Published in final edited form as:

Ann N Y Acad Sci. 2019 August ; 1450(1): 268–280. doi:10.1111/nyas.14175.

Data needed to respond appropriately to anemia when it is a public health problem

Anne M. Williams[1,2,3], **O. Yaw Addo**[2,3], **Scott D. Grosse**[4], **Nicholas J. Kassebaum**[5,6], **Zane Rankin**[5], **Katherine E. Ballesteros**[5], **Helen Elizabeth Olsen**[7], **Andrea J. Sharma**[3,8], **Maria Elena Jefferds**[3], **Zuguo Mei**[3]

[1]McKing Consulting Corporation, Atlanta, Georgia

[2]Department of Global Health, Emory University, Atlanta, Georgia

[3]Division of Nutrition, Physical Activity and Obesity, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention (CDC), Atlanta, Georgia

[4]National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC), Atlanta, Georgia

[5]The Institute for Health Metrics and Evaluation, University of Washington, Seattle, Washington

[6]Seattle Children's Hospital, Seattle, Washington

[7]The Bill and Melinda Gates Foundation, Seattle, Washington

[8]The U.S. Public Health Service Commissioned Corps, Atlanta, Georgia

Address for correspondence: Anne Williams, McKing Consulting Corporation, 2900 Chamblee Tucker Road, Building 10, Suite 100, Atlanta, GA 30341. nql3@cdc.gov.

Author contributions

All authors had substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; contributed to the drafting of the work or revising it critically for important intellectual content; have given final approval of the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Statement

This manuscript was presented at the WHO technical consultation "Use and Interpretation of Haemoglobin Concentrations for Assessing Anaemia Status in Individuals and Populations," held in Geneva, Switzerland on November 29–30 and December 1, 2017. This paper is being published individually but will be consolidated with other manuscripts as a special issue of *Annals of the New York Academy of Sciences,* the coordinators of which were Maria Nieves Garcia-Casal and Sant-Rayn Pasricha. The special issue is the responsibility of the editorial staff of *Annals of the New York Academy of Sciences,* who delegated to the coordinators preliminary supervision of both technical conformity to the publishing requirements of *Annals of the New York Academy of Sciences* and general oversight of the scientific merit of each article. The workshop was supported by WHO, the Centers for Disease Control and Prevention (CDC), the United States Agency for International Development (USAID), and the Bill & Melinda Gates Foundation. The authors alone are responsible for the views expressed in this paper; they do not necessarily represent the views, decisions, or policies of the WHO. The opinions expressed in this publication are those of the authors and are not attributable to the sponsors, publisher, or editorial staff of *Annals of the New York Academy of Sciences.*

Supporting information

Additional supporting information may be found in the online version of this article.

Competing interests

The authors declare no competing interests.

Disclosure

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Abstract

Although the proportion of anemia amenable to change varies by population, the World Health Organization (WHO) criteria used to describe the public health severity of anemia are based on population prevalences. We describe the importance of measuring iron and other etiologic indicators to better understand what proportion of anemia could be responsive to interventions. We discuss the necessity of measuring inflammation to interpret iron biomarkers and documenting anemia of inflammation. Finally, we suggest assessing nonmodifiable genetic blood disorders associated with anemia. Using aggregated results from the Global Burden of Disease 2016, we compare population prevalence of anemia with years lived with disability (YLD) estimates, and the relative contributions of mild, moderate, and severe anemia to YLD. Anemia prevalences correlated with YLD and the relative proportion of moderate or severe anemia increased with anemia prevalence. However, individual-level survey data revealed irregular patterns between anemia prevalence, the prevalence of moderate or severe anemia, and the prevalence of iron deficiency anemia (IDA). We conclude that although the WHO population prevalence criteria used to describe the public health severity of anemia are important for policymaking, etiologic-specific metrics that take into account IDA and other causes will be necessary for effective anemia control policies.

Keywords

anemia; iron deficiency anemia; disability-adjusted life years; public health significance

Introduction

Anemia is defined as a “condition in which the number of red blood cells or their oxygencarrying capacity is insufficient to meet physiologic requirements,” and is diagnosed by low blood hemoglobin (Hb) concentrations.[1–3] The health consequences of anemia adversely influence development through reduced attention spans and intelligence in children[4–6] and diminished work productivity.[7,8] Anemia is the most common blood disorder in the world,[9] disproportionally affecting children under 5 years and women of reproductive age (WRA, 15–49 years old) in low-income settings.[10–13] Substantial reductions in global anemia prevalence will require addressing the multifaceted etiology of anemia.[14–16]

The World Health Assembly target is to reduce anemia prevalence among WRA by 50% between 2012 and 2025.[17] To achieve this target, countries that are currently experiencing a 1–2% annual average rate of reduction need to achieve and maintain a 6–7% annual average rate of anemia reduction.[18] Universal iron supplementation may have contributed to the modest reduction in anemia among WRA from 1995 to 2011 (approximately 4 percentage points).[19] However, low blood Hb concentration is influenced by multiple health conditions other than inadequate iron intake such as malaria,[3] HIV,[20] inflammation,[14] gastrointestinal bleeding (e.g., intestinal parasites[12,21] or peptic ulcer disease[12]), nonmodifiable genetic blood disorders and hemoglobinopathies,[22,23] multiple micronutrient deficiencies,[24] and physiologic state (e.g., pregnancy and menstruation). Iron provided to populations without iron deficiency (ID) may lead to unnecessary health risks in the context of infection,[25,26]

because bacteria and parasites propagate in iron-rich environments. Therefore, assessment of context-specific data is required to understand and respond appropriately to the drivers of low Hb.

The World Health Organization (WHO) classifications for public health severity of anemia are based on population prevalence of low Hb.[1,3] At-risk population groups, such as women or children, with prevalence ranges of <4.9%, 5.0–19.9%, 20.0–39.9%, or ≥40.0%, are classified with a normal, mild, moderate, or severe public health problem of anemia, respectively.[3] These classifications not only describe disease burden, but are used for program prioritization and targeting. For example, in areas where anemia is a moderate or severe public health problem, global guidance suggests iron supplementation or multiple micronutrient powder provision and scheduled deworming should be carried out among vulnerable populations.[3,27,28] However, the proportion of anemia that is amenable to iron or deworming interventions is often unknown and will depend on population-specific etiology. The Global Burden of Disease (GBD) project estimates that anemia accounts for 8–9% of the years lived with disability (YLD) in the world, and is similarly constrained in the estimation of iron as an etiologic driver of anemia given the paucity of data on iron status.[11,12] Therefore, the WHO population thresholds used to describe the public health severity of anemia may be insufficient for program prioritization and targeting without simultaneously assessing population iron status.[1] The objectives of our study were twofold: (1) to examine population cutoffs for public health anemia severity using an economic metric, and (2) to describe the proportion of anemia amenable to intervention based on data that have been collected in population-based surveys.

Methods

Data sources

GBD 2016 results were accessed from the Global Health Data Exchange (GHDX, http://ghdx.healthdata.org). The GBD anemia prevalence estimates were compared with anemia-specific YLD rates, and used to illustrate the relative contributions of mild, moderate, and severe anemia on the YLD estimates. The YLD estimates depend on the prevalence of disease and the corresponding disability weights, which have been refined using two large (n ~ 30,000) international studies.[29,30] Further details on the GHDX and methods to calculate YLD are available in Appendix A (online only). The Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project has merged nationally and regionally representative nutrition survey data from multiple countries.[31] These population-based survey data were used to estimate the proportion of anemia amenable to intervention by examining the prevalence of iron deficiency anemia (IDA), and among those with anemia, the proportion with ID, evidence of recent malaria infection, genetic blood disorder, or hemoglobinopathy variants (where available). There were 24 surveys available for preschool children (6–59 months old) and 19 surveys available for WRA in the BRINDA database (www.brinda-nutrition.org).

Accounting for etiology

Etiologic indicators of anemia available in the population-based surveys in the BRINDA data set included iron status (ferritin), inflammatory markers (alpha-1-acid glycoprotein (AGP) and C-reactive protein (CRP), required to interpret ferritin concentrations), malaria status, genetic blood disorders, and hemoglobinopathies. We compare the prevalence of any anemia to the prevalence of IDA. The proportion of individuals with concomitant anemia and ID was also calculated to describe the maximum proportion of anemia that could be treated with an iron intervention, which would inform national anemia reduction strategies. We calculated the proportion of malaria among individuals with anemia, and the proportion of individuals with anemia displaying any genetic blood disorder or hemoglobinopathy variant that was measured as part of the population-based survey. Such data were available in two of the child surveys within the BRINDA data set (Malawi, 2016 and Kenya, 2010). Alpha thalassemia, sickle cell anemia (HbSS) and sickle cell trait (HbAS), and glucose-6-phosphate dehydrogenase (G6PD) deficiency were assessed in Malawi,[32] and in Kenya each of those genotypes was measured in addition to haptoglobin.[22,33]

[Correction added on July 8, 2019, after online publication: In the previous sentence, “(HbSA)” was changed to “(HbAS)”.]

Variable definitions

Anemia was defined as Hb < 110 g/L for children 6–59 months of age and <120 g/L for nonpregnant women, and individual-level moderate and severe anemia were assigned per current WHO classifications (Table 1). Hb was adjusted for smoking and altitude,[34] when those data were available (Table S1, online only). ID was defined as low ferritin, adjusted for inflammation using the BRINDA regression correction approach,[35] <12.0 μg/L for children 6–59 months of age and <15.0 μg/L for nonpregnant WRA.[36] Because there are multiple methods to address iron status in the context of inflammation, we also presented unadjusted ID for WRA, and ferritin <30 μg/L for children under 5 years who had evidence of elevated inflammatory proteins (CRP > 5 mg/L or AGP > 1 g/L).[2] IDA was defined as concomitant anemia and ID. Malaria was available among malaria-endemic countries but assessed in a variety of ways. In Malawi and Liberia, rapid diagnostic kits were used; Kenya and Cote d’Ivoire used microscopy but the malaria variable was dichotomized; and a plasma histidine-rich protein 2 test (Cellaba Pty Ltd.) was used in Cameroon.[15,32] Inflammation was defined as elevated CRP > 5 mg/L or AGP > 1 g/L.[37] Genetic blood disorder variant data were grouped to describe the magnitude of burden in Malawi and Kenya.

Results

Comparing anemia prevalence with YLD

Country-level analyses comparing anemia prevalence rate and anemia YLD rate revealed a positive correlation consistent across age groups, gender, and regions (Fig. 1). There was a clustering of countries from the African Region that fell above the trend line for females aged 15–49 years, revealing higher YLD rates compared with countries with similar anemia prevalence. The positive relationship was to be expected because YLD is the product of anemia prevalence and disability weights (Table 2). However, the slight increase in slope at

higher anemia prevalence rates illustrates the influence of moderate and severe anemia on YLD rate. The prevalence of moderate or severe anemia carries greater population burden in YLD analyses because they have substantially higher disability weights than mild anemia (Table 2). The majority of YLD within regions was attributable to moderate anemia (Fig. 2). The relatively small proportion of severe anemia contributed more to the YLD among women and children than mild anemia in the African, Eastern Mediterranean, and Southeast Asia regions (Fig. 2).

Accounting for etiology

Among BRINDA countries that had iron status and inflammatory marker data available, there were irregular patterns between anemia prevalence and IDA prevalence. These irregularities persisted when iron was not adjusted for inflammation (in WRA) or adjusted using the cutoff of <30 μg/L among children with elevated inflammatory proteins (Tables S2 and S3, online only). For example, the Bangladesh 2010 preschool child survey had the highest prevalence of anemia (83.5%), but had only 15.1% IDA, while among the three surveys reporting the next highest prevalence of anemia for preschool children (65.7–71.7%), the IDA prevalence ranged from 28.4% to 47.5%. Among the 11 countries with preschool child surveys classifying anemia as a severe public health problem (>40% prevalence of anemia), two countries had less than 20% ID among children with anemia (18.1% in Bangladesh, 2012, and 8.2% in Cambodia, 2014, see Table 3). Among the seven country surveys where anemia was categorized as a moderate public health problem, Ecuador stands out, with 24.7% prevalence of anemia among preschool children, but IDA of 16.2%, while in the other six countries IDA ranged from 0.05% to 8.8%. Malaria prevalence was available in six of the child surveys, and among children with anemia, the prevalence of recent malaria ranged from 23.1% (Kenya, 2007) to 48.1% (Malawi, 2016). Among the two child surveys that collected data on genetic blood disorder variants, more than half of children with anemia had one of these variants (61.4% in Malawi, and 59.7% in Kenya, 2010, data not shown). Cambodia had the most pronounced pattern of high anemia (>45%) and low IDA (<4%) in both children and WRA.

The public health problem of anemia among the WRA surveys were severe in four surveys where IDA ranged from 2.9% to 27.1%, moderate in eight surveys where IDA prevalence ranged from 0.9% to 16.6%, and mild in seven surveys where IDA ranged from 4.5% to 11.1% (Table 4). All surveys that had prevalence of anemia 5–19.9% (or a mild public health problem) had greater than 50% of women with anemia also having ID (Table 4). Genetic blood disorder and hemoglobinopathy variant data were unavailable for any survey targeting WRA. Although the number of surveys with malaria data was limited, children with anemia were more likely to have had recent malaria infection than women with anemia (Tables 3 and 4).

Discussion

We offer evidence to suggest that the current WHO thresholds to define anemia as a public health problem based on population prevalence may be insufficient for the purpose of guiding effective program prioritization and targeting of iron interventions. Based on the

BRINDA surveys, the median proportion of anemia amenable to iron treatment among surveys classified as having a severe public health problem of anemia was estimated to be 41.5% (range: 8.2–76.0%) for preschool children and 42.3% (range: 6.6–69.0%) for WRA. For countries classified in the lower half of this range (e.g., Bangladesh and Cambodia), national anemia policies that focus on iron delivering interventions and deworming programs may be insufficient to reduce anemia prevalence. Therefore, additional data may be critical to inform program design for effective anemia reduction. Without additional data on iron and inflammation status, as well as genetic and environmental (e.g., malaria) conditions, mounting an appropriate response to anemia is challenging. Many years have passed with too little progress in anemia reduction; however, interpreting additional data alongside Hb will enable program planners to best respond to a high burden of anemia.

Measuring Hb, iron, and inflammation biomarkers

Differentiating anemia from IDA is a vital first step for effective public health programming, but it cannot be done if Hb is measured without a more sensitive and specific measure of iron status. Using surveys from the BRINDA project as an example, approximately one-third and one-half of child and women surveys categorized as severe (>40% anemia prevalence), respectively, had IDA prevalence less than 20%, suggesting that less than half of anemia in those settings could be resolved by iron interventions. A recent meta-analysis similarly demonstrated that the proportion of anemia associated with ID was less than the previously expected 50% “rule of thumb,”[38] and varied by the level of country development.[39] The fact that the target populations for iron interventions are also more likely to have co-occurring infections, which reduce iron absorption via hepcidin regulation,[40] further hinders the effectiveness of iron interventions in reducing IDA. Although hepcidin is valuable for assessing iron status and the likelihood of iron intervention success simultaneously,[41] hepcidin cutoffs to define ID are not standardized for population-based surveys.

Inflammation regardless of iron status is associated with anemia.[15,16] Therefore, measuring and accounting for inflammation is important above and beyond the utility for interpreting iron status.[35,42,43] Take the example of Cote d’Ivoire, where approximately one in two women had anemia, one in seven had IDA, and one in three had elevated inflammatory proteins (Table 4). In this type of context, anemia reduction programs may also need to prioritize strategies that reduce nonnutritional causes of anemia. We use published information on Bangladesh[44–46] and Cambodia,[23,47–50] two countries that have recent relevant data on anemia etiology and program effectiveness to reduce anemia, as examples of how different data may help inform and understand the anemia public health response and effectiveness.

Malaria is a cause of anemia as well as causing inflammation and important to measure when assessing the etiology of anemia. Recent evidence indicates that unabsorbed iron may be detrimental to the gut microflora,[26,51,52] Given iron absorption regulation, iron-replete individuals may have more unabsorbed supplemental iron in the upper and lower gastrointestinal tract. This evidence further illustrates the value of characterizing a population’s iron status prior to giving preventive iron interventions. Utilizing other available data sources, such as population-based surveys that measure iron and

inflammation, or surveys such as the Malaria Indicator Survey, to better understand the context-specific etiology of anemia is a practical approach to fill data gaps.

The role of genetics and anemia severity in defining public health significance

Although we present limited information on concomitant genetic blood disorder or hemoglobinopathy variants and anemia, a number of studies show the association between anemia and various genetic blood disorders.[23,46,53,54] Among the two countries that assessed genetic variants, more than half of children with anemia had an inherited blood disorder or variant. None of the BRINDA surveys for WRA collected data on hemoglobinopathies, but more adults than children would be expected to be carriers of blood disorder traits, given the selective pressures of malaria. Although we did not differentiate between alpha thalassemia heterozygotes (e.g., −α/αα) and homozygotes (e.g., −α/−α), the alpha thalassemia homozygous genotype is more strongly associated with mild anemia than heterozygotes.[22,54] If the prevalence of inherited red blood cell disorders or carriers is unknown in a population, and a large proportion of the anemia is mild and not IDA, then testing for genetic blood disorder variants will help elucidate how much of the anemia maybe modifiable. Innovative technologies are enabling data gaps to be filled for sickle cell disease detection, as screening has been combined with HIV programs,[55] and anemia assessment in East Africa.[56]

The data suggest that efforts focused on reducing moderate and severe anemia may have the greatest influence on reducing YLD. Moderate anemia, described as “making daily activities more difficult,” is responsible for the largest proportion of YLD across regions, ages, and gender (Fig. 2). Severe anemia presents the greatest risk for adverse health and functional outcomes, including maternal and child mortality.[57–60] Therefore, the proportion of anemia classified as moderate or severe deserves greater attention than the overall population prevalence of any anemia. In 1997, Stoltzfus[57] suggested that the population prevalence of severe anemia, defined as Hb < 70 g/L, be considered to assess the public health severity of anemia; specifically, >10% would be considered high, 1–9% moderate, and < 1% low. These cutoffs were not adopted by the WHO, but prevalence estimates of moderate and severe anemia may be pragmatic for defining a public health problem of anemia severity, given the concerns of potential misclassification of anemia with cutoffs higher than necessary among certain populations.[34,61]

Examples of two countries with different types of data to help interpret anemia etiology

We describe two country situations from the BRINDA project surveys supported by additional evidence to illustrate the challenges of a “one-size-fits-all” iron delivering interventions address anemia. The first is Cambodia (2014), where the prevalence of anemia was 45.4% for WRA and 55.6% for children aged 6–59 months. There was a high (>20%) proportion of moderate or severe anemia and the burden of elevated inflammatory proteins was nearly 40% for both population groups. Among those with anemia, <10% had ID (irrespective of if iron was adjusted for inflammation). Karakochuk *et al.*[23] reported IDA prevalence 10 times higher among women with Hb disorders, compared with those without Hb disorders in a rural province of Cambodia, but nationally representative analyses suggest that anemia could not be explained by nutritional deficiencies or Hb disorders.[47,49] Based on

the national ID prevalence (<7% regardless of inflammation-adjustment), national iron delivery interventions are likely not needed.[3] Dijkhuizen *et al.*[50] suggest that nutrition-specific interventions (e.g., food aid) beyond single micronutrient interventions and nutrition-sensitive (e.g., infectious disease control) interventions are needed to reduce anemia prevalence, with targeting that extends beyond pregnant women. A second example is Bangladesh (2012), where the prevalence of anemia in women and children was moderate (20–40%) and among those with anemia, 25–30% had ID (and the prevalence was higher if ferritin was not adjusted for inflammation). Regions of Bangladesh are known to have iron in groundwater.[45] Based on dietary intake data,[62] population-based provision of multiple micronutrients may be justified. Yet, a recent trial showed no change in anemia prevalence among pregnant women in Bangladesh randomized to receive a daily multiple micronutrient supplement or iron and folic acid during pregnancy.[44] Trial authors concluded that baseline micronutrient status and other covariates explained the majority of the micronutrient and Hb status in late pregnancy.[44] Given these examples, improving nutritional and nonnutritional modifiable factors may be required to reduce anemia among vulnerable populations (e.g., children and WRA, and lower socioeconomic status).

Utility of using YLD to assign public health severity of anemia

Prevalence and severity of anemia are the underlying components of YLD. What the YLD reveals that is not apparent from population prevalence estimates alone is the increasing disability associated with moderate and severe anemia. Although YLD is an important tool for policymakers and donors, it does not contain the etiologic specific information that would help inform effective anemia control programs, such as the proportion of individuals with anemia and ID, genetic blood disorders or hemoglobinopathy variants, and other causes of anemia, such as malaria, tuberculosis, and HIV/AIDS, or other micronutrient deficiencies. The YLD rate may be most useful at the within-country setting for prioritizing anemia across other disease burdens faced at a national level.

Strengths and limitations

Using anemia prevalence estimates from the 2016 GBD to compare with YLD rates, and comparing the relative contributions of mild, moderate, and severe anemia on the YLD estimates is a strength of this analysis. However, working with the 2016 GBD data reminds us of the challenge of characterizing IDA within published GBD work. The GBD 2013 anemia collaborators state the shortcomings of generating etiologic specific estimates of anemia without iron biomarker data.[12] As such, the strength of this study is the BRINDA database that includes serum ferritin and inflammatory protein concentrations. However, the BRINDA database has a relatively small number of surveys and the availability of additional micronutrient data is inconsistent and genetic blood disorder or hemoglobinopathy variant data within these surveys are extremely limited. Potentially the most important limitation of this work was the reliance on individual Hb cutoffs defined by WHO that were determined using statistical thresholds rather than having health outcome data available, and therefore may not reflect adverse outcomes.

Conclusion

It has long been known that anemia is caused by multiple factors besides ID,[1,3,12] yet the collection of etiologic characteristics of anemia in a single survey is rare. We argue that even if a single survey does not collect all of the necessary data to interpret anemia etiology within a country, compiling data from various recent surveys and other data sources in a country would help inform anemia control programs. As a starting point, however, iron status and inflammation status assessment in population-based surveys, although complex, can be done in resources constrained settings,[63] and need not be considered out of reach. Resources are limited to target anemia reduction, giving further credence to programing etiologically appropriate interventions. Where the anemia burden is high and the underlying cause is unknown, efforts to understand the etiology of anemia would be useful. When the anemia prevalence is high and amenable to iron interventions, supporting effective iron interventions is expected to reduce the prevalence of anemia and ID. When the anemia prevalence is high and amenable to other micronutrients, such as folate, vitamin B12, vitamin A, or zinc, delivering multiple micronutrients to a population, coupled with malaria control (if endemic), may be appropriate. Yet these decisions are difficult to make in the absence of data. We conclude that although the WHO population prevalence criteria used to describe the public health severity of anemia are important for national policymakers and for setting global designations of severity and policymaking, etiologic-specific metrics that take into account IDA and other causes of anemia are necessary for effective anemia control policies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was commissioned by the Evidence and Programme Guidance Unit, Department of Nutrition for Health and Development of the WHO, Geneva, Switzerland. We appreciate the critical review and insights from CDC colleagues, Julie R. Gutman and Meghna Desai, in the Malaria Branch of the Center for Global Health, and Emory University health economist, Deborah McFarland. Tom Fleming, Laura Kemmer, and Brian Whetter all contributed to the anemia estimates generated by the Institute for Health Metrics and Evaluation team. Contributions of data sets from the BRINDA working group are acknowledged as well as the BRINDA steering committee members. The steering committee consists of the following people (in alphabetical order): Erick Boy, Rafael Flores, Janet King, Sorrel Namaste, Lynnette M. Neufeld, Daniel Raiten, Parminder Suchdev, James Wirth, and Melissa F. Young. We also acknowledge the contributions of the BRINDA working group and country representatives (in alphabetical order): O. Yaw Addo, Tahmeed Ahmed, Moira Angel, Zulfiqar Bhutta, Reina Engle-Stone, Wilma Freire, Junjie Guo, Sanober Ismaily, Roland Kupka, Rebecca Lander, Leila M. Larson, Nino Lortkipanidze, Maria Jose Ramirez Luzuriaga, Pragya Mathema, Christine McDonald, Zuguo Mei, Purnima Menon, Sabiha Nasrin, Polly Page, Jan Peerson, Tamerlan Rajabov, Rahul Rawat, Pura Rayco-Solon, Fabian Rohner, Ofelia Saniel, Olga Lucia Sarmiento, Mary Serdula, Victor Temple, Andres Tschanne, Salvador Villapando, Frank Wieringa, Anne M. Williams, and Emma Yu.

References

1. WHO. 2001. Iron Deficiency Anaemia. Assessment, Prevention and Control. A Guide for Programme Managers Geneva: World Health Organization.
2. WHO. 2011. Hemoglobin Concentrations for the Diagnosis of Anemia and Assessment of Severity. Geneva:World Health Organization.

3. WHO. 2017. Nutritional Anaemias: Tools for Effective Prevention and Control. Geneva:World Health Organization.
4. Lozoff B, Beard J, Connor J, et al. 2006. Long-lasting neural and behavioral effects of iron deficiency in infancy. Nutr. Rev 64(Pt. 2): S34–S43; discussion S72–S91. [PubMed: 16770951]
5. Stoltzfus RJ, Mullany LC & Black RE. 2004. Iron Deficiency Anemia. Geneva:World Health Organization.
6. Sachdev H, Gera T & Nestel P. 2005. Effect of iron supplementation on mental and motor development in children: systematic review of randomised controlled trials. Public Health Nutr. 8: 117–132. [PubMed: 15877905]
7. Horton S & Levin C. 2001. Commentary on "evidence that iron deficiency anemia causes reduced work capacity." J. Nutr 131: 691S–696S. [PubMed: 11160599]
8. Haas JD & Brownlie T. 2001. Iron deficiency and reduced work capacity: a critical review of the research to determine a causal relationship. J. Nutr 131: 676S–688S; discussion 688S–690S. [PubMed: 11160598]
9. McLean E, Cogswell M, Egli I, et al. 2009. Worldwide prevalence of anaemia, WHO Vitamin and Mineral Nutrition Information System, 1993–2005. Public Health Nutr. 12: 444–454. [PubMed: 18498676]
10. WHO. 2015. The Global Prevalence of Anemia in 2011. Geneva:World Health Organization.
11. Kassebaum NJ, Jasrasaria R,Naghavi M, et al. 2014.Asystematic analysis of global anemia burden from 1990 to 2010. Blood 123: 615–624. [PubMed: 24297872]
12. Kassebaum NJ & GBD 2013 Anemia Collaborators. 2016. The global burden of anemia. Hematol. Oncol. Clin. North Am 30: 247–308. [PubMed: 27040955]
13. Black RE, Victora CG, Walker SP, et al. 2013. Maternal and child undernutrition and overweight in low-income and middle-income countries. Lancet 382: 427–451. [PubMed: 23746772]
14. Pasricha SR, Armitage AE, Prentice AM & Drakesmith H. 2018. Reducing anaemia in low income countries: control of infection is essential. BMJ 362: k3165. 10.1136/bmj.k3165. [PubMed: 30068664]
15. Engle-Stone R, Aaron GJ, Huang J, et al. 2017. Predictors of anemia in preschool children: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. Am. J. Clin. Nutr 106(Suppl. 1): 402S–415S. [PubMed: 28615260]
16. Wirth JP, Woodruff BA, Engle-Stone R, et al. 2017. Predictors of anemia in women of reproductive age: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. Am. J. Clin. Nutr 106(Suppl. 1): 416S–427S. [PubMed: 28615262]
17. WHO. 2015. World Health Assembly Nutrition Targets. Accessed February 10, 2015. http://www.who.int/nutrition/topics/nutrition_globaltargets2025/en/.
18. WHO. 2018. Global targets tracking tool, nutrition. Accessed June 15, 2018. http://www.who.int/nutrition/trackingtool/en/.
19. Stevens GA, Finucane MM, De-Regil LM, et al. 2013. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. Lancet Glob. Health 1: e16–e25. [PubMed: 25103581]
20. Redig AJ & Berliner N. 2013. Pathogenesis and clinical implications of HIV-related anemia in 2013. Hematology Am. Soc. Hematol. Educ. Program 2013: 377–381. [PubMed: 24319207]
21. Barabino A 2002. *Helicobacter pylori*-related iron deficiency anemia: a review. Helicobacter 7: 71–75. [PubMed: 11966864]
22. Suchdev PS, Ruth LJ, Earley M, et al. 2014. The burden and consequences of inherited blood disorders among young children in western Kenya. Matern. Child Nutr 10: 135–144. [PubMed: 22973867]
23. Karakochuk CD, Whitfield KC, Barr SI, et al. 2015. Genetic hemoglobin disorders rather than iron deficiency are a major predictor of hemoglobin concentration in women of reproductive age in rural prey Veng, Cambodia. J. Nutr 145: 134–142. [PubMed: 25527668]
24. Nguyen PH, Gonzalez-Casanova I, Nguyen H, et al. 2015. Multicausal etiology of anemia among women of reproductive age in Vietnam. Eur. J. Clin. Nutr 69: 107–113. [PubMed: 25205323]

25. Prentice AM, Ghattas H & Cox SE. 2007.Host–pathogen interactions: can micronutrients tip the balance? J. Nutr 137: 1334–1337. [PubMed: 17449601]
26. Tang M, Frank DN, Hendricks AE, et al. 2017. Iron in micronutrient powder promotes an unfavorable gut microbiota in Kenyan infants. Nutrients 9: 776. 10.3390/nu9070776.
27. Stoltzfus RJ & Dreyfuss ML. 1998. Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anemia. Washington, DC: International Life Science Institute Press.
28. WHO. 2016. Guideline: Daily Iron Supplementation in Infants and Children. Geneva:World Health Organization.
29. Salomon JA, Vos T, Hogan DR, et al. 2012. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. Lancet 380: 2129–2143. [PubMed: 23245605]
30. Salomon JA, Haagsma JA, Davis A, et al. 2015. Disability weights for the Global Burden of Disease 2013 study. Lancet Glob. Health 3: e712–e723. [PubMed: 26475018]
31. Suchdev PS, Namaste SM, Aaron GJ, et al. 2016. Overview of the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) Project. Adv. Nutr 7: 349–356. [PubMed: 26980818]
32. National Statistical Office (NSO), CHSUCM, Centers for Disease Control and Prevention (CDC), and Emory University. 2016. Malawi Micronutrient Survey 2015–16: Key Indicators Report. Atlanta, GA: NSO, CHSU, CDC, and Emory University.
33. Tsang BL, Sullivan KM, Ruth LJ, et al. 2014. Nutritional status of young children with inherited blood disorders in western Kenya. Am. J. Trop. Med. Hyg 90: 955–962. [PubMed: 24639300]
34. Sullivan KM, Mei Z, Grummer-Strawn L & Parvanta I. 2008. Haemoglobin adjustments to define anaemia. Trop. Med. Int. Health 13: 1267–1271. [PubMed: 18721184]
35. Namaste SM, Rohner F, Huang J, et al. 2017. Adjusting ferritin concentrations for inflammation: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project.Am. J. Clin. Nutr 106(Suppl. 1): 359S–371S. [PubMed: 28615259]
36. WHO. 2011. Serum Ferritin Concentrations for the Assessment of Iron Status and Iron Deficiency in Populations. Geneva:World Health Organization.
37. Raiten DJ, Sakr Ashour FA, Ross AC, et al. 2015. Inflammation and Nutritional Science for Programs/Policies and Interpretation of Research Evidence (INSPIRE). J. Nutr 145: 1039S–1108S. [PubMed: 25833893]
38. DeMaeyer E & Adiels-Tegman M. 1985. The prevalence of anaemia in the world. World Health Stat. Q 38: 302–316. [PubMed: 3878044]
39. Petry N, Olofin I, Hurrell RF, et al. 2016. The proportion of anemia associated with iron deficiency in low, medium, and high human development index countries: a systematic analysis of national surveys. Nutrients 8: 693.
40. Ross AC 2017. Impact of chronic and acute inflammation on extra- and intracellular iron homeostasis. Am. J. Clin. Nutr 106(Suppl. 6): 1581S–1587S. [PubMed: 29070546]
41. Spottiswoode N, Armitage AE, Williams AR, et al. 2017. Role of activins in hepcidin regulation during malaria. Infect. Immun 85. pii: e00191–17. 10.1128/IAI.00191-17. [PubMed: 28893916]
42. Thurnham DI, McCabe LD, Haldar S, et al. 2010. Adjusting plasma ferritin concentrations to remove the effects of subclinical inflammation in the assessment of iron deficiency: a meta-analysis. Am. J. Clin. Nutr 92: 546–555. [PubMed: 20610634]
43. Rohner F, Namaste SM, Larson LM, et al. 2017.Adjusting soluble transferrin receptor concentrations for inflammation: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. Am. J. Clin. Nutr 106(Suppl. 1): 372S–382S. [PubMed: 28615256]
44. Schulze KJ, Mehra S, Shaikh S, et al. 2019. Antenatal multiple micronutrient supplementation compared to iron-folic acid affects micronutrient status but does not eliminate deficiencies in a randomized controlled trial among pregnant women of rural Bangladesh. J. Nutr 10.1093/jn/nxz046.
45. Merrill RD, Shamim AA, Ali H, et al. 2011. Iron status of women is associated with the iron concentration of potable groundwater in rural Bangladesh. J. Nutr 141: 944–949. [PubMed: 21451130]

46. Merrill RD, Shamim AA, Ali H, et al. 2012. High prevalence of anemia with lack of iron deficiency among women in rural Bangladesh: a role for thalassemia and iron in groundwater. Asia Pac. J. Clin. Nutr 21: 416–424. [PubMed: 22705433]
47. Wieringa FT, Dahl M, Chamnan C, et al. 2016. The high prevalence of anemia in Cambodian children and women cannot be satisfactorily explained by nutritional deficiencies or hemoglobin disorders. Nutrients 8: 348. 10.3390/nu8060348.
48. Whitfield KC, Karakochuk CD, Liu Y, et al. 2015. Poorthiamin and riboflavin status is common among women of childbearing age in rural and urban Cambodia. J. Nutr 145: 628–633. [PubMed: 25733481]
49. Greffeuille V, Sophonneary P, Laillou A, et al. 2016. Inequalities in nutrition between Cambodian women over the last 15 years (2000–2014). Nutrients 8: 224. [PubMed: 27104556]
50. Dijkhuizen MA, Greffeille V, Roos N, et al. 2019. Interventions to improve micronutrient status of women of reproductive age in Southeast Asia: a narrative review on what works, what might work, and what doesn't work. Matern. Child Health J 23(Suppl. 1): 18–28. [PubMed: 30357535]
51. Paganini D &Zimmermann MB. 2017. The effects of iron fortification and supplementation on the gut microbiome and diarrhea in infants and children: a review. Am. J. Clin. Nutr 106(Suppl. 6): 1688S–1693S. [PubMed: 29070552]
52. Soofi S, Cousens S, Iqbal SP, et al. 2013. Effect of provision of daily zinc and iron with several micronutrients on growth and morbidity among young children in Pakistan: a cluster-randomised trial. Lancet 382: 29–40. [PubMed: 23602230]
53. Campbell RK, Aguayo VM, Kang Y, et al. 2018. Epidemiology of anaemia in children, adolescent girls, and women in Bhutan. Matern. Child Nutr. 14(Suppl. 4): e12740. [PubMed: 30499252]
54. McGann PT, Williams AM, Ellis G, et al. 2018. Prevalence of inherited blood disorders and associations with malaria and anemia in Malawian children. Blood Adv. 2: 3035–3044. [PubMed: 30425067]
55. Ndeezi G, Kiyaga C, Hernandez AG, et al. 2016. Burden of sickle cell trait and disease in the Uganda Sickle Surveillance Study (US3): a cross-sectional study. Lancet Glob. Health 4: e195–e200. [PubMed: 26833239]
56. Smart LR, Ambrose EE, Raphael KC, et al. 2018. Simultaneous point-of-care detection of anemia and sickle cell disease in Tanzania: the RAPID study. Ann. Hematol 97: 239–246. [PubMed: 29147848]
57. Stoltzfus RJ 1997. Rethinking anaemia surveillance. Lancet 349: 1764–1766. [PubMed: 9193395]
58. Stoltzfus RJ 2001. Iron-deficiency anemia: reexamining the nature and magnitude of the public health problem. Summary: implications for research and programs. J. Nutr 131: 697S–700S; discussion 700S–701S. [PubMed: 11160600]
59. Calis JC, Phiri KS, Faragher EB, et al. 2016. Severe anemia in Malawian children. Malawi. Med. J 28: 99–107. [PubMed: 27895843]
60. Daru J, Zamora J, Fernández-Félix BM, et al. 2018. Risk of maternal mortality in women with severe anaemia during pregnancy and post partum: a multilevel analysis. Lancet Glob. Health 6: e548–e554. [PubMed: 29571592]
61. Yip R, Johnson C & Dallman PR. 1984. Age-related changes in laboratory values used in the diagnosis of anemia and iron deficiency. Am. J. Clin. Nutr 39: 427–436. [PubMed: 6695842]
62. Arsenault JE, Yakes EA, Islam MM, et al. 2013. Very low adequacy of micronutrient intakes by young children and women in rural Bangladesh is primarily explained by low food intake and limited diversity. J. Nutr 143: 197–203. [PubMed: 23256144]
63. Suchdev PS, Williams AM, Mei Z, et al. 2017. Assessment of iron status in settings of inflammation: challenges and potential approaches. Am. J. Clin. Nutr 106(Suppl. 6): 1626S–1633S. [PubMed: 29070567]

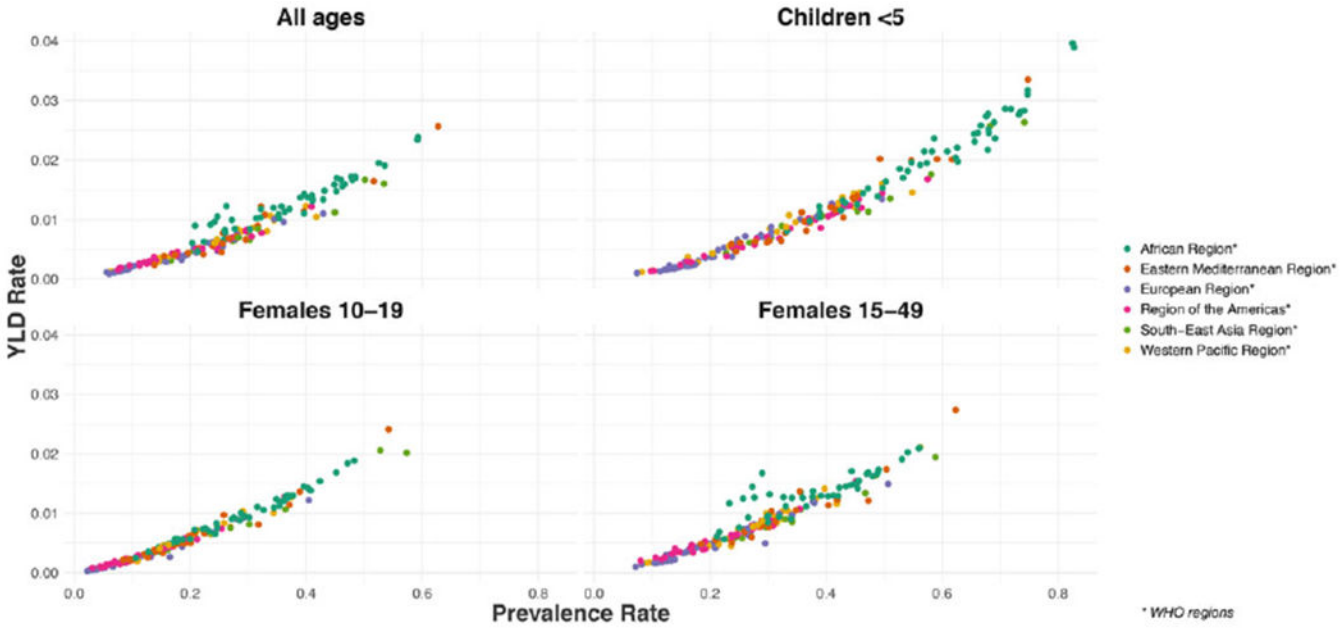

Figure 1.

Country-level anemia prevalence rate by YLD rate for 2016 by WHO regions. NOTE: Global Health Data Exchange estimates of years lived with disability (YLD, per 100,000) from anemia and anemia prevalence rate (per 100) among all age groups (women and men at all available ages), children under 5 years, adolescent females (10–19 years old), and women of reproductive age (15–49 years old). World Health Organization (WHO) regions are designated by color; each dot represents a unique country.

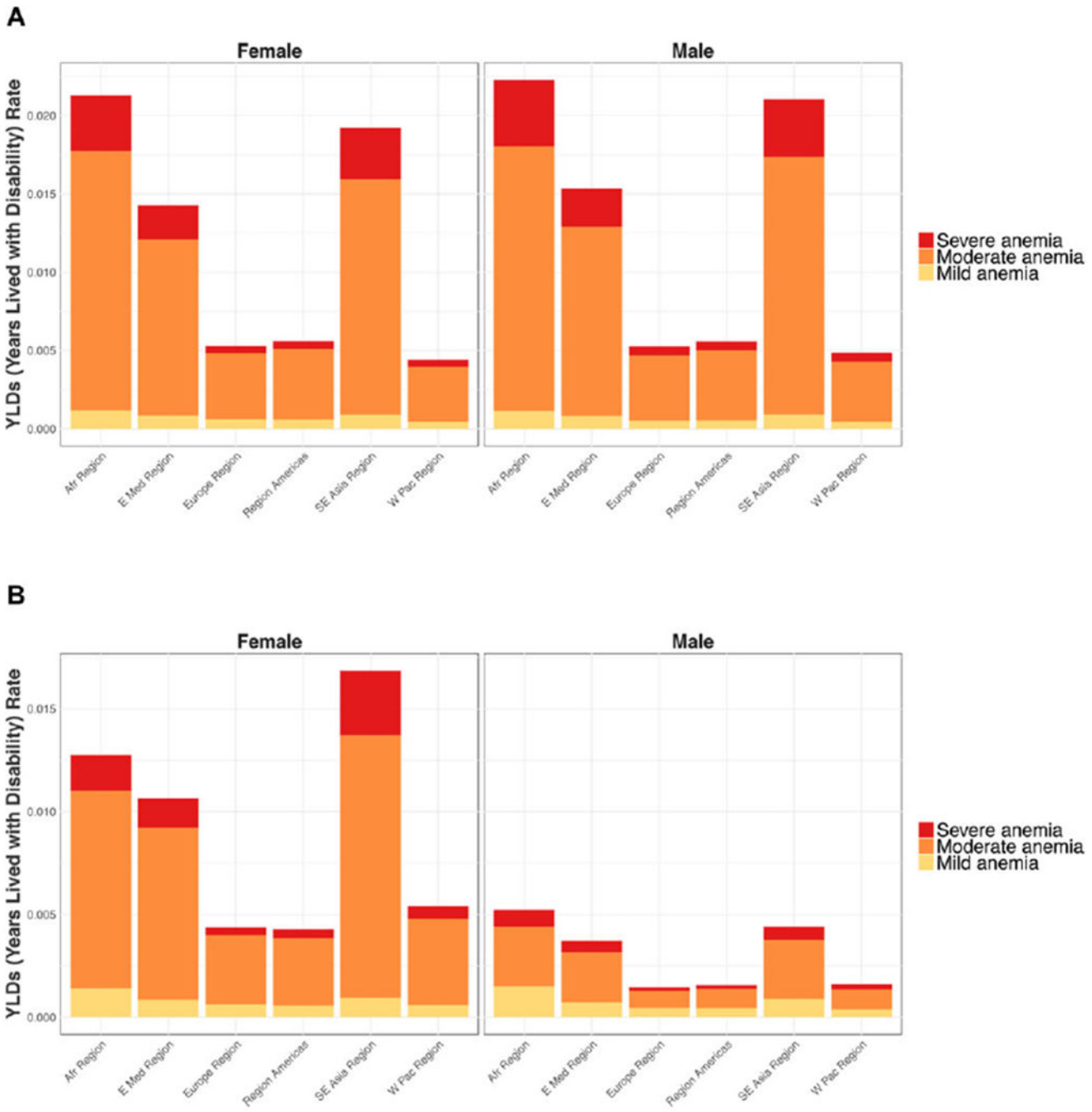

Figure 2.

Age-standardized 2016 YLD rate according to the severity of anemia among children under 5 years (A) and adults 15–49 years old (B) stratified by gender and WHO region. Note: Global health data exchange estimates of anemia years lived with disability (YLD, per 100,000) and anemia severity among children under 5 years and adults 15–49 years old (World Health Organization (WHO)).

Table 1.

Hemoglobin concentrations for categorizing anemia severity at the individual level for children from 6 months to 5 years of age and pregnant women of reproductive age (15–49 years)[a]

Anemia severity	WHO recommendations[1–3]	GBD criteria 1990–2010[11]	GBD criteria 2013–2016[12]
Any anemia	<110 g/L	<120 g/L	<110 g/L
Mild	100–109 g/L	110–119 g/L	100–109 g/L
Moderate	70–99 g/L	80–109 g/L	70–99 g/L
Severe	<70 g/L	50–79 g/L	<70 g/L

[a]The World Health Organization (WHO) does not provide cutoffs for hemoglobin in children <6 months old. Global Burden of Disease (GBD) 2013–2016 estimates included children <6 months old; range in the table above represents 1 month to 5 years old. The 2013–2016 GBD cycles estimated individual anemia severity in children < 1 month old using the following classifications: mild (130–149 g/L), moderate (90–129 g/L), and severe (<90 g/L); in GBD 2017, the 1 month to 5 years old thresholds were used from birth to 5 years old. WHO cutoffs for nonpregnant women of reproductive age are 10 g/L higher than pregnant women (any anemia <120 g/L; mild 110–119 g/L; moderate 80–109 g/L; severe <80 g/L).

Ann N Y Acad Sci. Author manuscript; available in PMC 2021 July 20.

Table 2.

Descriptions of anemia severity and Global Burden of Disease disability weights for anemia, 1990–2016[a]

Anemia severity	Description	GBD 1990–2004	GBD 2010[29]	GBD 2013–2016[30]
Mild	Feels slightly tired and weak at times, but this does not interfere with normal daily activities.	0.000	0.005 (0.002–0.011)	0.004 (0.001–0.008)
Moderate	Feels moderate fatigue, weakness, and shortness of breath after exercise, making daily activities more difficult.	0.011 (0.011–0.012)	0.058 (0.038–0.086)	0.052 (0.034–0.076)
Severe	Feels very weak, tired and short of breath, and has problems with activities that require physical effort or deep concentration.	0.090 (0.087–0.093)	0.164 (0.112–0.228)	0.149 (0.101–0.209)

[a]Between 2004 and 2013, the GBD disability weights were adjusted to better reflect population perception of disease updating the 1990 designations, which were based on expert opinion.

GBD, Global Burden of Disease.

Table 3.

Prevalence of any anemia, moderate or severe anemia, inflammation, ID, and IDA, alongside the proportion of individuals with concomitant anemia and ID or malaria among preschool children within the BRINDA data set[a]

							BRINDA inflammation-adjusted			
WHO classification	**Country, survey year**	***n***	**Any anemia (%)**	**Moderate or severe anemia (%)[b]**	**Elevated CRP or AGP (%)[c]**	**ID (ferritin <30 μg/L among inflamed) (%)[d]**	**ID (%)[e]**	**IDA (%)[f]**	**ID among those with anemia (%)[g]**	***Plasmodium falciparum* parasitemia among those with anemia (%)[h]**
Severe	Bangladesh, 2010	1492	83.5	48.6	35.7	17.7	16.0	15.1	18.1	–
	Kenya, 2010	845	71.7	52.2	61.8	32.3	53.7	39.9	55.9	40.9
	Côte d'Ivoire, 2007	768	71.0	48.0	67.5	24.1	39.0	29.6	41.5	28.8
	Kenya, 2007	934	65.7	35.8	65.5	61.3	72.5	50.9	76.0	23.1
	Pakistan, 2011	4099	63.0	39.4	35.5	57.9	45.1	33.4	53.5	–
	Liberia, 2011	1444	59.3	28.6	59.1	37.0	51.0	32.2	54.1	37.6
	Cambodia, 2014	455	55.6	25.6	38.5	6.3	5.3	4.4	8.2	–
	Cameroon, 2009	787	54.1	30.0	48.1	23.6	34.1	22.5	41.4	40.7
	PNG, 2005	454	48.0	25.0	57.2	–	–	–	–	–
	Afghanistan, 2013	703	43.7	23.6	24.8	28.9	23.7	10.7	30.3	–
	Philippines, 2011	1777	41.8	16.6	26.0	34.2	34.9	21.6	51.5	–
	Laos, 2006	488	40.7	19.0	43.8	27.6	25.6	15.5	38.0	–
Moderate	Bangladesh, 2012	568	33.1	5.4	29.5	15.4	13.7	8.4	25.9	–
	Malawi, 2016	1140	31.6	13.2	56.9	25.4	21.8	9.3	30.4	48.1
	Azerbaijan, 2013	1076	24.6	8.4	30.9	18.9	22.3	8.8	37.5	–
	Ecuador, 2012	2020	24.7	8.2	12.5	12.9	49.0	16.2	65.7	–
	Georgia, 2009	2200	22.8	10.0	24.7	0.9	0.3	0.05	0.2	–
	Mexico, 2006	5264	20.7	9.7	10.8	26.9	33.9	8.8	42.8	–
	Nicaragua, 2005	1156	20.0	5.3	26.9	44.8	24.0	5.2	39.3	–
Mild	Mexico, 2012	6338	16.8	6.9	12.0	16.4	18.1	4.0	23.9	–
	Colombia, 2010	5955	13.2	8.3	18.8	17.1	13.5	2.5	18.9	–
	Vietnam, 2010	395	7.1	1.8	12.4	17.5	18.8	3.2	42.9	–
Normal	The U.S., 2006	1529	1.9	0.4	5.9	11.5	13.3	1.2	57.0	–

[a] Values represent weighted percentage, taking into account cluster, strata, and weight. "-" means no data. Prevalences greater than 20% were colored dark gray, and 10–20% were colored light gray for comparison, throughout.

[b] Moderate or severe anemia was defined as altitude-adjusted Hb < 100 g/L. Not all surveys measured altitude (see Table S1, online only, for details).

[c] Elevated inflammatory protein was defined as CRP > 5 mg/L or AGP > 1 g/L. Not all surveys measured both inflammatory proteins (see Table S1, online only, for details).

[d] ID defined using serum ferritin <30 μg/L for individuals with CRP > 5 mg/L or AGP > 1 g/L.

[e] Inflammation-adjusted ID was defined as serum ferritin < 12 μg/L after regression correction for inflammation according to the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia project.

[f] IDA was defined as Hb < 110 g/L and BRINDA inflammation-adjusted serum ferritin <12 μg/L.

[g] Inflammation-adjusted serum ferritin < 12 μg/L restricted to individuals with anemia

[h] Recent malaria restricted to individuals with anemia was defined based on results from rapid diagnostic test kits or microscopy. Malaria was assessed using microscopy in Kenya and Cote d'Ivoire, and rapid diagnostic test kits in Malawi, Liberia, and Cameroon.

AGP, alpha-1-acid glycoprotein; CRP, C-reactive protein; ID, iron deficiency; IDA, iron deficiency anemia; PNG, Papua New Guinea.

Ann N Y Acad Sci. Author manuscript; available in PMC 2021 July 20.

Table 4.

Prevalence of any anemia, moderate or severe anemia, inflammation, ID, and IDA, alongside the proportion of individuals with concomitant anemia and ID or malaria among nonpregnant women of reproductive age within the BRINDA data set[a]

							BRINDA inflammation-adjusted			
WHO classification	**Country, survey year**	***n***	**Any anemia (%)**	**Moderate or severe anemia (%)[b]**	**Elevated CRP or AGP (%)[c]**	**ID (unadjusted) (%)[d]**	**ID (%)[e]**	**IDA (%[f]**	**ID among those with anemia (%)[g]**	***Plasmodium falciparum* parasitemia among those with anemia (%)[h]**
Severe	Pakistan, 2011	10,787	50.4	29.5	26.0	36.4	42.5	27.1	54.1	–
	Côte d'Ivoire, 2007	850	49.9	25.7	33.5	13.5	22.7	15.3	30.4	5.6
	Cambodia, 2014	447	45.4	21.0	38.9	2.2	3.5	2.9	6.6	–
	Azerbaijan, 2013	2713	38.1	19.2	34.4	30.8	42.7	26.3	69.0	–
Moderate	Cameroon, 2009	775	36.3	17.0	20.4	13.0	19.5	13.3	37.1	18.6
	Laos, 2006	823	36.0	18.4	13.9	22.8	26.3	15.9	44.1	–
	PNG, 2005	760	35.1	18.1	24.8	–	–	–	–	–
	Afghanistan, 2013	1308	34.7	16.7	20.3	26.2	30.7	16.6	42.8	–
	Liberia, 2011	1971	33.2	11.5	18.4	17.9	29.1	14.9	44.7	19.7
	Bangladesh, 2012	1033	26.0	8.4	16.8	7.5	9.3	5.2	20.0	–
	Georgia, 2009	1711	23.3	9.3	29.3	1.3	1.8	0.9	3.6	–
	Malawi, 2016	789	22.7	7.3	13.1	11.4	15.0	8.0	36.2	22.5
Mild	Ecuador, 2012	8118	14.5	5.2	17.4	14.8	37.4	11.1	76.4	–
	Mexico, 2006	3050	13.9	5.3	24.2	26.9	34.5	8.8	63.3	–
	Mexico, 2012	4174	12.9	5.4	20.9	27.8	43.7	9.8	72.8	–
	Vietnam, 2010	1491	11.4	3.2	6.6	13.1	18.0	5.8	50.6	–
	The United Kingdom, 2014	937	10.9	1.9	16.7	18.7	29.7	5.7	51.2	–
	Colombia, 2010	9678	8.0	4.9	22.0	23.0	25.6	4.5	59.4	–
	The United States, 2006	3226	6.7	2.7	25.6	13.1	20.7	5.1	77.6	–

[a]Values represent weighted percentage, taking into account cluster, strata, and weight. "-" means no data. Prevalences greater than 20% were colored dark gray, and 10–20% were colored light gray for comparison, throughout.

[b]Moderate or severe anemia was defined as altitude- and smoking-adjusted Hb < 110 g/L. Not all surveys measured smoking and altitude (see Table S1, online only, for details).

[c] Elevated inflammatory proteins were defined as CRP > 5 mg/L or AGP > 1 g/L. Not all surveys measured both inflammatory proteins (see Table S1, online only, for details).

[d] Unadjusted ID was defined as serum ferritin < 15 μg/L.

[e] Inflammation-adjusted ID was defined as serum ferritin < 15 μg/L after regression correction for inflammation according to the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia project.

[f] IDA was defined as Hb < 120 g/L and inflammation-adjusted serum ferritin < 15 μg/L.

[g] Inflammation-adjusted serum ferritin <5 μg/L restricted to individuals with anemia.

[h] Recent malaria restricted to individuals with anemia was defined based on results from rapid diagnostic test kits or microscopy. Malaria was assessed using microscopy in Cote d'Ivoire, and rapid diagnostic test kits in Malawi Liberia, and Cameroon.

AGP, alpha-1-acid glycoprotein; CRP, C-reactive protein; ID, iron deficiency; IDA, iron deficiency anemia; PNG, Papua New Guinea.