La relation entre les règles abondantes, la carence en fer et l'anémie ferriprive

La relation entre les règles abondantes, la carence en fer et l'anémie ferriprive

- Chez les femmes en âge de procréer, le symptôme des règles abondantes constitue un facteur important de carence en fer et de sa manifestation la plus grave, l'anémie ferriprive

- HMB : Un symptôme caractérisé par des pertes sanguines menstruelles d'un volume suffisant pour avoir un impact négatif sur la qualité de vie physique, émotionnelle, sociale et/ou matérielle d'une femme (QdV)

- Il ne s'agit que de l'un des symptômes caractérisant les saignements utérins anormaux (SUA) chez les femmes non enceintes en âge de procréer

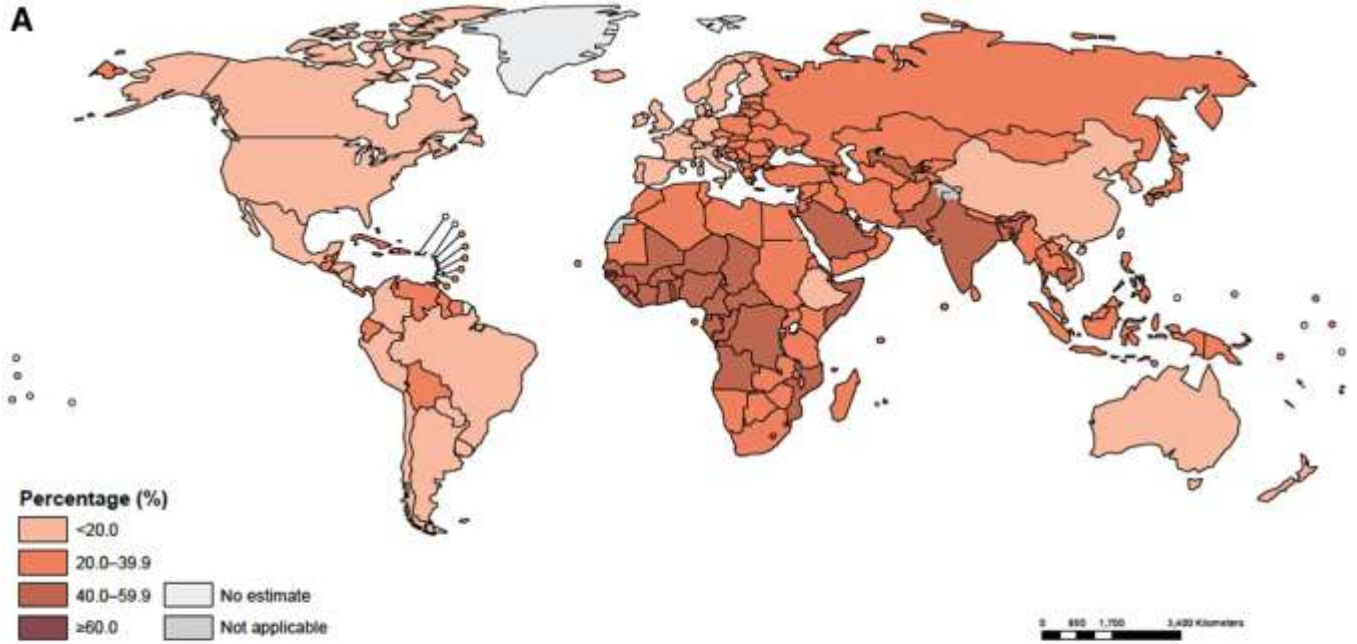
- Outre les règles abondantes, une alimentation déficiente en fer, répandue chez les adolescentes et en particulier chez les femmes habitant dans les pays à revenu faible ou intermédiaire, contribue à un bilan ferrique négatif et à la carence en fer qui en découle

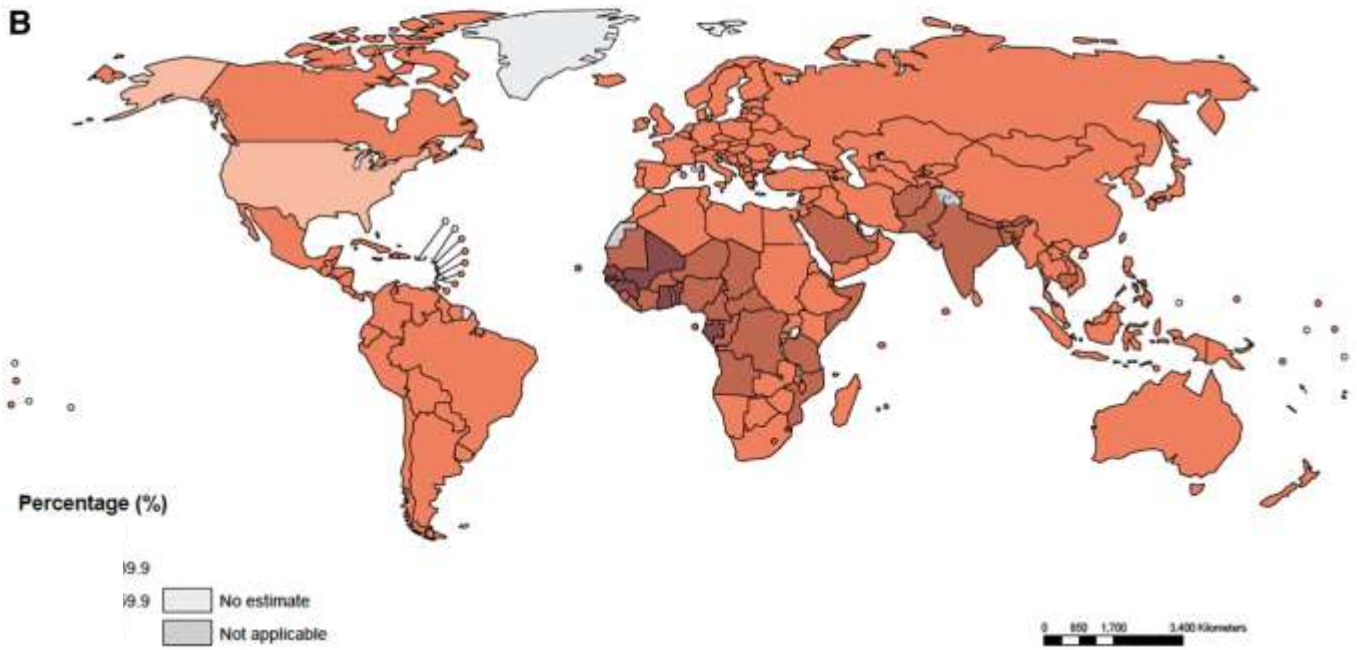
- Lorsque les femmes souffrant d'une carence en fer tombent enceintes, et en particulier en cas d'anémie, l'impact sur la grossesse et le développement du fœtus peut être grave et se traduire par des troubles du développement neurologique et un dysfonctionnement neurologique à long terme qui persiste à l'âge adulte

- Souvent, les réserves de fer ne sont pas reconstituées pendant la période postnatale, ce qui ouvre la voie à des événements répétés au cours des grossesses suivantes

Munro MG, et al. Am J Obstet Gynecol. 2023 Jan 24;S0002-9378(23)00024-8.

La figure A illustre la prévalence mondiale de l'anémie chez toutes les femmes. La figure B illustre la prévalence de l'anémie chez les femmes enceintes. La carence en fer constitue la cause ou le facteur d'au moins la moitié des cas d'anémie chez les femmes en âge de procréer dans le monde. Les chiffres sont tirés de la publication de l'Organisation mondiale de la santé, consultée le 1er juin 2022





The relationship between heavy menstrual bleeding, iron deficiency, and iron deficiency anemia

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For reproductive-aged women, the symptom of heavy menstrual bleeding is highly prevalent and a major contributor to iron deficiency and its most severe manifestation, iron deficiency anemia. It is recognized that these 2 clinical entities are not only highly prevalent, but their interrelationship is poorly appreciated and frequently normalized by society, healthcare providers, and affected girls and women themselves. Both heavy menstrual bleeding and iron deficiency, with or without anemia, adversely impact quality of life—heavy menstrual bleeding during the episodes of bleeding and iron deficiency on a daily basis. These combined issues adversely affect the lives of reproductive-aged girls and women of all ages, from menarche to menopause, and their often-insidious nature frequently leads to normalization. The effects on cognitive function and the related work and school absenteeism and presenteeism can undermine the efforts and function of women in all walks of life, be they students, educators, employers, or employees. There is also an increasing body of evidence that suggests that iron deficiency, even in early pregnancy, may adversely impact fetal neurodevelopment with enduring effects on a spectrum of cognitive and psychological disorders, critically important evidence that begs the normalization of iron stores in reproductive-aged women. The authors seek to raise individual, societal, and professional awareness of this underappreciated situation in a fashion that leads to meaningful and evidence-based changes in clinical guidance and healthcare policy directed at preventing, screening, diagnosing, and appropriately managing both disorders. This manuscript provides evidence supporting the need for action and describes the elements necessary to address this pervasive set of conditions that not only affect reproductive-aged girls and women but also the lives of children everywhere.

Key words: abnormal uterine bleeding, heavy menstrual bleeding, iron deficiency, iron deficiency anemia

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Introduction

The objective of this expert review was to raise awareness of the related conditions of heavy menstrual bleeding (HMB) and iron deficiency (ID), along with the extreme manifestation of ID, iron deficiency anemia (IDA). These interrelated conditions have broad and far-reaching consequences for adolescent girls and women on a global scale and, as a consequence of the impact of iron deficiency on fetal brain development, on males as well. This expert group of coauthors met virtually on multiple occasions to discuss the need for consensus on the appropriate screening and diagnosis procedures and consistent management of HMB, ID, and IDA. It is apparent that these related clinical entities cross a number of specialty boundaries in a way that has impeded public and professional awareness of the depth and breadth of the problem. This has impaired the development and implementation of appropriate policies and screening, diagnosis, and treatment guidelines necessary to address this critically important clinical situation.

Heavy menstrual bleeding and iron deficiency

Heavy menstrual bleeding

HMB is a symptom that is defined as menstrual blood loss that is of sufficient volume to adversely impact a woman's physical, emotional, social, and/or material quality of life (QoL).[1] It is but one of the symptoms that comprise abnormal uterine bleeding (AUB) in nonpregnant, reproductive-aged women. The symptom of HMB is one of the most common gynecologic complaints, and although data from healthcare systems suggest a prevalence of 3% to 5%, population-based studies using definitions like that described previously suggest that it may affect up to 50% of women of reproductive age.[2,3] AUB accounts for 18% to 30% of all gynecologic visits and leads to more than half of the 600,000 hysterectomies performed annually for benign disorders in the United States.[4,5]

The perceived underreported prevalence of HMB is likely because of a lack of recognition by patients and a wide variability in reporting by physicians and other healthcare providers (HCPs), with data sources typically comprising data of private or government-funded provider systems.[2,6,7] One reason for the disparity in prevalence data on HMB is the historic and cultural aversion to discussing menstruation and its management, even among HCPs.[7] This lack of awareness of normal vs heavy bleeding can lead to acceptance and normalization of HMB symptoms by HCPs and reproductive-aged women, including adolescents and their parents, instead of being recognized as excessive or at least problematic.[2,3,7] Societal and cultural values influence patient reporting and attendance of HCP appointments in a fashion that undermines appropriate assessment and management of HMB. It is estimated that fewer than half of the women who experience HMB visit their HCP, and when they do, the diagnostic evaluation and treatment are often suboptimal.[2,7,8] Collectively, these observations likely explain the underestimation of HMB prevalence when the data sources are healthcare system databases.

Iron deficiency and iron deficiency anemia

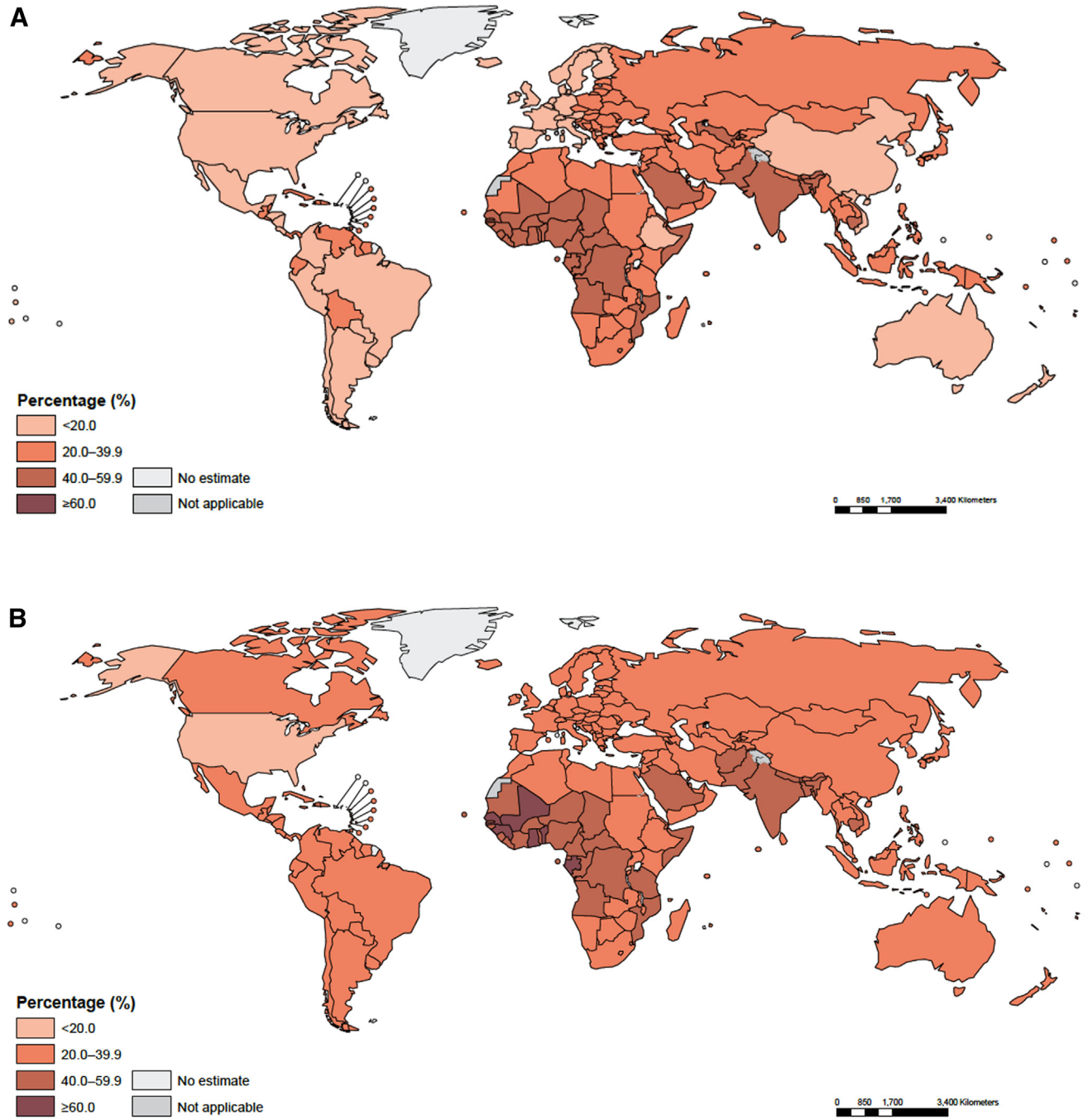
Anemia is a decreased hemoglobin concentration, which in nonpregnant, reproductive-aged women has been defined by the World Health Organization (WHO) as being below the threshold value of 12 g/dL.[9] The disorder is a major global public health problem affecting about one-quarter of the world's population, predominantly women and children[10,11] (Figure 1). Although the prevalence varies among populations and according to region, ID accounts for approximately 75% of all anemia cases. Indeed, the WHO has recognized ID as the most common micronutrient deficiency worldwide and a top 10 cause of disability,[12] affecting more than 20% of women of reproductive age[12–17].

Understanding the potential impact of ID requires knowledge of iron metabolism. The role of iron in humans is critical and multifaceted to an extent that is frequently not appreciated by both the lay public and many HCPs. Iron is important not just for its role in the synthesis of hemoglobin needed for oxygen transport but also as an essential trace mineral that is a critically important component of many organismal processes. Iron is necessary for mitochondrial energy metabolism and many enzymatic processes across multiple tissue sites, affecting myocardial and skeletal muscle activity, the production of neurotransmitters, and the function of the immune system.[18]

The body tightly regulates iron metabolism, but there is no mechanism for active iron excretion. Therefore, ID occurs via 2 principal mechanisms, namely insufficient iron intake because of diet or poor iron absorption or iron loss in excess nutritional intake secondary to clinical problems such as HMB or chronic gastrointestinal bleeding. Another important mechanism contributing to iron depletion occurs in individuals who donate blood, a population disproportionately comprising adolescents aged 16 to 18 years who make up about 15% of the United States donor pool.[19]

When ID develops, iron is initially mobilized from ferritin, its stored form, located predominantly in the liver. As deficiency worsens, iron also is taken from iron enzymes and iron proteins to maintain erythropoiesis.[20] This diversion of iron resources to heme comes at the expense of enzymatic and other essential body functions well before the appearance of anemia, which is the final stage of ID.[18] Consequently, ID itself is associated with a multitude of symptoms that affect both mental and physical health and work productivity. In adolescent females, there is evidence that ID alone can be associated with physical[21] and cognitive impairment.[22,23] Investigators have found a relatively high prevalence of ID in apparently healthy women[24] and especially in young females presenting for the first time as blood donors.[20,25,26] The symptoms related to ID are similar to those of IDA, including fatigue and exhaustion, brain fog, muscle weakness, shortness of breath, dizziness, pica, insomnia, restless legs, and hair loss[13,14,27]. Treatment of

FIGURE 1
The global prevalence of anemia



A, Depicts the worldwide prevalence of anemia in all women. **B**, Demonstrates the prevalence of anemia among those who are pregnant. Iron deficiency is the cause or contributor to at least half the worldwide cases of anemia in reproductive-aged women. Figure reproduced with permission (#389518) from the World Health Organization publication accessed June 1, 2022.[15]

Munro. Relationship between heavy menstrual bleeding, iron deficiency, and iron deficiency anemia. Am J Obstet Gynecol 2023.

ID in nonanemic women has been shown to improve skeletal muscle and physical function.[24] Collectively, these circumstances indicate a need for routine screening of otherwise healthy, nonpregnant, reproductive-aged women for ID by measuring ferritin and hemoglobin levels.

Our current understanding of the prevalence of ID and IDA in the female population is primarily informed by studies of adolescent girls and women

presenting for blood donation. The US-based Comparison of Donation History and Iron Levels in Teenage Blood Donors study of adolescent girls presenting for blood donation demonstrated a prevalence of absent iron stores of 18% (<12 ng/mL) and of iron deficiency of 50% (here defined as <26 ng/mL), approximately twice that of adult women.[28] These data are similar to those reported in the Recipient Epidemiology and Donor Evaluation Study (REDS) in the United States,[29] Canada,[30] and Australia. However, the latter study defined absent iron stores as <15 ng/mL.[31] Although the overall prevalence of anemia in these cohorts is often difficult to determine, the REDS reported that 17.7% of all females are deferred from blood donation for a hemoglobin level below 12.5 g/dL,[32] and the Australian study described a prevalence of anemia of 8.5%.[31] Regardless, all of these studies demonstrated that the measurement of hemoglobin is an inadequate surrogate for the measurement of ferritin for the diagnosis of ID.

Relationship between HMB and ID or IDA

Although HMB is caused by 1 or a combination of conditions, chronic blood loss from HMB is a key contributor to the development of ID and IDA.[33] The extent of the bleeding is often unappreciated by the woman and her HCP despite the continuous depletion of iron that makes HMB the most common cause of IDA, at least in the developed world.[13] This circumstance may be amplified in low- and middle-income countries (LMICs); a report from Pakistan demonstrated a prevalence of anemia among adolescent girls of 50.6% with a highly significant association with HMB.[34] Indeed, HMB, often associated with acute episodes of heavy bleeding, may start at menarche, which is a time when previously undiagnosed coagulopathies, such as von Willebrand disease (vWD), are uncovered. Hundreds of girls are admitted to United States children's hospitals yearly for complications related to severe anemia caused by HMB.[35] Data on the true relationship between HMB and ID or IDA are limited mainly because of an absence of guidelines that direct laboratory screening in adolescent girls and adult women and underreporting of the symptom of HMB. It can be hypothesized that the impact of HMB on ID and IDA may be even more striking in LMICs and other settings with a higher prevalence of malnutrition. In these regions, the monthly iron depletion induced by HMB would propel already vulnerable girls and women into ID and IDA, as reflected in data on the prevalence of anemia among women of childbearing age (Figure 1, A).

The combined impact of HMB, ID, and IDA

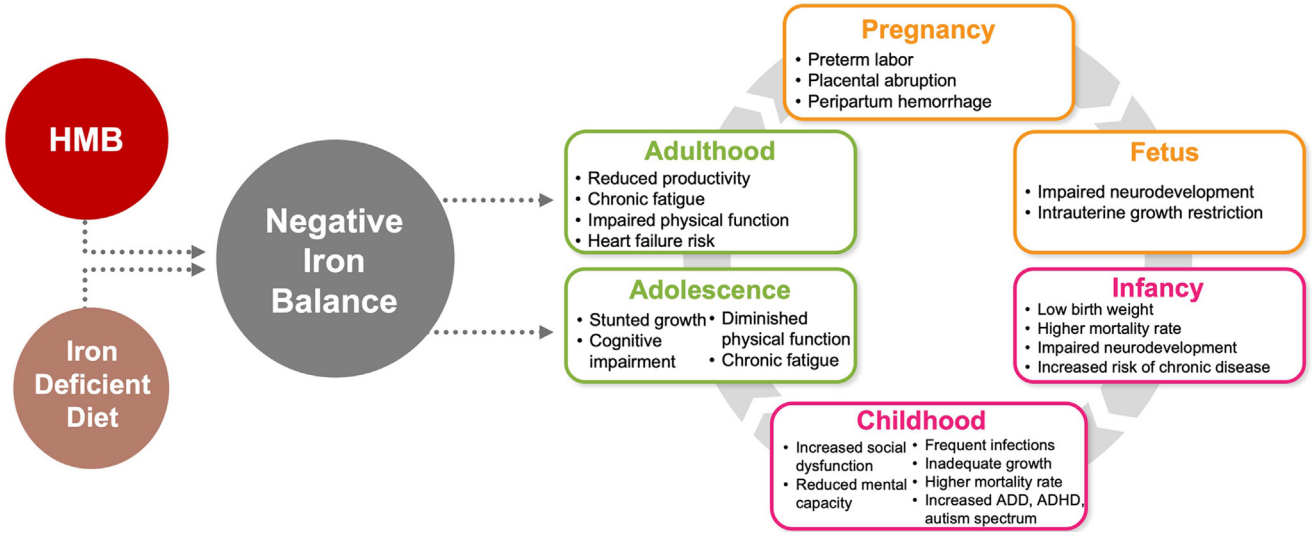
It is apparent that HMB and, when present, ID have insidious and potentially far-reaching clinical and economic impacts experienced not only by the individual woman but also by her children, her employers, her healthcare system, and society at large. The combination of HMB and ID, with or without anemia, negatively impacts QoL parameters for various reasons and from several perspectives. The intermittent symptom of HMB, by definition, interferes with a woman's physical, social, emotional, and/or material QoL.[1,36,37] However, ID can impact a woman's health and QoL daily.[21,22,38–40] Women with HMB scored significantly lower on studies[41] using validated patient-reported QoL instruments such as the 36-Item Short Form survey (SF-36), which comprises 36 questions in 8 domains, including physical function, bodily pain, general health, vitality, social function, emotional and mental health, and psychological and physical composite scores.[42–44] In a systematic review of 5 studies reporting on 1171 women, there was a significantly lower SF-36 score among those with HMB (called menorrhagia in this paper) than among those without HMB.[41] Subsequent investigators from multiple countries have found similar results, demonstrating the significant impact that the symptom of HMB has on QoL.[37,45–47]

The economic burden that HMB and ID or IDA place on women and their families, employers, and national healthcare systems is substantial. Work absenteeism has been reported in almost 14% of those with HMB, whereas presenteeism, the symptom affecting work quality, was reported by more than 80%.[48] Studies performed in the early 2000s showed that the annual costs for women with HMB were estimated to exceed $2000 per family primarily because of the cost of menstrual products, work absence, and absenteeism.[49,50] In 2007, the United States total direct and indirect costs were estimated to be between $12 billion and $37 billion US dollars.[6]

Issues in the diagnosis and management of ID and IDA

Several issues confound or impair the diagnosis and treatment of ID and IDA. Failure to address these issues will prolong the morbidity experienced by millions, if not billions, of untold women worldwide. For example, a number of conditions, including pregnancy, thalassemia, and inflammatory disorders, impact ferritin levels, potentially obscuring the diagnosis.[51] The recognition of ID is also impeded by inconsistent and highly variable local laboratory reference ranges for women with lower limits of normal that are often below the WHO criteria for iron deficiency (<15 ng/mL) and well below the threshold at which oral iron supplementation has been shown to improve hemoglobin status (<50 ng/mL),[20] as well as below a recently determined physiological threshold of 25.4 ng/mL for females of reproductive age.[52] These suboptimal reference ranges likely reflect the inclusion in the sample of so called healthy females who fail to appreciate their ID status, highlighting the hidden burden of this condition. Setting the threshold for ID artificially low runs the risk of reassuring women with ID that they have a normal iron status with the consequent failure to provide appropriate treatment. Indeed, even the generally accepted lower limit of normal for hemoglobin in nonpregnant women, 12 g/dL, can be challenged because the available evidence suggests that when iron-deficient women are removed from the analysis, the lower limit for women is 13 g/dL, which is the same as for men.[53] These

FIGURE 2
Iron deficiency represents an intergenerational challenge



In addition to heavy menstrual bleeding, an iron-deficient diet, prevalent in adolescents and especially women residing in low- and middle-income countries, contributes to a negative iron balance and the consequent iron deficiency. When iron-deficient women become pregnant, and especially when anemia is present, the impact on pregnancy and the developing fetus can be severe and include neurodevelopmental impairment and long-term neurologic dysfunction that exists into adulthood. Often, iron stores are not restored in the postpartum woman, a circumstance that sets the stage for repeated events in subsequent pregnancies. By Malcolm G. Munro and Richard Derman with permission, as adapted from Bailey, R. et al.[54]

Munro. Relationship between heavy menstrual bleeding, iron deficiency, and iron deficiency anemia. Am J Obstet Gynecol 2023.

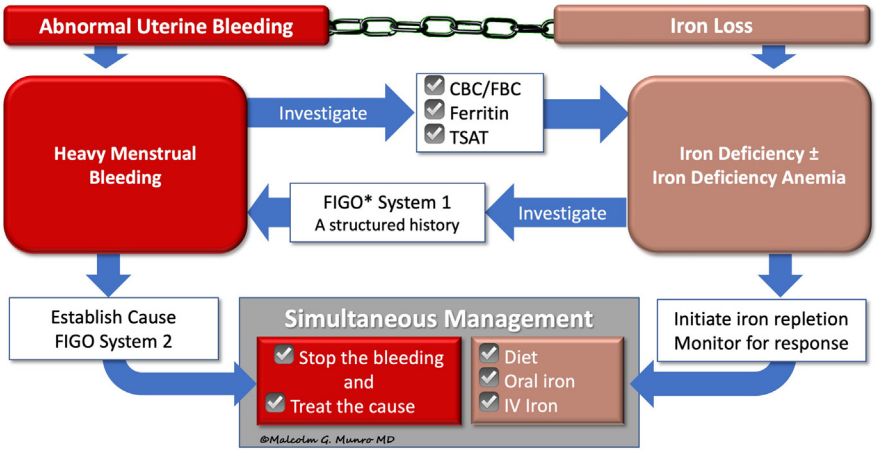
observations further emphasize the need to develop and implement evidence-based screening guidelines for ID and IDA in nonpregnant women.

The recognition and early management of ID and IDA among women of childbearing age are of particular importance because IDA in pregnant women can be associated with adverse outcomes, including preterm labor, low birthweight, and postpartum hemorrhage, as well as neurodevelopmental delay in the newborn (Figure 2). These associations may even apply to ID alone.[55,56] The common identification of IDA in pregnancy is likely a consequence of the high prevalence of undetected and untreated ID before pregnancy (Figure 1). The detection of IDA in pregnancy is likely associated with guidelines, including those by the American College of Obstetricians and Gynecologists (ACOG), that recommend screening of all pregnant women.[57] However, no formal guidance exists for the detection of ID itself despite a reported prevalence of >50% even in developed countries such as Canada.[56] Furthermore, no US-based guidelines exist that support the detection and treatment of ID or IDA among women planning to conceive, including those with HMB. In the United Kingdom, the National Institute for Health and Care Excellence (NICE) recommends obtaining a "full blood count…on all women with HMB." It explicitly recommends that screening for ID should not be done by measuring ferritin levels.[58,59]

There are also barriers to effective therapy. Although increased dietary intake of iron is important, iron therapy remains the first-line treatment for both ID and IDA, usually with orally administered formulations.[60] However, oral iron supplementation is frequently ineffective because of patient compliance issues typically related to the gastrointestinal side effect profile that includes nausea and constipation. These symptoms can often be mitigated with strategies such as low-dose daily schedules[61] or alternate-day, low-dose administration, approaches that may not be appreciated by many HCPs.[62,63] Indeed, alternate-day administration allows hepcidin levels to fall before the next dose, enhancing total iron absorption and reducing the incidence and severity of gastrointestinal side effects.[62,63] Clinicians also frequently seem to be unaware of follow-up protocols designed to assess for an appropriate response to oral iron administration; for IDA, if there is not at least a 1 g/dL response by 2 weeks, there is likely either a problem with compliance or absorption.[64] In addition, many are unsure of the endpoint of oral iron administration because the return to normal hemoglobin levels does not indicate that iron stores have been repleted. For those unable to tolerate oral therapy, those who exhibit an inadequate response, or for whom the rapid restoration of iron stores is needed, such as those planning imminent surgery, intravenous iron is an appropriate and effective option.

Historically, parenteral iron therapy was associated with a concerning side-effect profile, leading to prolonged infusions of low iron doses that required frequent administration to counter the risks of adverse reactions. However, improvements in the design of parenteral

FIGURE 3
The symptom of HMB and ID are frequently related



One of the most common abnormal uterine bleeding symptoms is HMB, which may be present in up to 50% of nonpregnant, reproductive-aged girls and women. When the structured history described in the FIGO System 1[67] suggests HMB, the individual should be simultaneously investigated for the cause of the bleeding according to FIGO System 2[67] and for ID and anemia using appropriate laboratory tests. Similarly, when reproductive-aged girls and women are shown to have ID, they should be investigated for the presence of HMB. Management should include treatment of both the ID and the cause of the HMB as appropriate. From Malcolm G. Munro MD, with permission.

FIGO, International Federation of Gynecology and Obstetrics; *ID*, iron deficiency; *HMB*, heavy menstrual bleeding.

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formulations have dramatically mitigated the risks, reduced the need for allergy prophylaxis, and increased the dosing to allow, for some formulations, iron repletion in a single infusion. Many clinicians remain unaware of these advances, a circumstance that seems to have limited the use of parenteral iron therapy to the detriment of patients with ID and IDA. One of the issues restricting the use of intravenous iron therapy is cost, an important consideration for employers and payers, patients and providers, and those who reside in LMICs.[65] Unfortunately, despite the benefit of iron therapy for women with ID or IDA, no widespread, evidence-based guidance has been developed.

Challenges in the diagnosis and therapy for HMB

We have mentioned the problem of normalizing HMB by society, families, HCPs, and women themselves. However, even if symptoms are recognized, there exists inconsistent use of appropriate and available diagnostic techniques to identify the cause or causes of HMB and to inform the selection of medical and minimally invasive surgical options for affected women. The International Federation of Gynecology and Obstetrics (FIGO) has developed 2 systems to facilitate and standardize the evaluation of reproductive-aged women with AUB, System 1 to characterize symptoms, including HMB, and System 2 to identify potential causes of the problem.[66,67] These causes include structural abnormalities in the uterus such as polyps (AUB-P), adenomyosis (AUB-A), and leiomyomas (AUB-L), as well as disorders of systemic or local functions such as inherited coagulopathies (AUB-C), ovulatory disorders (AUB-O), and endometrial dysfunction (AUB-E), each of which can manifest with excessive menstrual blood loss or HMB.

It is not clear if such a diagnostic approach is widely used. For example, when HMB occurs in adolescents, there is evidence that about one-third have an underlying disorder of hemostasis, such as vWD or platelet aggregation abnormalities.[68,69] Even in adult women, the prevalence of vWD is about 13%.[70] This cause of HMB, called AUB-C in FIGO System 2, is often unrecognized by HCPs.[71] For these and other reasons, therapy varies greatly by provider in that a broad range of medical, procedural, and surgical interventions are offered for seemingly similar conditions.[72,73] Hysterectomy remains an exceedingly common procedure for women with menstrual disorders, including HMB, despite the introduction of a variety of medical and minimally invasive procedural options starting more than 20 years ago.[74] These inconsistencies reflect variable education and training of gynecologists, in combination with disproportionate incentives for procedural interventions that are often performed instead of offering safe, effective, and often less-expensive medical options.

The reasons for such suboptimal and inconsistent care vary but, at least in part, seem to be the consequence of heterogeneity in clinical guidelines on the appropriate assessment methods to use, including imaging and laboratory evaluation, and a lack of knowledge on the extent and appropriate use of available medical and procedural management options.

The unmet need

As we have shown, HMB and associated ID are underappreciated disorders that are prevalent among adolescents and women of reproductive age and that negatively impact QoL, school and workplace performance, as well as physical and cognitive function, all the while adding to the global healthcare financial burden. The potential adverse impacts of ID on pregnancy outcomes in the developing fetus is an additional justification for urgent action to address this situation. Solutions are attainable because the diagnosis and treatment of ID and related anemia can be easily achieved and the causes of HMB can be identified and effectively managed often with inexpensive medical options or with appropriate and typically minimally invasive procedural interventions (Figure 3).

TABLE
Call to action

A comprehensive approach to the identification and management of HMB, ID, and IDA

Proposed is a broad strategy designed to address the unmet needs around the issues of HMB and ID, including IDA.

I. Increase awareness of the relationship between the symptom of HMB and ID or IDA

Raise awareness of both HMB and ID or IDA and their interrelationship in all identified stakeholders, including, but not limited to girls, women and their families, and healthcare providers, employers, educators, payors, and clinical investigators. Other important stakeholders include members of the life sciences industry, healthcare provider systems, and those in government, medical societies, and other influential organizations charged with the development and implementation of healthcare policy

II. Harmonize definitions of ID and anemia across systems and jurisdictions:
   a. Recognize the limitations of current "normal" reference ranges for hemoglobin based on populations that include individuals with ID
   b. Develop consensus on appropriate, evidence-based thresholds for normal ferritin values
III. Advocate for routine screening of adolescent girls and reproductive-aged women
   a. Routine screening for ferritin and hemoglobin that begins during adolescence and continues at appropriate intervals.
   b. Screening for disorders of hemostasis (coagulopathies) in girls and women with chronic HMB
   c. Screening for HMB in girls and women with ID with or without IDA
IV. Facilitate further research on the impact of ID without anemia in adolescents and adult women of reproductive age considering:
   a. Cognitive function
   b. Physical function
   c. Pregnancy. Liaise with and support those investigators exploring the relationships of ID with pregnancy and pediatric neurodevelopmental outcomes.
V. Improve implementation of appropriate iron replacement therapy regimens
   a. Provide appropriate guidance on diet, including for those with comorbidities that may adversely affect iron absorption.
   b. Develop evidence-based guidelines for the optimal dose and schedule for oral iron administration for both ID and IDA to improve absorption and minimize side effects.
   c. Develop evidence-based guidelines for the use of intravenous iron supplementation for those who are intolerant of or not suited to oral iron supplementation, including use as an alternative for blood transfusion.
   d. Facilitate the development and implementation of systems and guidelines designed to normalize hemoglobin levels before major surgery on women. Such guidance should include some combination of medical interventions designed to minimize uterine bleeding and appropriate route, dose, and schedule of iron therapy.
VI. Improve provider education on the detection, evaluation, and appropriate counseling and management of girls and women with the symptom of HMB
   a. Defining the symptoms using a structured history (FIGO System 1).
   b. Case-appropriate evaluation for cause (FIGO System 2; PALM-COEIN).
   c. Include routine assessment for the detection of ID and IDA "If you see HMB, think ID."
   d. Preferential selection of cause-specific medical and minimally invasive procedural interventions.
VII. Develop and maintain comprehensive ID, IDA, and HMB databases to support real world evidence-based research
   a. Collaboration with healthcare systems, particularly those using electronic medical records.
   b. Include co-stakeholders including payors, the life sciences industry, and government agencies.

The expert group calls on governments, policymakers, clinicians, researchers, educators, advocacy groups, and the life science industry to take steps designed to address the virtual, debilitating, and pervasive condition that is iron deficiency.

FIGO, International Federation of Gynecology and Obstetrics; *ID*, iron deficiency; *IDA*, iron deficiency anemia; *HMB*, heavy menstrual bleeding; *PALM-COEIN*, polyp, adenomyosis, leiomyoma, malignancy and hyperplasia, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified.

Munro. Relationship between heavy menstrual bleeding, iron deficiency, and iron deficiency anemia. Am J Obstet Gynecol 2023.

Unfortunately, it will be necessary to surmount several hurdles before these paired issues are consistently and simultaneously addressed in a fashion that demonstrably improves the relevant outcomes (Table). National and international guidelines and initiatives do not seem to be aligned. The WHO issued recommendations encouraging the assessment, prevention, and control of ID and IDA in 2001, emphasizing the removal of nutritional barriers and promoting the use of iron supplementation.[75] However, there was no mention of the role of HMB in the genesis of IDA in nonpregnant, reproductive-aged girls and women. An ACOG guideline emphasized the importance of coordinating care with hematology to ensure serum ferritin levels are assessed in pregnant women with anemia but provides no guidance on the screening for ID and IDA in women with HMB, including those who are planning to conceive.[76] The American Gastroenterology Association has recently recommended bidirectional endoscopy, a costly and invasive procedure, to exclude gastrointestinal malignancy in essentially all reproductive-aged women with IDA,[77] but it does not address the role of HMB at all in this category of women, a recommendation that is at odds with the guidance of the British Society of Gastroenterology.[78] Such an approach, if implemented, would likely elevate the morbidity and cost associated with the investigation of anemia without addressing what seems to be the most common cause in reproductive-aged women.

An unmet need exists for a multipronged strategy to raise awareness of the high prevalence and societal impact of these related conditions, including increased screening and improved diagnosis and therapy. A necessary component of the strategy is to identify existing evidence gaps related to epidemiology, screening and diagnostic alignment, optimization of therapeutic interventions, and appropriate follow-up care for both conditions. It is clear that girls and reproductive-aged women worldwide are frequently disadvantaged, adversely affecting society as a whole and not just those affected by these disorders. Consequently, our governments, granting agencies, medical organizations, and clinical investigators, to name only a few, must urgently address this issue in a well-designed, comprehensive, and effective fashion. ■

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