Force guidelines focus on iron deficiency anemia screening and iron supplementation among asymptomatic pregnant women and children aged 6 to 24 months, not on iron deficiency.[7,8] Furthermore, foundational guidelines on screening for anemia, iron deficiency, and iron deficiency anemia are outdated[5,6] or inconclusive[7,8] and do not follow recent updated World Health Organization (WHO) guidance.[4,19] As a result, US clinical guidelines and practices vary widely.[1,6–8,24–29]

National prevalence data on anemia, iron deficiency, and iron deficiency anemia among infants, younger children, and pregnant women are limited. Prevalence data are almost nonexistent at the state and local levels, including, in the highest-risk subgroups (e.g., minority racial/ethnic groups and people with low incomes), infants who are exclusively breastfed and people who are in the third trimester of pregnancy.[24,30,31] Furthermore, the biochemical indicators and diagnostic thresholds used in clinical and surveillance settings vary, and they measure different aspects of iron metabolism; this creates inconsistency and complexity in understanding US iron status.[32–34] For example, Healthy People 2030 monitors total body iron index (TBII), which is calculated from ferritin and soluble transferrin receptor (sTfR) concentrations,[35] whereas sTfR has limited availability in clinical settings. Data sparsity and inconsistency limit the ability to monitor trends, direct interventions, evaluate programs and policies, reduce health inequities, and inform guidelines.

OUTDATED IRON DEFICIENCY GUIDANCE

The 1998 CDC recommendations for prevention and control of iron deficiency in the United States[5] is a foundational reference for many federal, clinical, and program guidelines[1,7,8,27,29]; however, it does not reflect the evidence available for both primary and secondary prevention of iron deficiency. The recommendations, published almost 25 years ago, were based on the recommendations of a 1993 Institute of Medicine report,[6] a 1994 expert panel convened by the CDC, and input from multidisciplinary experts. With the release of the *2020–2025 Dietary Guidelines for Americans*, which for the first time includes comprehensive guidelines for infants and children younger than 2 years, guidance on primary prevention of iron deficiency centering on diet has been recently reviewed and updated.[36] However, there remain key areas that lack updated foundational guidance for assessment and diagnosis of iron deficiency, including primary laboratory tests, thresholds defining deficiency, and interpretation of results. These are critical for informing and updating screening guidance, as current guidance relies on hematologic indicators known to lack sensitivity in identifying iron deficiency and focuses only on end-stage iron deficiency anemia, and so misses treatable iron deficiency.

Biomarkers to Assess Iron Status

Despite stating that serum ferritin is the most specific indicator available of depleted iron stores, the CDC recommendations propose multiple iron biomarkers reflecting various aspects of iron metabolism, including iron depletion, iron transport, iron-deficient erythropoiesis, and iron deficiency anemia, resulting in differences in iron deficiency identification and, consequently, clinical decisions and population prevalence (Table A).[5] Unclear criteria for defining iron deficiency increases complexity and limits consistency in tests used and diagnosis, so that clinical iron assessment in the United States is not systematic.[32–34] Recent reviews conclude that ferritin and hemoglobin are important or recommended when measuring uncomplicated iron deficiency (no inflammation or infection),[37] and other reviews additionally recommend C-reactive protein (CRP) in the context of inflammation.[14,38] In 2020, after following an evidence-based methodology,[39] the WHO updated their guidance recommending ferritin to assess the iron status of individuals and populations.[4]

Thresholds to Define Iron Deficiency

CDC recommendations for ferritin thresholds to define iron deficiency specify 15 or less micrograms per liter (μg/L) among people older than 6 months.[5] No rationale for this threshold among children is provided, and for women a single publication examining ferritin and bone marrow is cited. The American College of Obstetricians and Gynecologists recently increased their recommended ferritin threshold to define iron deficiency among pregnant women as from less than 10 μg/L to less than 30 μg/L,[1] based on a 90% probability that iron stores are depleted when ferritin is less than 30 μg/L, even in the absence of anemia.[38] In the 2020 guideline, the WHO determined that insufficient data were available to revise the ferritin thresholds of less than 12 μg/L for children younger than 5 years and less than 15 μg/L for individuals aged 5 years and older.[4] The WHO includes a ferritin threshold of less than 15 μg/L for pregnant women in the first trimester but no thresholds for later pregnancy. Furthermore, the WHO concluded that all the thresholds were supported by a low to very low certainty of evidence.

More recent publications have identified methods to derive ferritin thresholds based on physiologically linked processes reflecting multiple indicators of iron status and metabolism, such as the onset of iron-deficient erythropoiesis or upregulation of iron absorption from the diet.[40–44] Results obtained using these methods suggest that ferritin thresholds among healthy populations could be higher to identify treatable iron deficiency than those currently recommended by the WHO and the CDC. Evidence used to calculate TBII warrants revisiting, as the equation was validated in a small number of adults and the cutoff of less than 0 milligrams per kilogram[45] may need to be reexamined for pregnant women and children.

Influence of Inflammation and Infection

Ferritin is a positive acute phase protein strongly influenced by inflammation and infection that results in elevated ferritin values that may mask true iron deficiency.[4,5] CDC recommendations do not provide guidance on interpreting the effect of inflammation or infection on ferritin concentrations or using alternative indicators—guidance that is necessary for correctly interpreting results. Inflammation is common and thus may be especially important for those at high risk for both iron deficiency and inflammation or infection, such as younger children and those who are pregnant,

experience underweight or obesity, or have other chronic conditions.[46–48] Furthermore, acute phase proteins are known to increase with gestational age,[49,50] suggesting that when ferritin is used for testing, unidentified iron deficiency might be even higher among pregnant women in the second and third trimesters of pregnancy. Updated WHO guidance recommends that ferritin be assessed along with measures of inflammation (CRP and α-1-acid glycoprotein [AGP]) and that those assessing ferritin values account for the influence of inflammation and infection in both clinical and public health settings by following one of several suggested approaches.[4]

Anemia Assessment

In addition to iron deficiency guidance, the CDC has guidance on anemia assessment that needs to be revisited, considering new evidence in the decades since publication, including recommended laboratory tests, blood source, thresholds to define anemia, and interpretation of results. When screening for anemia to presumptively diagnose iron deficiency, the CDC recommends measuring either hemoglobin or hematocrit, while acknowledging that hemoglobin is the more direct and sensitive measure and that hematocrit declines only after hemoglobin has already decreased (Table A).[5]

The US Preventive Services Task Force states that there is insufficient evidence to recommend specific screening tests for iron deficiency anemia, but usually either hemoglobin or hematocrit is assessed first.[7,8] Professional medical organizations suggest measuring hemoglobin or hematocrit as a first step for anemia screening (Table A); their guidance could be driven by health objectives other than that of primarily identifying iron deficiency. For example, anemia during childbirth decreases tolerance for blood loss during delivery and increases the risk of hemorrhagic shock, cardiovascular failure, blood transfusion, and infection.[21,51]

Hemoglobin and hematocrit are frequently listed as interchangeable, but these indicators measure different hematologic processes. Hemoglobin is a direct measure of the iron-containing protein in red blood cells, which is critical for both red blood cell production and oxygen delivery to tissues. Hematocrit is a measure of the proportion of whole blood filled by red blood cells; red blood cell volume can also be influenced by other nutritional deficiencies, disease processes, and genetic blood disorders.[19] A recent study looked at the electronic health records (EHRs) of 1045 pregnant women with anemia who had both hemoglobin and hematocrit values and were assessed on the same day and seen in the first trimester. The study found that the concordance in identifying anemia with both tests was 45% and that agreement by anemia severity (i.e., mild; moderate or severe) was 37%.[52] Similar findings have been reported for other population groups in the United States, such as men in the military.[53] If hemoglobin and hematocrit are used interchangeably, they will frequently diagnose different people with anemia, leaving anemia and iron deficiency untreated in some individuals. Furthermore, prevalence estimates of anemia will differ depending on definitions. WHO 2017 guidance focuses primarily on hemoglobin to assess anemia.[19]

The CDC's recommended hemoglobin thresholds to define anemia for most population groups vary slightly from the WHO's guidance, whereas the recommendations for adjusting hemoglobin concentrations for elevation and smoking are the same (Table A). The WHO is in the process of reexamining evidence for the use of hemoglobin to assess anemia among individuals and populations to update their guideline. Since 2017, updated evidence has been presented at WHO technical consultations and during guideline development group meetings on analyzers and point-of-care devices (both invasive and noninvasive),[54,55] blood sources in different settings,[54,56] and adjustments to hemoglobin concentrations for elevation and smoking,[57,58] as well as for thresholds to define anemia for various population groups,[59,60] among other topics. Updating foundational guidance, systematizing recommendations on assessment and interpretation of laboratory results, and addressing guidance and data gaps can improve measurement and diagnosis and strengthen surveillance and prevalence estimates.

SURVEILLANCE GAPS AND PREVALENCE

National and state-level surveillance data gaps limit the ability to describe the problems of anemia and iron deficiency among high-risk population groups. The National Health and Nutrition Examination Survey (NHANES) produces nationally representative prevalence estimates of anemia and iron deficiency published in 2-year cycles, and these data are used to monitor the iron indicators for Healthy People 2030.[35] There is currently no state surveillance system producing state representative estimates for either anemia or iron deficiency, although state-level anemia data (and data for the District of Columbia, US territories, and Indian tribal organizations) are available every

2 years for low-income pregnant and postpartum women and children included in the Special Supplemental Nutrition Program for Women, Infants, and Children Participant and Program Characteristics survey (WIC-PC).[29]

NHANES measures hemoglobin, ferritin, sTfR, and CRP, but the number of children aged 12 to 23 months included in each 2-year cycle is small (~150) and no blood is collected among infants younger than 12 months; dietary transitions are known to be associated with increased risk of iron deficiency among children younger than 24 months.[61,62] NHANES stopped oversampling pregnant women in 2007 to 2008; sample sizes during each 2-year cycle are so small (~50 women) that reliable estimates by race and Hispanic origin or trimester can only be produced by combining data over approximately 10 years. Sample sizes for pregnant women and children aged 12 to 23 months limit the ability to monitor trends, particularly among higher-risk subgroups, and even with combining multiple survey cycles many estimates are still considered unreliable and not reportable. Oversampling pregnant women and younger children is a possible strategy, but feasibility needs to be determined.

The risk of both anemia and iron deficiency increases with gestational age, but the trimester of pregnancy is no longer collected after NHANES 2013–2014. Including pregnancy trimester in future NHANES cycles would support the monitoring of trends in disparities that occur in the third trimester. Because of funding gaps, iron indicators were not measured in some years (e.g., no ferritin and sTfR assessment during NHANES 2011–2014) or were not measured in younger children (e.g., no sTfR assessment among children younger than 3 years in NHANES 1999–2002). Similarly, CRP has not been measured consistently in all age groups over time, limiting the ability to adjust for inflammation and infection, particularly among children. Data on AGP has been lacking, but surplus specimens from NHANES 2015–2018 are being analyzed for AGP, and both CRP and AGP are now assessed in NHANES 2021–2022. Geographic location data are restricted to reduce risk of disclosure, so adjusting for the influence of elevation on hemoglobin values is challenging, potentially limiting identification of anemia among those residing at higher elevations.[5]

Anemia and Iron Deficiency Prevalence

For national anemia and iron deficiency prevalence estimates among pregnant women, NHANES data from 1999 to 2010 and from 2015 to 2018 show a positive increasing trend in anemia (*P* value for trend = .046; Table 1; supplementary text describes methods, available as a supplement to the online version of this article at https://www.ajph.org). The WHO defines public health problem severity thresholds for anemia based on hemoglobin[19] and iron deficiency based on ferritin[4] (Table A). This anemia prevalence meets the criteria for a mild public health problem.[19] During the same period, iron deficiency (inflammation-adjusted ferritin[63]) trends show no improvement (*P* for trend = 0.26), signifying a moderate public health problem. The prevalence of iron deficiency identified by ferritin was double that of TBII. Among those with iron deficiency identified by ferritin, inflammation-adjusted ferritin, or TBII, the percentages of women who also had anemia were identified. For those identified by ferritin, 19.5% (95% confidence interval [CI] = 13.1, 27.4) had anemia; by inflammation-adjusted ferritin, 19.5% (95% CI = 13.3, 27.0) had anemia; and by TBII, 30.4% (95% CI = 19.9, 42.6) had anemia. This indicates that approximately 70% to 80% or more of pregnant women with treatable iron deficiency are missed by relying on hemoglobin alone as a screen for iron deficiency.

There are important disparities by race and Hispanic origin and trimester of pregnancy (Table 1). Both anemia and iron deficiency are highest among non-Hispanic Black women and third trimester pregnant women, with iron deficiency prevalence for both indicating moderate public health problems. Data are too limited to report prevalence by trimester among race and Hispanic origin groups. Overall, iron deficiency anemia was rare (inflammation-adjusted ferritin and hemoglobin = 4.3% 95% CI = 3.0, 6.3).

Among children aged 12 to 23 months, anemia varied little between NHANES 2003–2010 and 2015–2018 (*P* for trend = .43) and is indicative of a mild public health problem (Table 2; supplementary text describes methods). Trends in iron deficiency (ferritin < 15 μg/L) were also stable over that period (*P* for trend = .10). Among the 563 children aged 12 to 23 months in NHANES 2003–2006 and 2015–2018 where CRP was measured, iron deficiency (ferritin < 15 μg/L) was 16.6% (95% CI = 13.2, 20.6) and inflammation-adjusted iron deficiency (inflammation-adjusted ferritin[63] < 15 μg/L) was 27.4% (95% CI = 22.9, 32.2), with the latter meeting the criteria of a moderate public health problem. Not using inflammation-adjusted ferritin among children aged 12 to 23 months results in a meaningful amount of treatable iron deficiency being missed in this group.

Using a physiologically based ferritin threshold of less than 20 μg/L to identify

TABLE 1— Prevalence of Anemia per Hemoglobin and Iron Deficiency per Ferritin, Inflammation-Adjusted Ferritin, and Total Body Iron Index Among Pregnant Women Aged 15–49 Years: United States, NHANES 1999–2010 and 2015–2018

	No.	Anemia, % (95% CI)	Iron Deficiency (Ferritin < 15 µg/L),[a] % (95% CI)	Iron Deficiency (Ferritin adjusted < 15 µg/L),[b] % (95% CI)	Iron Deficiency (TBII < 0 mg/kg),[c] % (95% CI)
Total (1999–2010, 2015–2018)[d]	1371	7.5 (5.5, 10.0)	20.9 (17.7, 24.5)	22.7 (19.4, 26.4)	10.8 (8.7, 13.3)
Survey years					
1999–2002	567	5.3 (2.8, 8.9)	16.5 (12.4, 21.3)	20.0 (15.0, 25.7)	8.5 (6.1, 11.5)
2003–2006	585	6.6 (3.0, 12.4)[e]	22.4 (17.3, 28.1)	23.0 (17.9, 28.7)	13.2 (9.8, 17.3)
2007–2010	113	9.6 (4.7, 17.0)	20.8 (12.7, 31.1)	21.4 (13.4, 31.4)	8.6 (3.1, 18.1)[e]
2015–2018	106	11.1 (5.8, 18.6)	26.9 (16.4, 39.6)	28.5 (18.3, 40.6)	13.3 (7.1, 22.0)
Trimester[d]					
1st	178	2.3 (0.5, 6.4)[e]	5.2 (2.4, 9.9)[e]	5.2 (2.4, 9.9)[e]	3.3 (1.1, 7.5)[e]
2nd	345	4.3 (1.3, 10.0)[e]	17.6 (12.0, 24.6)	18.1 (12.4, 25.0)	8.6 (5.0, 13.5)
3rd	323	12.4 (7.2, 19.6)	33.6 (25.9, 42.0)	34.6 (26.8, 42.9)	20.1 (14.0, 27.5)
Unknown	525	8.3 (5.5, 11.9)	21.8 (16.7, 27.6)	24.9 (19.6, 30.8)	10.3 (7.2, 14.2)
Race and Hispanic origin[d]					
Non-Hispanic White	570	3.6 (1.6, 6.9)[e]	15.9 (11.8, 20.7)	17.5 (13.0, 22.8)	7.7 (5.3, 10.7)
Non-Hispanic Black	222	18.0 (12.0, 25.3)	32.7 (23.7, 42.7)	34.8 (25.9, 44.6)	17.4 (11.2, 25.2)
Mexican American	400	7.4 (4.0, 12.5)	25.6 (20.6, 31.1)	27.0 (21.9, 32.5)	14.0 (9.8, 19.1)
Other	179	11.0 (5.5, 19.0)	22.4 (14.2, 32.6)	24.9 (16.6, 34.9)	12.1 (6.1, 20.8)

Note. CDC = Centers for Disease Control and Prevention; CI = confidence interval; NHANES = National Health and Nutrition Examination Survey; TBII = total body iron index. Counts (No.) are unweighted. Anemia defined as smoking-adjusted hemoglobin < 11.0 grams per deciliter (g/dL) during first, third, or unknown trimester, and < 10.5 g/dL during second trimester. Trimester was not collected during 2015–2018, thus all are categorized as unknown. Hemoglobin is not elevation adjusted, as NHANES does not report these data. Smoking adjustments and trimester thresholds to define anemia and thresholds to define iron deficiency using serum ferritin are based on CDC.[5] Ferritin and soluble transferrin receptor were not assessed during 2011–2014. All analyses were weighted and accounted for the complex survey design.

[a]Thresholds to define iron deficiency from CDC. Ferritin was not inflammation adjusted.[5]
[b]Thresholds to define iron deficiency from CDC.[5] Ferritin inflammation adjusted using regression-based approach with C-reactive protein based on Namaste et al.[63]
[c]TBII based on Cook et al.[45]
[d]All survey years combined.
[e]Estimate considered unreliable based on National Center for Health Statistics Data Presentation Standards for Proportions (www.cdc.gov/nchs/data/series/sr_02/sr02_175.pdf).

iron deficiency based on new emerging evidence,[40,42] the prevalence almost doubles to 30.5%, reflecting a moderate public health problem even before adjusting for inflammation. Among those with iron deficiency identified by ferritin less than 15 µg/L, only 12.3% (95% CI = 6.6, 20.3) also had anemia; by ferritin less than 20 µg/L, 7.1% (95% CI = 3.9, 11.7) had anemia; by TBII, 18.5% (95% CI = 10.3, 29.4) had anemia. These findings indicate that more than 80% to 90% of children with treatable iron deficiency are missed by relying on hemoglobin alone to screen for iron deficiency.

Disparities by race and Hispanic origin in anemia and iron deficiency are evident, with the highest anemia prevalence among non-Hispanic Black children (10.7%), signifying a mild public health problem. Mexican American children had the highest iron deficiency prevalence across all indicators, indicating a moderate public health problem (Table 2). Overall, iron deficiency anemia was rare (2.0%; 95% CI = 1.0, 3.5).

Alternatives for Pregnancy Surveillance

Because iron deficiency surveillance during pregnancy is limited, alternative data sources, such as WIC-PC and EHRs, may help fill data gaps. WIC-PC, conducted by the US Department of Agriculture every other year, is a census of persons certified to receive WIC.[64] Anemia, not iron deficiency, screening is part of WIC certification; hemoglobin or hematocrit is reported from clinical

TABLE 2— Prevalence of Anemia per Hemoglobin and Iron Deficiency per Ferritin (Different Thresholds) and Total Body Iron Index Among Children Aged 12–23 Months: United States, NHANES 2003–2010 and 2015–2018

	No.	Anemia, % (95% CI)	Iron Deficiency (Ferritin < 15 µg/L)[a] % (95% CI)	Iron Deficiency (Ferritin < 20 µg/L),[b] % (95% CI)	Iron Deficiency (TBII < 0 mg/kg),[c] % (95% CI)
Total (2003–2010, 2015-2018)[d]	881	4.7 (3.4, 6.4)	16.2 (13.4, 19.4)	30.5 (27.3, 34.0)	10.3 (8.1, 12.8)
Survey years					
2003–2006	295	4.6 (1.9, 9.2)[e]	18.2 (12.9, 24.5)	30.9 (24.8, 37.5)	14.2 (9.1, 20.6)
2007–2010	320	3.6 (1.9, 6.3)	17.0 (12.8, 22.0)	31.3 (25.5, 37.5)	8.6 (4.9, 13.6)
2015–2018	266	6.0 (3.4, 9.5)	13.7 (9.0, 19.6)	29.5 (24.1, 35.4)	6.5 (3.7, 10.3)
Race and Hispanic origin[d]					
Non-Hispanic White	276	2.4 (1.0, 5.0)	14.1 (9.7, 19.5)	31.5 (25.9, 37.4)	7.1 (4.0, 11.5)
Non-Hispanic Black	207	10.7 (6.7, 16.0)	12.1 (7.5, 18.1)	20.6 (14.7, 27.7)	11.1 (6.6, 17.0)
Mexican American	249	4.1 (2.0, 7.4)[e]	23.6 (18.4, 29.5)	36.3 (30.3, 42.7)	15.1 (10.9, 20.1)
Other	149	7.7 (2.9, 16)[e]	18.3 (11.2, 27.4)	29.7 (21.1, 39.6)	14.2 (8.5, 21.7)

Note. CDC = Centers for Disease Control and Prevention; CI = confidence interval; NHANES = National Health and Nutrition Examination Survey; TBII = total body iron index. Counts (No.) are unweighted. Hemoglobin is not elevation adjusted, as NHANES does not report these data. Threshold to define anemia based on CDC.[5] Soluble transferrin receptor was not assessed during 1999–2002 and 2011–2014. C-reactive protein was not assessed 1999–2002 and 2007–2010. All analyses were weighted and accounted for the complex survey design.

[a]Ferritin not inflammation adjusted. Thresholds to define iron deficiency based on CDC.[5]
[b]Ferritin not inflammation adjusted. Thresholds to define iron deficiency based on Mei Z et al.[42]
[c]TBII based on Cook et al.[45]
[d]All survey years combined.
[e]Estimate considered unreliable based on National Center for Health Statistics Data Presentation Standards for Proportions (www.cdc.gov/nchs/data/series/sr_02/sr02_175.pdf).

documentation in a specified time or measured at the WIC clinic.[29] Data limitations include that they are not representative of all pregnant women in the United States, nor all pregnant women who meet income eligibility for WIC. Benefits include that sample sizes are large and can provide state-based estimates of anemia stratified by demographic characteristics (e.g., in 2018 overall the WIC-PC sample size was 609 775 pregnant women[31] compared with 106 pregnant women in NHANES 2015–2018).

In an analysis of WIC-PC trends, anemia among pregnant women showed a steady increase in prevalence from 10.1% in 2008 to 11.4% in 2018,[31] indicating a mild public health problem overall. Across 56 WIC state agencies (states and territories), a significant increase in prevalence was observed in 36 agencies, and a significant decrease was observed in 11 agencies. Consistent with NHANES, there were notable disparities by race/ethnicity and trimester of pregnancy. The highest anemia prevalence was among non-Hispanic Black women (> 20%), indicating a moderate public health problem. Among women with hemoglobin assessed in the third trimester, anemia prevalence was higher than 20% across women of all racial/ethnic groups and nearly 50% among non-Hispanic Black women. As WIC-PC reflects a population at high risk for iron deficiency and is a key source of data for pregnant women, it is important to continue monitoring these trends for pregnant and postpartum women and younger children.

EHR data can potentially answer identifiable data gaps, such as the prevalence of iron deficiency, health care provider practices, and the benefits and harms of screening and supplementation. EHR data vary in their data structure and content, (e.g., only outpatient visit data vs inpatient data, actual laboratory results or only *International Classification of Diseases* [*ICD*] diagnostic codes, data in text fields, or structured variables). Other factors that influence the availability of EHR data include clinical guidelines and workflow, protocols, processes, and practices in a given setting.

A recent analysis explored whether EHR data are a feasible data source for surveillance of anemia, iron deficiency, and iron deficiency anemia in pregnancy and provider practices[52] and for

filling data gaps identified by the US Preventive Services Task Force.[8] Provider practices explored included screening patterns, tests ordered, use of *ICD* codes, and use of iron supplements and prescriptions. This study of 41 991 pregnant women in their first trimester found that first trimester anemia screening measured by hemoglobin or hematocrit was nearly universal (93%).

Overall, anemia prevalence was low (3%); similar to data from NHANES and WIC-PC, non-Hispanic Black women had an anemia prevalence that was 2 to 5 times (10.9%) higher than did any other racial/ethnic group. Among pregnant women with anemia, less than 19% had ferritin assessed; among those without anemia, about 3% had it assessed. Less than 0.1% had CRP assessed, limiting the ability to account for the influence of inflammation or infection on ferritin. Among women with iron status assessed, 90% had ferritin assessed. It is unknown why more than 80% of women with anemia did not have ferritin measured but providers potentially assumed a presumptive diagnosis of iron deficiency anemia.[1]

Prescribing iron supplementation or advice for over-the-counter supplementation was not readily available in the EHR data. Laboratory test results were required, as the use of *ICD* codes was not a reliable indicator of laboratory-confirmed anemia prevalence. Among those with measured ferritin, regardless of anemia status, 48% had iron deficiency (i.e., ferritin of < 15 µg/L). Among women with both a determination of anemia and a measure of ferritin, the prevalence of iron deficiency and iron deficiency anemia was 27% and 7%, respectively.[52] The study concludes that EHR may potentially be used as a surveillance source for anemia. However, a standard case definition of anemia is required (e.g., low hemoglobin, low hematocrit, or both low).[52] With scant and selective screening for iron deficiency, the study concludes that EHR data cannot be used for surveillance of first trimester iron deficiency based on current practices in this EHR setting.

For EHR data to be used for surveillance of iron deficiency and iron deficiency anemia in pregnancy, the following are needed: laboratory test results, a systematic assessment of iron status, and the use of clear and consistent case definitions. An additional data source to explore to confirm whether data availability and provider practices differ in a larger EHR data source is IQVIA. This source has recent ambulatory EHR data that is national in scope and includes more than 80 million patients (IQVIA E360TM SaaS Platform; https://bit.ly/3KEjOov).

Another possibility is to explore working with clinical settings that serve higher-risk populations as a source of data (either existing routinely available data or primary data collection), such as federally qualified health centers or others, for iron deficiency and iron deficiency anemia prevalence; screening, diagnosis, and treatment practices; and over-the-counter micronutrient supplementation prescribing and dispensing practices. Laboratory innovations, such as the development of point-of-care ferritin and CRP devices, if the Food and Drug Administration approved and adopted them, could result in changes to clinical practices that increase the screening and diagnosis of iron deficiency. The federal government working with partners and clinical professional organizations could also strengthen and systematize screening practices and surveillance. Ultimately, a viable data source for surveillance will require a consistent assessment of iron status and case definitions.

CONCLUSIONS

Iron deficiency, iron deficiency anemia, and anemia assessment are related and can reflect a spectrum of severity. However, the lack of updated and specific guidelines results in treating them as interchangeable proxies for screening, which is problematic because it results in the pragmatic use of anemia to assess iron deficiency even though anemia is not sensitive for identifying iron deficiency in the United States versus directly assessing iron status. Consequently, results do not identify, and thus do not address, the vast majority of treatable iron deficiency in the US context. Foundational guidelines influencing clinical practice recommendations for assessment and diagnosis of iron deficiency need to be updated. Given the age of the CDC guideline, the available evidence relevant to the assessment and diagnosis of iron deficiency warrants revisiting the guidelines, especially those for laboratory assessment, thresholds for ferritin and hemoglobin (including by gestational age), and data adjustments and interpretation. Based on CDC standards required to develop evidence-based guidelines,[65] the first step to assess the need for an updated foundational guideline for assessment and diagnosis of iron deficiency and anemia has been met. AJPH

ABOUT THE AUTHORS

At the time of writing, Maria Elena D. Jefferds, Zuguo Mei, Yaw Addo, Heather C. Hamner, Cria G. Perrine, Rafael Flores-Ayala, and Andrea J. Sharma were with the National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention (CDC), Atlanta, GA. Christine M. Pfeiffer was with the Nutritional Biomarkers Branch, National Center for Environmental Health, CDC, Atlanta.

Note. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC or the Department of Health and Human Services.

CORRESPONDENCE

Correspondence should be sent to Maria Elena D. Jefferds, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 4770 Buford Hwy NE, Mail-Stop S107-5, Atlanta, GA 30341-3717 (e-mail: mnj5@cdc.gov). Reprints can be ordered at http://www.ajph.org by clicking the "Reprints" link.

PUBLICATION INFORMATION

Full Citation: Jefferds MED, Mei Z, Addo Y, et al. Iron deficiency in the United States: limitations in guidelines, data, and monitoring of disparities. *Am J Public Health*. 2022;112(S8):S826–S835.

Acceptance Date: June 4, 2022.

DOI: https://doi.org/10.2105/AJPH.2022.306998

CONTRIBUTORS

M. E. D. Jefferds and A. J. Sharma wrote the first draft, are cofirst authors, and contributed equally to the article. A. J. Sharma analyzed the data. All authors participated fully in subsequent writing, revising, and approved the final version.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

HUMAN PARTICIPANT PROTECTION

No protocol approval was necessary because this work did not involve human participants.

REFERENCES

1. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins–Obstetrics. Anemia in pregnancy: ACOG Practice Bulletin, number 233. *Obstet Gynecol.* 2021;138(2):e55–e64. https://doi.org/10.1097/AOG.0000000000004477
2. Georgieff MK. Long-term brain and behavioral consequences of early iron deficiency. *Nutr Rev.* 2011;69(suppl 1):S43–S48. https://doi.org/10.1111/j.1753-4887.2011.00432.x
3. McCarthy EK, Murray DM, Hourihane JOB, Kenny LC, Irvine AD, Kiely ME. Behavioral consequences at 5 y of neonatal iron deficiency in a low-risk maternal-infant cohort. *Am J Clin Nutr.* 2021;113(4):1032–1041. https://doi.org/10.1093/ajcn/nqaa367
4. World Health Organization. *WHO Guideline on Ferritin Concentrations to Assess Iron Status in Individuals and Populations.* 2020. Available at: https://apps.who.int/iris/bitstream/handle/10665/331505/9789240000124-eng.pdf?sequence=1&isAllowed=y. Accessed September 1, 2022
5. Centers for Disease Control and Prevention. Recommendations to prevent and control iron deficiency in the United States. *MMWR Recomm Rep.* 1998;47(RR-3):1–29.
6. Earl RO, Woteki CE, Calloway DH; US Institute of Medicine, eds. *Iron Deficiency Anemia: Recommended Guidelines for the Prevention, Detection, and Management Among U.S. Children and Women of Childbearing Age.* Washington, DC: National Academies Press; 1993.
7. Siu AL; US Preventive Services Task Force. Screening for iron deficiency anemia in young children: USPSTF recommendation statement. *Pediatrics.* 2015;136(4):746–752. https://doi.org/10.1542/peds.2015-2567
8. Siu AL; US Preventive Services Task Force. Screening for iron deficiency anemia and iron supplementation in pregnant women to improve maternal health and birth outcomes: US Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2015;163(7):529–536. https://doi.org/10.7326/M15-1707
9. McCann JC, Ames BN. An overview of evidence for a causal relation between iron deficiency during development and deficits in cognitive or behavioral function. *Am J Clin Nutr.* 2007;85(4):931–945. https://doi.org/10.1093/ajcn/85.4.931
10. Sanghavi M, Rutherford JD. Cardiovascular physiology of pregnancy. *Circulation.* 2014;130(12):1003–1008. https://doi.org/10.1161/circulationaha.114.009029
11. Thompson RA, Nelson CA. Developmental science and the media. Early brain development. *Am Psychol.* 2001;56(1):5–15. https://doi.org/10.1037/0003-066x.56.1.5
12. Georgieff MK, Brunette KE, Tran PV. Early life nutrition and neural plasticity. *Dev Psychopathol.* 2015;27(2):411–423. https://doi.org/10.1017/S0954579415000061
13. Lozoff B, Jimenez E, Smith JB. Double burden of iron deficiency in infancy and low socioeconomic status: a longitudinal analysis of cognitive test scores to age 19 years. *Arch Pediatr Adolesc Med.* 2006;160(11):1108–1113. https://doi.org/10.1001/archpedi.160.11.1108
14. McCarthy EK, Murray DM, Kiely ME. Iron deficiency during the first 1000 days of life: are we doing enough to protect the developing brain? *Proc Nutr Soc.* 2022;81(1):108–118. https://doi.org/10.1017/S0029665121002858
15. Drakesmith H, Pasricha S-R, Cabantchik I, et al. Vaccine efficacy and iron deficiency: an intertwined pair? *Lancet Haematol.* 2021;8(9):e666–e669. https://doi.org/10.1016/S2352-3026(21)00201-5
16. Guthrie B, Picciano MF. Macronutrient minerals. In: Guthrie HA, Picciano MF, Scott A, eds., *Human Nutrition*. St. Louis, MO: Mosby Year Book; 1995:334–351.
17. Auerbach M, Abernathy J, Juul S, Short V, Derman R. Prevalence of iron deficiency in first trimester, nonanemic pregnant women. *J Matern Fetal Neonatal Med.* 2021;34(6):1002–1005. https://doi.org/10.1080/14767058.2019.1619690
18. Teichman J, Nisenbaum R, Lausman A, Sholzberg M. Suboptimal iron deficiency screening in pregnancy and the impact of socioeconomic status in a high-resource setting. *Blood Adv.* 2021;5(22):4666–4673. https://doi.org/10.1182/bloodadvances.2021004352
19. World Health Organization. Nutritional anaemias: tools for effective prevention and control. November 13, 2017. Available at: https://www.who.int/publications/i/item/9789241513067. Accessed September 1, 2022.
20. Smith C, Teng F, Branch E, Chu S, Joseph KS. Maternal and Perinatal Morbidity and Mortality Associated With Anemia in Pregnancy. *Obstet Gynecol.* 2019;134(6):1234–1244. https://doi.org/10.1097/AOG.0000000000003557
21. Zofkie AC, Garner WH, Schell RC, et al. An evidence-based definition of anemia for singleton, uncomplicated pregnancies. *PLoS One.* 2022;17(1):e0262436. https://doi.org/10.1371/journal.pone.0262436
22. Alper BS, Kimber R, Reddy AK. Using ferritin levels to determine iron-deficiency anemia in pregnancy. *J Fam Pract.* 2000;49(9):829–832.
23. Carsley S, Fu R, Borkhoff CM, et al. Iron deficiency screening for children at 18 months: a cost-utility analysis. *CMAJ Open.* 2019;7(4):E689–E698. https://doi.org/10.9778/cmajo.20190084
24. Baker RD, Greer FR. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0–3 years of age). *Pediatrics.* 2010;126(5):1040–1050. https://doi.org/10.1542/peds.2010-2576
25. Cantor AG, Bougatsos C, Dana T, Blazina I, McDonagh M. Routine iron supplementation and screening for iron deficiency anemia in pregnancy: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2015;162(8):566–576. https://doi.org/10.7326/M14-2932
26. McDonagh MS, Blazina I, Dana T, Cantor A, Bougatsos C. Screening and routine supplementation for iron deficiency anemia: a systematic review. *Pediatrics.* 2015;135(4):723–733. https://doi.org/10.1542/peds.2014-3979
27. Short MW, Domagalski JE. Iron deficiency anemia: evaluation and management. *Am Fam Physician.* 2013;87(2):98–104.
28. Wang M. Iron deficiency and other types of anemia in infants and children. *Am Fam Physician.* 2016;93(4):270–278.
29. US Department of Agriculture Food and Nutrition Service. Special Supplemental Nutrition Program for Women, Infants, and Children (WIC): bloodwork requirements. Final rule. *Fed Regist.* 1999;64(241):70173–70178.
30. Brotanek JM, Gosz J, Weitzman M, Flores G. Secular trends in the prevalence of iron deficiency among US toddlers, 1976–2002. *Arch Pediatr Adolesc Med.* 2008;162(4):374–381. https://doi.org/10.1001/archpedi.162.4.374
31. Centers for Disease Control and Prevention. Anemia among pregnant women participating in the Special Supplemental Nutrition Program for Women, Infants, and Children—United States, 2008–2018. *MMWR Morb Mortal Wkly Rep.* 2022;71(25):813–819. https://doi.org/10.15585/mmwr.mm7125a1
32. Mansour D, Hofmann A, Gemzell-Danielsson K. A review of clinical guidelines on the management of iron deficiency and iron-deficiency anemia in women with heavy menstrual bleeding. *Adv Ther.* 2021;38(1):201–225. https://doi.org/10.1007/s12325-020-01564-y
33. Peyrin-Biroulet L, Williet N, Cacoub P. Guidelines on the diagnosis and treatment of iron deficiency across indications: a systematic review. *Am J Clin Nutr.* 2015;102(6):1585–1594. https://doi.org/10.3945/ajcn.114.103366
34. Read AJ, Waljee AK, Sussman JB, et al. Testing practices, interpretation, and diagnostic evaluation of iron deficiency anemia by US primary care physicians. *JAMA Netw Open.* 2021;4(10):e2127827. https://doi.org/10.1001/jamanetworkopen.2021.27827
35. Office of Disease Prevention and Health Promotion. Healthy People 2030. US Department of Health and Human Services.

36. US Department of Agriculture; US Department of Health and Human Services. *2020–2025 Dietary Guidelines for Americans*. 9th ed. December 2020. Available at: https://www.dietaryguidelines.gov/sites/default/files/2021-03/Dietary_Guidelines_for_Americans-2020-2025.pdf. Accessed September 1, 2022.
37. Pfeiffer CM, Looker AC. Laboratory methodologies for indicators of iron status: strengths, limitations, and analytical challenges. *Am J Clin Nutr.* 2017;106(suppl 6):1606S–1614S. https://doi.org/10.3945/ajcn.117.155887
38. Breymann C, Honegger C, Hosli I, Surbek D. Diagnosis and treatment of iron-deficiency anaemia in pregnancy and postpartum. *Arch Gynecol Obstet.* 2017;296(6):1229–1234. https://doi.org/10.1007/s00404-017-4526-2
39. World Health Organization. *WHO Handbook for Guideline Development*. 2nd ed. Geneva; 2014. Available at: https://apps.who.int/iris/bitstream/handle/10665/145714/9789241548960_eng.pdf. Accessed September 1, 2022.
40. Abdullah K, Birken CS, Maguire JL, et al. Re-Evaluation of serum ferritin cut-off values for the diagnosis of iron deficiency in children aged 12–36 months. *J Pediatr.* 2017;188:287–290. https://doi.org/10.1016/j.jpeds.2017.03.028
41. Galetti V, Stoffel NU, Sieber C, Zeder C, Moretti D, Zimmermann MB. Threshold ferritin and hepcidin concentrations indicating early iron deficiency in young women based on upregulation of iron absorption. *EClinicalMedicine.* 2021;39:101052. https://doi.org/10.1016/j.eclinm.2021.101052
42. Mei Z, Addo OY, Jefferds ME, Sharma AJ, Flores-Ayala RC, Brittenham GM. Physiologically based serum ferritin thresholds for iron deficiency in children and nonpregnant women: a US National Health and Nutrition Examination Surveys (NHANES) serial cross-sectional study. *Lancet Haematol.* 2021;8(8):e572–e582. https://doi.org/10.1016/S2352-3026(21)00168-X
43. Sezgin G, Monagle P, Loh TP, et al. Clinical thresholds for diagnosing iron deficiency: comparison of functional assessment of serum ferritin to population based centiles. *Sci Rep.* 2020;10(1):18233. https://doi.org/10.1038/s41598-020-75435-5
44. Addo OY, Mei Z, Hod EA, et al. Physiologically based serum ferritin thresholds for iron deficiency in women of reproductive age who are blood donors. *Blood Adv.* 2022;6(12):3661–3665. https://doi.org/10.1182/bloodadvances.2022007066
45. Cook JD, Lipschitz DA, Miles LE, Finch CA. Serum ferritin as a measure of iron stores in normal subjects. *Am J Clin Nutr.* 1974;27(7):681–687. https://doi.org/10.1093/ajcn/27.7.681
46. Alley DE, Seeman TE, Ki Kim J, Karlamangla A, Hu P, Crimmins EM. Socioeconomic status and C-reactive protein levels in the US population: NHANES IV. *Brain Behav Immun.* 2006;20(5):498–504. https://doi.org/10.1016/j.bbi.2005.10.003
47. Ford ES, Galuska DA, Gillespie C, Will JC, Giles WH, Dietz WH. C-reactive protein and body mass index in children: findings from the Third National Health and Nutrition Examination Survey, 1988–1994. *J Pediatr.* 2001;138(4):486–492. https://doi.org/10.1067/mpd.2001.112898
48. Sjaarda LA, Radin RG, Swanson C, et al. Prevalence and contributors to low-grade inflammation in three US populations of reproductive age women. *Paediatr Perinat Epidemiol.* 2018;32(1):55–67. https://doi.org/10.1111/ppe.12409
49. Mei Z, Li H, Serdula MK, et al. C-reactive protein increases with gestational age during pregnancy among Chinese women. *Am J Hum Biol.* 2016;28(4):574–579. https://doi.org/10.1002/ajhb.22837
50. Ferguson KK, McElrath TF, Chen YH, Mukherjee B, Meeker JD. Longitudinal profiling of inflammatory cytokines and C-reactive protein during uncomplicated and preterm pregnancy. *Am J Reprod Immunol.* 2014;72(3):326–336. https://doi.org/10.1111/aji.12265
51. Peace JM, Banayan JM. Anemia in pregnancy: pathophysiology, diagnosis, and treatment. *Int Anesthesiol Clin.* 2021;59(3):15–21. https://doi.org/10.1097/AIA.0000000000000320
52. Sharma AJ, Ford ND, Bulkley JE, Jenkins LM, Vesco KK, Williams AM. Use of the electronic health record to assess prevalence of anemia and iron deficiency in pregnancy. *J Nutr.* 2021;151(11):3588–3595. https://doi.org/10.1093/jn/nxab254
53. Nguyen WB, Wyse JM, Drollinger SM, Cheng K. Anemia screening in naval aviation: is hemoglobin a better indicator than hematocrit as the primary index? *Mil Med.* 2020;185(3–4):461–467. https://doi.org/10.1093/milmed/usz243
54. Larson LM, Braat S, Hasan MI, et al. Preanalytic and analytic factors affecting the measurement of haemoglobin concentration: impact on global estimates of anaemia prevalence. *BMJ Glob Health.* 2021;6(7):e005756. https://doi.org/10.1136/bmjgh-2021-005756
55. Young MF, Raines K, Jameel F, et al. Non-invasive hemoglobin measurement devices require refinement to match diagnostic performance with their high level of usability and acceptability. *PLoS One.* 2021;16(7):e0254629. https://doi.org/10.1371/journal.pone.0254629
56. Neufeld LM, Larson LM, Kurpad A, Mburu S, Martorell R, Brown KH. Hemoglobin concentration and anemia diagnosis in venous and capillary blood: biological basis and policy implications. *Ann N Y Acad Sci.* 2019;1450(1):172–189. https://doi.org/10.1111/nyas.14139
57. Gassmann M, Mairbäurl H, Livshits L, et al. The increase in hemoglobin concentration with altitude varies among human populations. *Ann N Y Acad Sci.* 2019;1450(1):204–220. https://doi.org/10.1111/nyas.14136
58. Sharma AJ, Addo OY, Mei Z, Suchdev PS. Reexamination of hemoglobin adjustments to define anemia: altitude and smoking. *Ann N Y Acad Sci.* 2019;1450(1):190–203. https://doi.org/10.1111/nyas.14167
59. Addo OY, Yu EX, Williams AM, et al. Evaluation of hemoglobin cutoff levels to define anemia among healthy individuals. *JAMA Netw Open.* 2021;4(8):e2119123. https://doi.org/10.1001/jamanetworkopen.2021.19123
60. Ohuma EO, Young MF, Martorell R, et al. International values for haemoglobin distributions in healthy pregnant women. *EClinicalMedicine.* 2020;29-30:100660. https://doi.org/10.1016/j.eclinm.2020.100660
61. Griebler U, Bruckmüller MU, Kien C, et al. Health effects of cow's milk consumption in infants up to 3 years of age: a systematic review and meta-analysis. *Public Health Nutr.* 2016;19(2):293–307. https://doi.org/10.1017/S1368980015001354
62. Obbagy JE, English LK, Psota TL, et al. Complementary feeding and micronutrient status: a systematic review. *Am J Clin Nutr.* 2019;109(suppl_7):852s–871s. https://doi.org/10.1093/ajcn/nqy266
63. Namaste SM, Rohner F, Huang J, et al. Adjusting ferritin concentrations for inflammation: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *Am J Clin Nutr.* 2017;106(suppl 1):359S–371S. https://doi.org/10.3945/ajcn.116.141762
64. Kline N, Thorn B, Bellows D, Wroblewska K, Wilcox-Cook E. *WIC Participant and Program Characteristics 2018.* Alexandria, VA: US Department of Agriculture, Food and Nutrition Service; 2020.
65. Centers for Disease Control and Prevention. Standards required for the development of CDC evidence-based guidelines. *MMWR Suppl.* 2022;71(1):1–6. https://doi.org/10.15585/mmwr.su7101a1