Iron deficiency anaemia: Managing symptoms and supporting self-care. 2024 - Part 1

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Summary

Anaemia is a global public health concern, affecting individuals of all ages and demographic groups, with implications for health, morbidity and mortality. It stems from many factors, including diet, chronic illnesses, infections, hereditary blood disorders and other conditions related to blood loss and reduced haemoglobin levels. While anaemia manifests as decreased haemoglobin or haematocrit levels, iron deficiency anaemia is the most prevalent type, and iron is a crucial element for growth and development and a component of haemoglobin.

In 2022, the International Pharmaceutical Federation (FIP) explored the role of pharmacists in anaemia management, emphasising the need for an educational guide to support pharmacists, particularly in addressing iron deficiency anaemia (IDA). IDA, which affects 1.2 billion individuals worldwide, is preventable and treatable, highlighting the importance of early detection. Pharmacists, as accessible healthcare providers, bear a critical responsibility to educate patients, tailored to factors like age, sex, underlying conditions and the causes of IDA, encompassing self-care interventions and various management approaches. Pharmacists can promote a holistic approach to self-care and can support mitigation of the impact of this condition on overall health and well-being.

This handbook aims to provide a comprehensive guide for pharmacists to manage iron deficiency anaemia effectively, including for more vulnerable populations. It equips pharmacists with information on treatment options, managing special populations, screening and preventive measures for IDA. Nutrition, emphasising iron-rich diets and physical activity, is also described.

Addressing other types of anaemia is equally important, necessitating the identification and tailored treatment of their underlying causes. This handbook only covers anaemia treatment and management due to iron deficiency; there remains a need to further develop resources and guidelines for the management of other types of anaemia.

Further professional programmes designed to enhance pharmacists' competence in managing IDA, such as in a format of workshops, self-directed learning opportunities, or continuing professional development courses, are recommended. Collaboration with national professional leadership bodies would facilitate the organisation of workshops, self-directed learning initiatives, and the sharing of best practices.

In conclusion, this handbook serves as an invaluable resource for pharmacists in managing IDA, underpinning the importance of pharmacists' role in screening, managing, treating, patient education and holistic self-care practices. It is recommended to accompany this handbook with further CPD and resources for other types of anaemia.

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1. Introduction

The sections in this handbook were developed following a structured scoping review process using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guideline. The steps involved can be seen in Figure 1.

1.1 Background

Anaemia is a major global public health concern, closely tied to socioeconomic status and education,[1,2] and could indicate poor nutrition and health.[3] Anaemia involves a decreased red blood cell count or haemoglobin concentration, which impairs oxygen transport in the body.[3] The World Health Organization (WHO) defines anaemia as haemoglobin levels below 12.0 g/dl in non-pregnant, reproductive-aged women and 13.0 g/dl in males.[4-6] It is estimated that half of the global burden of anaemia[7] is due to iron deficiency.

Globally, anaemia affects around 40% of children (6–59 months), 37% of pregnant women, and 30% of women (15–49 years).[1,2] The WHO African and South-East Asian regions are most affected.[8] In 2019, 1.8 billion people (23% of the world) suffered from anaemia,[1,4] increasing to 1.9 billion in 2021.[9] Males exhibited a lower prevalence than females across all age groups. In 2021, the prevalence for all age groups was 17.5% in males and 31.2% in females.[9] A critical concern is for women of reproductive age, as anaemia contributes to maternal deaths,[10,11] and affects about two in five pregnant women and one in three non-pregnant women in this group.[8,11]

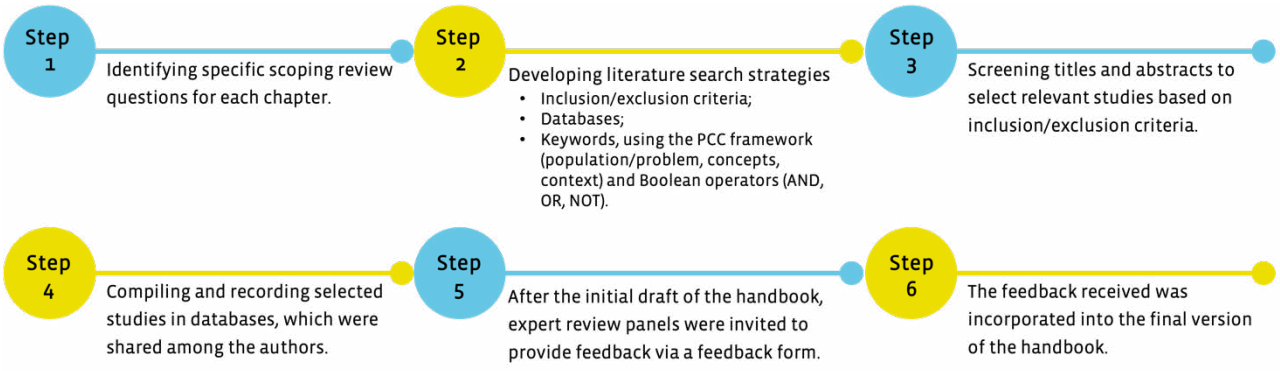

Figure 1: Steps involved in the development process of the handbook

The underlying causes of anaemia are multifactoral,[12] including biological, socioeconomic and ecological influences.[1] The causes may vary by population and age; for example, nutritional deficiencies and chronic diseases are the most common causes in children and older adults, respectively.[2] Causes of anaemia can be nutrition-specific (e.g., insufficient intake or poor absorption of micronutrients), non-nutritional specific (e.g., inherited haemoglobinopathies and infectious diseases), or a combination of these; each of these factors may have a social component.[8] Low socioeconomic status and limited education increase risk through poor living conditions, inadequate diets and restricted healthcare access.[1] There were variations in the distribution of anaemia cases based on gender and country, but dietary iron deficiency, haemoglobinopathies and haemolytic anaemias (13.7%) accounted for most cases worldwide.[4] Looking specifically at low and lower-middle income countries, iron deficiency and malaria are the most common causes of anaemia, particularly in rural and poor households with no formal education.[1] Comprehensive approaches are needed to address this multifaceted problem.[1]

1.2 Global policies and interventions on anaemia

As a health concern affecting maternal, infant and child well-being, anaemia recognition and treatment is significant for global policy and intervention agendas. As long ago as 2012, the World Health Assembly (WHA) approved global targets for maternal, infant and young child nutrition, which encompasses the ambitious objective of halving anaemia prevalence in women aged 15 to 49 by 2025.[1,13] This effort is reinforced by the United Nations 2030 Agenda for Sustainable Development Goals (SDGs), which highlights anaemia in women of the same age group as a key indicator of 2.2.3 of the SDGs.[1,8] This commitment was affirmed at the 2021 Nutrition for Growth Summit, where the WHO pledged to develop an encompassing framework for preventing, diagnosing and managing anaemia through a holistic approach.[1] Additionally, an Anaemia Action Alliance was created to align actions in reducing anaemia. [1]

Progress in reducing anaemia prevalence has been insufficient. While some progress has been made in combating anaemia, the most substantial declines have been seen among males and adults aged 20–74 years.[9] In contrast, young children (under five years) and women of reproductive age have not experienced the same improvement.[9] From 2000 to 2019, global estimates of anaemia prevalence slightly decreased from 31% to 30% among non-pregnant women and 41% to 36% among pregnant women. There is a global prevalence of 40% in 2019 for infants and children, exceeding 70% in specific countries. This status quo mandates comprehensive changes on multiple fronts, necessitating the involvement of policymakers, politicians, pharmacists and clinicians to address the complex factors contributing to anaemia.[12]

1.3 Iron deficiency anaemia

As stated above, it is estimated that half of the global burden of anemia[7] is due to iron deficiency (ID). ID is characterised by a reduction in the body's total iron content and is a global nutritional concern affecting over two billion people.[14,15] It may or may not progress to iron deficiency anaemia (IDA), a common form of chronic anaemia.[15] ID can result from insufficient iron intake or absorption and can also occur due to clinical issues such as chronic gastrointestinal bleeding or iron depletion, like blood donation.[16] As ID progresses, it initially mobilises iron from ferritin, primarily stored in the liver. This redirection of iron resources to support red blood cell production occurs at the expense of other essential bodily functions and precedes the onset of anaemia, leading to IDA.[16] According to International Classification of Diseases (ICD)-10 and Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT), IDA is categorised as nutritional anaemia (disorder) or nutritional deficiency associated condition (disorder) and it is interpreted as haemoglobin or red blood cell count below reference range.[17,18]

Both ID and IDA significantly impact an individual's well-being.[19] ID alone adversely affects quality of life and cognitive function.[16] Chronic conditions like chronic kidney disease, heart failure and inflammatory diseases are often associated with ID and contribute to increased mortality risk.[20] ID, with or without anaemia, is also a common complication of cancer.[20] In mild-to-moderate cases, symptoms such as fatigue, weakness and shortness of breath may occur.[16,20] However, some cases can remain asymptomatic.[21] Untreated ID, particularly IDA, leads to reduced cognitive function,[22] decreased work productivity and diminished overall quality of life.[4,21,23] During pregnancy, untreated ID hampers fetal brain maturation and development,[2,21,24] and contributes to low

birth weight and maternal complications.[19] Untreated ID can also affect child development, causing impaired school performance.[2] Addressing ID and IDA could yield substantial economic returns.[25]

Diagnosing and managing ID and IDA present challenges due to varying diagnostic criteria and tests.[19] Haemoglobin concentration lacks sensitivity and specificity, leading to potential underestimation of ID.[14] ID without anaemia can be elusive, with vague symptoms, necessitating investigation in patients with normal complete blood counts and low ferritin levels.[19,21] Conditions like pregnancy, thalassaemia and inflammatory disorders can complicate diagnosis by impacting ferritin levels.[20] Inconsistent laboratory reference ranges for ferritin in women further hinder accurate diagnosis.[19] Striking a balance between diagnostic thresholds is crucial, as setting it too low risks overlooking iron deficiency cases.[19] Comprehensive guidelines for early detection and management are essential, especially among women of childbearing age.[19] Implementing effective screening practices, including measuring ferritin and haemoglobin levels, can enhance outcomes and alleviate the associated health burdens.[19]

1.4 FIP contribution to support pharmacists' roles in managing anaemia

Historical efforts have often emphasised iron deficiency as the primary cause of anaemia; however, the complexity of anaemia demands a multifaceted approach.[26] A collaborative approach involving various stakeholders, including governments, civil society, healthcare professionals, academia, researchers and the media, is essential to drive meaningful progress. Each plays a specific role in reducing anaemia and promoting good health.[26] Associations and societies of healthcare professionals can promote education and awareness among association and society members, professionals and the general public about the importance of addressing anaemia comprehensively.[1]

The International Pharmaceutical Federation (FIP), a global professional leadership body for pharmacists, pharmaceutical scientists and educators, conducted an exploration study in May 2022 on pharmacists' role in anaemia, specifically IDA. This study underscored the imperative of enhancing the involvement of practising pharmacists, particularly community and hospital pharmacists, in IDA management.[27,28] With a foundation in clinical expertise and a widespread presence, pharmacists possess substantial opportunities to play a pivotal role in reducing IDA. This encompasses diverse aspects, including understanding the causes, participating in treatment strategies, engaging in preventive measures and promoting self-care practices.[27,28]

This explorative study also highlights the necessity to offer educational assistance to pharmacists, achieved through the provision of guidelines or toolkits for anaemia counselling, treatment, management, screening and prevention, complemented by comprehensive training sessions and

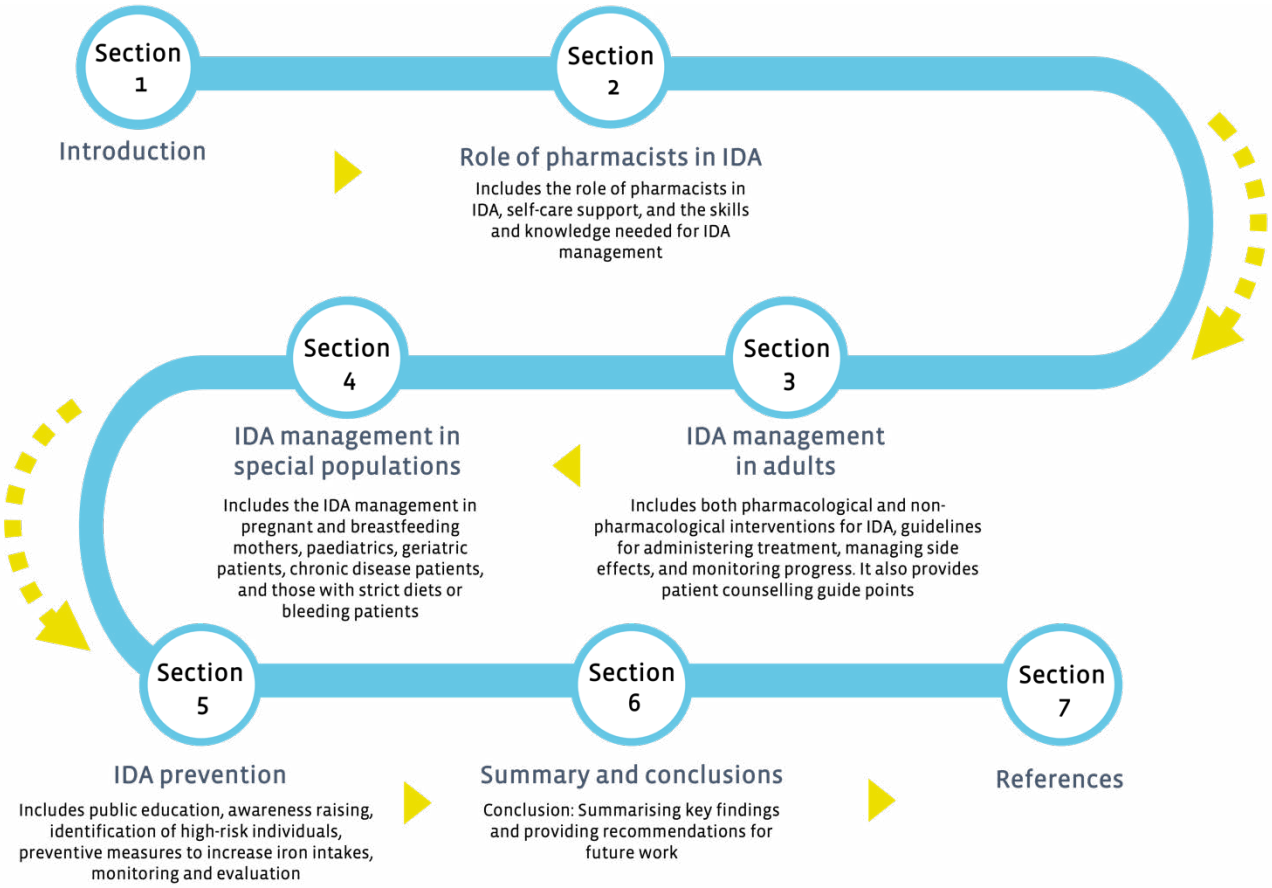

Figure 2: Sections included in this handbook

workshops.[27,28] It is recommended that national professional leadership bodies collaborate in developing practice support materials. These resources would empower pharmacists to excel in their role, ultimately contributing to the advancement of public health through comprehensive anaemia management strategies.[27,28]

1.5 Handbook development to support pharmacists' roles in IDA

This handbook is designed to be a valuable resource for a range of stakeholders:

- **Pharmacists** — This handbook serves as a comprehensive guide for pharmacists, offering guidance on screening, treating, managing, and preventing iron deficiency anaemia. It equips pharmacists with the knowledge and skills necessary for tasks like screening and counselling, enabling them to provide personalised patient care and stay updated on the latest guidelines and treatments.
- **Professional pharmacy leadership bodies** — Professional leadership bodies can share this handbook with their members to enhance their practice and improve patient care.
- **Pharmacy students** — Pharmacy students can use this handbook as a foundational resource to build their understanding of IDA.
- **Researchers and academics** — This handbook can serve as a valuable reference source for researchers and academics studying IDA, helping them identify and address research gaps in this field.

This handbook consists of seven sections (Figure 2).

2. Role of pharmacists in IDA

2.1 Pharmacists' roles in supporting self-care with regard to IDA

Pharmacists play a pivotal role in advancing self-care practices, including addressing IDA.[27-29] Defined by the WHO as individuals' ability to manage their health independently, self-care is vital to improving well-being and achieving universal health coverage.[29-31] Empowering patients to actively participate in their health management enhances patient-centred care and overall healthcare outcomes.[32] Self-care should not be confused with self-medication. Self- medication involves using medication to treat self-diagnosed disorders or symptoms or the intermittent or continued use of prescribed medicines for chronic or recurrent conditions.[33] Self-care empowers individuals to make informed health choices, and pharmacists, easily accessible healthcare professionals, can support individuals in making informed decisions on their health. Pharmacists are crucial in advocating and facilitating self-care, offering various interventions to enhance patient autonomy.[29,34] They act as promoters, supporters and overseers of self-care within their communities and can contribute as programme managers and policymakers.[29] Pharmacists' involvement in self-care helps address health system challenges,[29] such as limited access to healthcare, poor health literacy and financial barriers, ultimately benefiting individuals and communities in managing conditions[35] like IDA.

The Global Self-Care Federation established the Self-Care Readiness Index in 2021 and updated the index in 2022.[36] It serves as a comprehensive framework for implementing self-care and a powerful advocacy tool for elevating self-care's status in local and international contexts. This framework spotlights four critical enablers of self-care: stakeholder support and adoption, consumer and patient empowerment, self-care health policies, and a supportive regulatory environment.[36] Pharmacists play an essential role in advancing the second enabler, consumer and patient empowerment, as they engage with patients directly, empowering them to make well-informed health choices, particularly in managing conditions[29] such as IDA. This aligns with the index's recommendations to enhance the availability of quality self-care information and encourage healthcare providers, including pharmacists, to endorse self- care practices,[36] especially in the context of IDA prevention, screening and management. Furthermore, the call for interprofessional collaboration resonates with the need for a coordinated approach[1] to address IDA through self-care, ensuring the optimal delivery of information and services to patients facing this specific health challenge. The Self-Care Readiness Index,[36] in conjunction with pharmacists' role, underscores their significant contribution to promoting self- care practices in the context of IDA and other health concerns.

The seven pillars framework of self-care is also relevant in addressing IDA, for which it offers a comprehensive structure for individuals to bolster their self-care abilities.[29,37] Firstly, within the "Knowledge and health literacy" pillar, pharmacists empower individuals by providing crucial information about IDA, its underlying causes and the available treatment options, enabling patients to make well-informed decisions tailored to their specific needs.[27-29] They significantly contribute to the "Healthy eating" pillar by offering dietary guidance, emphasising the importance of incorporating iron-rich foods and supplements into the diet, which is especially pertinent for individuals managing IDA.[27-29] Furthermore, in the "Rational use of products and services" pillar, pharmacists play a central role in ensuring the responsible and effective use of iron supplements, offering expert advice on proper dosage and timing, crucial considerations for those dealing with IDA.[27-29] Additionally, they actively support the "Risk avoidance and mitigation" pillar by counselling patients on lifestyle modifications to prevent the recurrence of anaemia, such as addressing dietary deficiencies and advocating behaviours that mitigate risks.[27-29] In essence, by actively engaging with patients and applying their expertise, pharmacists bridge the gap between the seven pillars framework and effective self-care practices, providing invaluable guidance for individuals managing the complexities of IDA and ultimately contributing to improved health and quality of life.[27-29]

The self-care matrix (SCM)[38] is another valuable framework that pharmacists can leverage to enhance their role[29] in addressing IDA. The SCM encompasses the various facets of self-care,

acknowledging the influence of social and health systems, environmental factors and policy-based determinants on individuals' self-care practices.[38] Pharmacists equipped with an understanding of this framework can better support patients in maximising their autonomy and advocating person-centred decision-making when managing conditions like IDA. The SCM offers pharmacists a holistic perspective to comprehend the complex factors influencing self-care.[29,38] Specifically, pharmacists can align their interventions with the SCM's dimensions to empower patients with knowledge about IDA, foster self-awareness regarding its management, promote physical activity and healthy eating, and advise on risk avoidance and mitigation strategies. Furthermore, the SCM highlights the importance of considering external support and resources, making pharmacists pivotal in organising educational sessions or workshops to cater to individual needs. Additionally, in the realm of the self-care environment, pharmacists can advocate policy changes and community engagement initiatives to improve access to resources and healthcare services. By aligning their practices with the SCM's cardinal dimensions, pharmacists can enhance their role in improving individuals' health literacy in IDA, ensuring a comprehensive and effective approach to self-care in this context.[29,38]

2.2 Pharmacists' roles in managing IDA across practice sectors

Pharmacists are well-trained to effectively educate patients and provide evidence-based advice on a broad range of topics, including self-care interventions and the use of non-prescription medicines or supplements in IDA.[29,39] With their expertise, pharmacists can actively engage patients in discussions about IDA, explaining the importance of iron supplements and addressing any concerns or misconceptions. FIP has recently introduced toolkits for medication review and reconciliation to support pharmacists in improving medication adherence and health outcomes.[40] As pharmacists actively contribute to better medication management, they empower individuals to navigate IDA with confidence and competence, promoting a holistic approach to self-care and ultimately mitigating the impact of this condition on overall health and well-being. By fostering health literacy and advocating medication adherence, pharmacists play a pivotal role in supporting individuals on their journey to manage IDA and achieve optimal health outcomes effectively.[41] The increasing role of pharmacists in the healthcare system, coupled with being the most accessible members of the health workforce,[42-44] enable them to contribute significantly to the management of conditions such as IDA.[28]

In a community setting, pharmacists can provide health services and information on preventing and managing IDA.[45] Several studies have documented the role of pharmacists in IDA in community settings. A study carried out in Peru examined the feasibility and acceptability of training the pharmacy workforce to offer point-of-care testing for chronic diseases, including anaemia. It was reported that nearly 100% of 371 clients preferred the pharmacy for point-of-care testing due to better access, faster results, and faster and better attention. This study underscored the unique role of pharmacists in providing point-of-care testing services in the community setting. It also highlighted an opportunity to train the pharmacy workforce to conduct early detection and screening of the disease.[46] In Tanzania, a study revealed that private pharmacies were in closer proximity and offered greater convenience than government clinics, indicating the potential contributions of pharmacists in supporting maternal iron supplementation in rural areas.[47] This study recommended the importance of educating the public about the existing policies and treatments for anaemia, a role in which pharmacists actively participate by providing health education to the public and society.[47,48]

In a hospital setting, pharmacists can optimise patient outcomes by monitoring and adjusting treatment plans.[49] Studies in Jordan[50] and Thailand[51] explored how clinical pharmacist interventions in an outpatient clinic in a hospital improved patients' outcomes through pharmaceutical care programmes, such as providing comprehensive patient counselling for those with IDA.[50,51] Pharmacists' evolving roles include their ability to prescribe,[52,53] initiate or discontinue specific medicines, adjust the dosage[52-54] and order relevant laboratory tests.[52,53,55,56] Additionally, they are also actively involved in developing evidence-based practice guidelines in collaboration with fellow healthcare professionals.[54,56,57] Pharmacists are strategically positioned to influence drug formulary choices and healthcare management, thereby promoting adherence to guidelines and reducing costs tied to specific medicines.[52,57] Their active engagement in providing health advice was proven to yield significant therapeutic impact and garnered approval from fellow healthcare professionals.[56,58]

In addition to the role of community and hospital pharmacists, researchers in the field of pharmacy also play a significant role in addressing IDA alongside researchers from other fields. Their involvement in IDA research aligns with the broader goals of understanding, managing, and raising awareness of this condition. Pharmacy researchers contribute to understanding IDA's pathophysiology and its implications for medication management. Their research often intersects with areas such as pharmacokinetics and pharmacodynamics of different iron formulations, including exploring optimal dosing regimens and evaluating the safety and effectiveness of treatment options for IDA. Furthermore, they actively engage in clinical trials to assess the efficacy and tolerability of oral and intravenous iron supplements, focusing on patient adherence and outcomes. This research directly informs evidence-based guidelines for IDA treatment, ensuring that pharmacists and healthcare providers can offer the best possible care to patients. Their dissemination of research findings through publications, conferences and workshops can contribute to the body of knowledge on IDA, promoting best practices and ensuring access to appropriate iron repletion therapies.

The exploratory study conducted by FIP in May 2022 highlighted various roles of pharmacists in anaemia management, which

include screening and detection, medication management, patient counselling and monitoring patient progress. The conversation specifically underscored the pharmacist's role in taking patients' medical histories and ensuring the appropriate selection of supplements based on dietary habits and over-the-counter medicines. The participants also highlighted the need for guidelines or toolkits, along with subsequent training or workshops, to improve their competence in the management of IDA. A key enabler identified in this study was collaboration with other healthcare professionals, which is particularly pertinent to the development of community-based, point-of-care testing. Based on the findings in this study, it is evident that there is an increasing opportunity for pharmacists to contribute to the attainment of the WHO's global anaemia target, particularly through early detection, medication management and delivering health education to both individual patients and the broader community.[28]

2.3 *Educational needs to support pharmacists' role in IDA*

Roundtable participants of the exploratory study conducted by FIP in May 2022 shared a variety of competencies needed to support pharmacists' role in IDA.[27,28] The insights shared during this discussion are represented in Figure 3.

Specifically, regarding patient education and counselling, participants emphasised two key qualities that pharmacists should possess: confidence in patient management and effective communication skills. Furthermore, a strong foundational knowledge of IDA, as detailed in Figure 4, was identified as crucial to enhance their proficiency in this domain.[27,28]

An important suggestion from this roundtable was the need to develop a comprehensive guideline, toolkits or handbook tailored to individual pharmacists, addressing the topic of IDA. These resources would function as educational manuals, providing guidance on patient screening and counselling and encompassing critical information such as:[27,28]

- Diagnosis and severity assessment of anaemia;
- Appropriate medication selection, including details on iron preparations, their bioavailability, and pharmacokinetics to aid in supplement choice and formulation decisions;
- Common side effects associated with medicines and supplements; and
- Dietary guidelines to complement treatment strategies.

In addition to these resources, participants also recommended the establishment of professional programmes designed to enhance pharmacists' competence in managing IDA. These programmes could include workshops, self-directed learning opportunities, or continuing professional development courses, all centred around anaemia-related knowledge and skills. Collaboration with national professional leadership bodies would facilitate the organisation of workshops and self-directed learning initiatives, and the sharing of best practices.[27,28]

The handbook serves as an invaluable resource, providing pharmacists, specifically in patient-facing roles, with the essential knowledge needed to address the identified gaps above in their understanding of IDA.

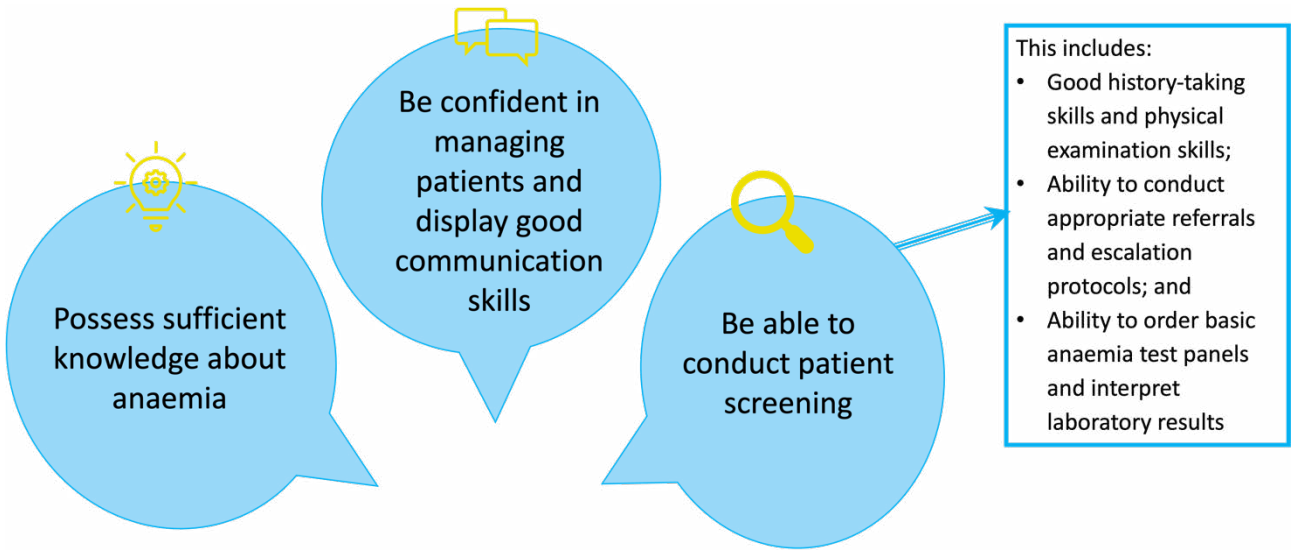

Figure 3: Competencies needed to support pharmacists' role in IDA

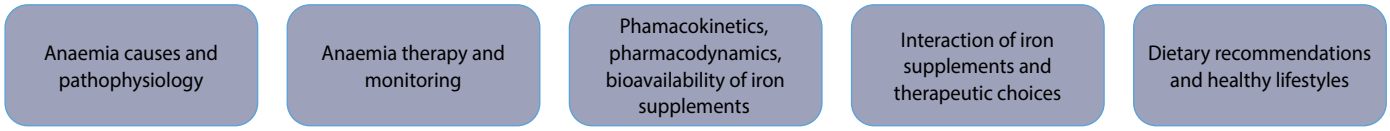

Figure 4. Knowledge that pharmacists should have related to IDA[27,28]

3. IDA management in adults

3.1 Identification and investigation of IDA

Early identification is pivotal in effectively managing IDA, and pharmacists can play a role in this process. They can support detecting potential cases, assessing patients' symptoms and signs, reviewing medical and medication histories, recommending additional tests and making referrals when necessary. This proactive approach can occur in various healthcare settings, including community pharmacies, hospitals and primary healthcare centres.[28]

3.1.1 Signs and symptoms

In community or primary healthcare settings, pharmacists can support identifying common signs and symptoms of ID, with or without anaemia, such as fatigue and weakness,[15,59-62] pale skin,[15,61] dizziness,[15,61] shortness of breath,[60] fast or irregular heartbeat,[59] strange cravings to eat items that are not food,[15,62] a tingling or crawling feeling in the legs,[62] cold hands and feet,[62] tongue swelling or soreness,[60,61] brittle nails,[15] hair loss[62] and headache.[15,61] By asking targeted questions during patient interactions, pharmacists can pick up on these symptoms and suggest further testing if necessary (see Figure 5).

3.1.2 Medical and medication histories

Examining medical and medication histories helps tailor the treatment according to the cause and severity of iron deficiency.[63,64] A comprehensive history-taking approach facilitates accurate diagnosis and guides appropriate management of IDA. Some key aspects to be considered are blood donation history, previous history of IDA, dietary intake, overt blood loss and haemoglobinopathies. Additionally, conducting a thorough medication history is crucial, particularly the use of NSAIDs or anticoagulants.[65] Individuals with underlying conditions leading to IDA should either be treated or referred to a specialist, such as a gastroenterologist or a gynaecologist, for comprehensive care.[66]

Pharmacists can ask the following questions to identify the common signs and symptoms of IDA:

- Have you been feeling unusually tired or fatigued lately?
- Do you often feel weak or find it difficult to perform routine tasks?
- Have you noticed that your skin appears paler than usual?
- Do you experience shortness of breath, especially after physical activity?
- Have you noticed any changes in your nails, such as brittleness or spooning (concave shape)?
- Do you often feel dizzy or lightheaded?
- Have you experienced any unusual cravings, such as a desire to eat ice, dirt or starch?
- Have you noticed any changes in your appetite or weight?

Figure 5: Questions that pharmacists can ask to identify signs and symptoms of ID, with or without anaemia

3.1.3 Examination and investigation

Some key aspects of examination include pallor assessment (conjunctiva, mucous membranes, nail),[15,61] vital signs (blood pressure, heart rate and respiratory rate),[59,60] cardiovascular examinations (heart murmurs),[67] respiratory assessment (shortness of breath),[59,60] skin and hair changes (koilonychia, dryness),[15,62] and evaluation of oral cavity.[60,61]

Some diagnostic tests contribute to the confirmation of IDA:

- **Serum haemoglobin —** Anaemia is defined as follows: Hb < 13 g/dl (men aged over 15 years), Hb < 12 g/dl (non pregnant women aged over 15 years and children aged 12–14 years of age).[68,69]
- **Red cell indices —** A mean corpuscular volume (MCV) less than 95 femtolitres has a sensitivity of 97.6% for iron deficiency anaemia. Other red blood cell changes associated with iron deficiency include reduced mean cell Hb (MCH) — hypochromia, increased percentage of hypochromic red cells, anisocytosis (variation in the size of red blood cells), and poikilocytosis (presence of irregularly shaped red blood cells)[69]
- **Serum ferritin levels —** Serum ferritin is the primary test to diagnose absolute iron deficiency for patients without inflammation.[70] While a ferritin level of ≤ 15 microgram/l was traditionally used for iron deficiency diagnosis in adults, a newer approach suggests a threshold of ≤ 30 microgram/l, providing 92% sensitivity and 98% specificity, which is now commonly used.
- **Transferrin saturation (TSAT) —** TSAT is not influenced by chronic inflammation as is the case with ferritin and is an important arbiter of iron status, especially in the face of chronic inflammation. A TSAT of < 20% is indicative of IDA.[59,71]
- **Hepcidin level —** Hepcidin level is decreased (< 6 ng/ml) or normal (6–46 ng/l) in IDA,[72] but this can be affected by factors such as circadian rhythm and hepatic and renal function. Hepcidin assessment can be useful to confirm Iron Refractory

1. **Prepare the patient:** Explain the procedure to the patient and ensure they are comfortable. Clean the area where the blood sample will be taken (usually a fingertip or a vein in the arm) with an alcohol swab.
2. **Collect the sample:** For a haemoglobin test, a sample of blood is taken by pricking the fingertip or inserting a needle into a vein in the patient's arm. For infants, the sample may be obtained by pricking the heel.
3. **Perform the test:** Apply the blood sample to the test strip or cuvette of the point-of-care testing device. Ensure that the sample adequately fills the required area.
4. **Analyse the results:** Insert the test strip or cuvette into the device and wait for it to process. The device will display a haemoglobin measurement.
5. **Interpret the results:** Compare the patient's haemoglobin level with reference ranges provided by the device manufacturer or relevant health guidelines.
6. **Document and communicate:** Record the results in the patient's health record and communicate them to the patient and their healthcare provider.

Figure 6: General steps on how to perform a point-of-care haemoglobin test[73]

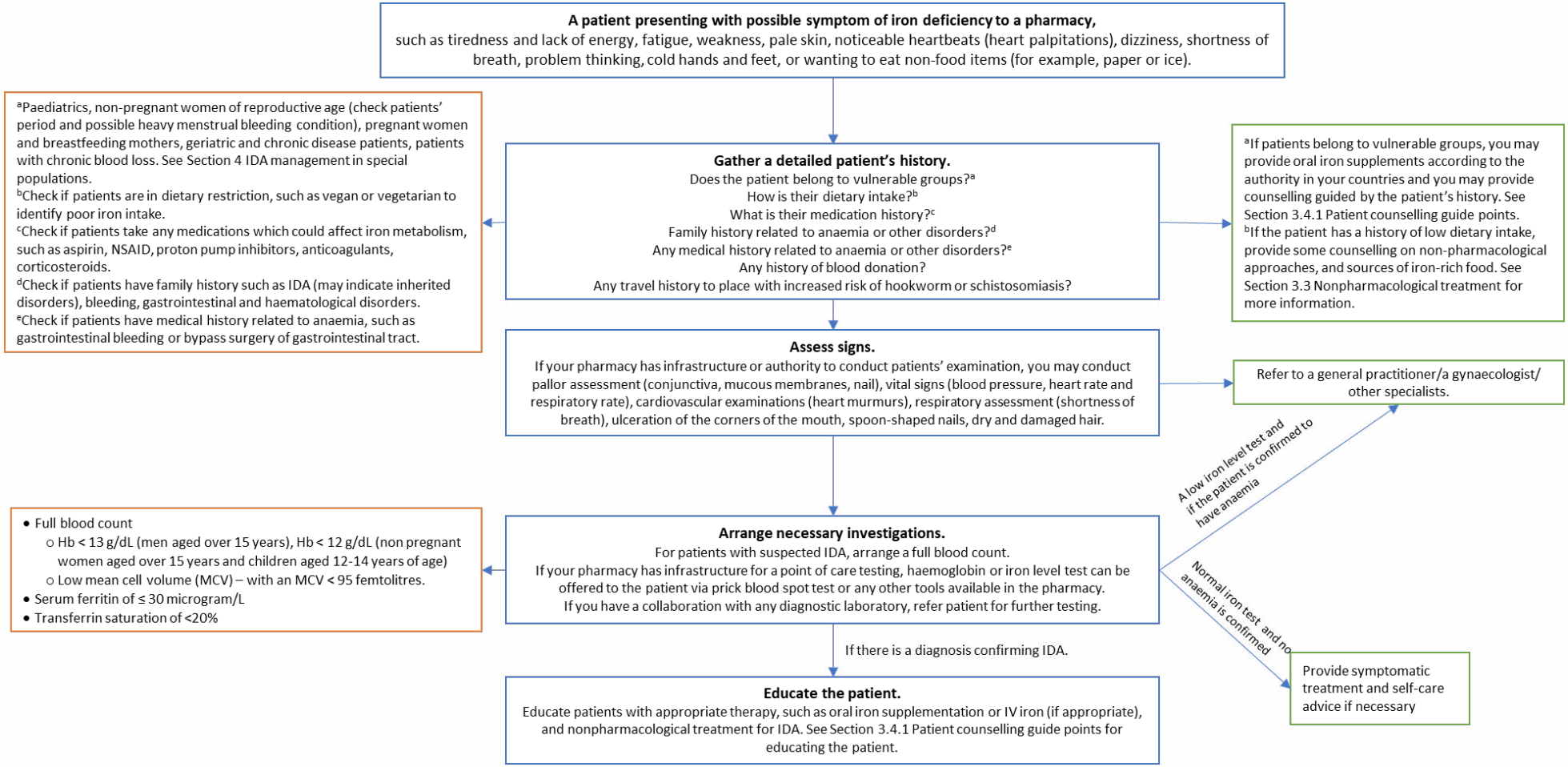

Figure 7: Flowchart to guide pharmacists in identifying patients with suspected IDA in a community pharmacy or primary healthcare setting[15,59-62,67,69,73-76]

Iron Deficiency Anemia (IRIDA), but this assessment is not routinely or widely used in clinical practice.[67,72]

- **Reticulocyte haemoglobin (RetHe) —** Combining hepcidin and reticulocyte haemoglobin levels can effectively differentiate between IDA and anaemia of chronic disease. When hepcidin levels are within the normal range, and RetHe is less than 30 pg, it suggests the presence of IDA.[72] Reticulocyte haemoglobin is accurate but frequently not accessible for many practitioners and patients.

Recognising that the accessibility of advanced tests can be a challenge for rural areas in certain nations, where such tests may not always be easily obtainable or affordable, it becomes imperative to explore alternative, cost-effective approaches for rural healthcare. Pharmacists should be vigilant in aligning their practices with the national guidelines regarding commonly employed diagnostic tests for IDA within their respective countries.

In some countries and facilities, pharmacists can conduct initial screening tests for anaemia, such as point-of-care testing for haemoglobin or iron level test. These tests are quick, easy to perform, and provide immediate results, enabling pharmacists to identify potential cases of IDA during a routine pharmacy visit. Some general steps on how to perform a point-of-care haemoglobin test are outlined in Figure 6.

3.1.4 Referrals

If the point-of-care test results or the presence of signs and symptoms suggest IDA, pharmacists can refer patients to a general practitioner, a gynaecologist or a specialist for further testing and diagnosis. This ensures that patients receive appropriate medical attention in a timely manner. Treating underlying causes of IDA is also critical, and pharmacists are advised to consult a general practitioner, a gynaecologist or a specialist. Interprofessional collaborative approaches are important in IDA management.

It is important to note that the scope of pharmacy practice in some countries may vary, and pharmacists need to refer patients directly to a general practitioner, a gynaecologist or other specialist for further evaluation before initiating treatment. Therefore, pharmacists are advised to follow national guidelines regarding their roles in screening, including the availability of point-of-care testing in pharmacy.

Figure 7 is a flowchart to guide pharmacists in identifying patients with suspected IDA in a community pharmacy or a primary healthcare setting.

3.2 Pharmacological treatments

3.2.1 Iron repletion therapy

Iron repletion therapy involves iron administration orally and parenterally (such as intravenous, intramuscular (not common in practice) or intradialytic (specific for patients with chronic kidney disease). The decision-making process between these options involves considering factors such as underlying cause, symptoms severity, therapy objectives, response to prior therapy, desired pace of haematological improvement, patient preference, cost and accessibility to treatment.[63,77]

3.2.1.1 Oral iron

Oral iron is commonly regarded as the first-line treatment option due to its affordability and widespread availability compared with intravenous iron (IV iron). While it is generally effective, in cases where oral iron is not poor tolerated or certain medical conditions are present, IV iron may be required.[78]

Dosing regimen and iron-containing preparations

The conventional therapeutic approach involving high dose iron supplementation has been demonstrated to increase hepcidin levels and reduce iron bioavailability, especially when taken multiple times a day.[79] The initial recommended dose of oral iron in adults is 100–200 mg elemental iron once daily or in two or three divided doses. However, there is growing evidence supporting the efficacy of lower daily doses,[80,81] which are found to have fewer gastrointestinal side effects. If patients exhibit poor tolerance to oral iron supplementation, it is advisable to use a lower dose, intermittent dosing schedules or try different formulations.[82] This therapeutic dose is determined by the severity of symptoms, patients' ferritin levels, their age and adverse gastrointestinal reactions.[83]

There is a wide range of iron-containing preparations available in the market. They vary in terms of dosage, type of iron salt and whether the iron is present in its ferrous or ferric form.[84] The ferrous form of iron (Fe^{2+}) found in the most widely used iron supplements

Table I: Common doses and elemental iron content of available oral iron formulations

Form	Strength (Elemental)	Formulation	Adult dosage
Ferrous bisglycinate chelate	24 mg tablet	24 mg ferrous bisglycinate chelate, 60 mg Vitamin C, 350 µg folate, 15 µg Vitamin B12	One tablet per day
Endosomal iron	24 mg capsule	24 mg endosomal iron, 60 mg Vitamin C, 350 µg folate, 15 µg Vitamin B12	One capsule per day
Sucrosomial iron	15 mg capsule	15 mg sucrosomial iron, 45 mg Vitamin C	One capsule per day
Sucrosomial iron	21 mg capsule	21 mg sucrosomial iron, 70 mg Vitamin C, 10 µg Vitamin D3, 1.75 ug Vitamin B12, 1 mg Vitamin B6	One sachet per day
Ferric polymaltose	50 mg capsule	50 mg iron(III)-hydroxide polymaltose complex, 150 µg folic acid	One tablet per day
Ferric polymaltose	100 mg tablet	100 mg iron(III)-hydroxide polymaltose complex	One tablet per day
Ferrous sulphate	50 mg tablet	50 mg ferrous sulphate	One tablet per day

is preferred due to its higher solubility, resulting in higher bioavailability in dietary supplements than ferric iron (Fe^{3+}).[85] All soluble iron molecules have side effects that impact absorption and bioavailability, with these side effects increasing as the dose rises. However, newer Ferric Pyrophosphates with micronised encapsulated iron molecules allows for a different absorption route due to molecule size. Therefore despite being insoluble, their modification with microencapsulation and alternative absorption pathways leads to much higher bioavailability without the associated side effects. There are several oral iron preparations available for the treatment of anaemia, as shown in Table I.

For the initial treatment of IDA, the British Society of Gastroenterology recommends taking one tablet of oral iron daily, containing ferrous sulfate, fumarate or gluconate.[60] This is attributed to their affordability, acceptable tolerability, good bioavailability, high efficacy, and availability in different formulations in correcting anaemia and restoring iron stores.[60,84] A recent review of 111 studies involving 10 695 participants looking at different oral iron preparations indicated that slow-release ferrous sulfate is more tolerable than conventional immediate-release ferrous iron salts.[91] Additional common types of iron formulations include ferrous ascorbate, ferrous succinate, carbonyl iron, ferric citrate, liposomal iron, haem iron polypeptide, endosomal irons, sucrosomal irons and polysaccharide iron complexes.[63]

Pharmacokinetic properties of oral iron

Bioavailability of iron depends on several factors, including the form of iron administered (with the ferrous form being more easily absorbed), the dosage, the level of erythropoiesis, dietary intake and existing iron reserves. The absorption of iron in the gastrointestinal tract increases in individuals with iron deficiency. The oral bioavailability of iron can range from less than 1% to over 50%, and one of the factors influencing the absorption of iron is the quantity of iron stored in the body.[92] Taking iron alongside meals can also reduce the bioavailability of oral iron by up to 75%.[93] This implies that iron should be taken either during fasting in the morning or during intervals between meals throughout the day.

Certain compounds found in foods, such as phytate in whole grains and calcium in milk, can hinder iron absorption.[94] In addition to phytate and calcium, phenolic compounds, including phenolic monomers and polyphenols (tannic acid and tannins), also hinder iron absorption through a complex formation of chelates with iron in the gastrointestinal lumen.[95] Polyphenols are particularly abundant in tea, coffee, cocoa, red wine and some herbal teas.[96,97] Drinking a cup of tea resulted in a 64% decrease in iron absorption from a test meal, whereas drinking a cup of coffee led to a reduction of 39%.[98] The inhibitory effect of tea on iron absorption disappears within an hour.[99]

Vitamin C may improve iron absorption by exerting its iron-reducing and chelating effects.[100] Some studies have shown that this may not be clinically effective at enhancing iron absorption, but many national guidelines recommend consuming iron in food or supplements with foods or drinks containing vitamin C, while avoiding substances that inhibit iron inhibitors is recommended.[100] Vitamin C can counteract and abolish the inhibitory effect of polyphenols on iron absorption, indicating that ascorbic acid has a higher affinity to iron than polyphenols.[101]

Commonly prescribed medicines, including proton pump inhibitors and histamine-2 receptor antagonists, can impede iron absorption.[102,103] Gastric acid plays a vital role in aiding the absorption of non-haem iron. It accomplishes this by releasing iron from food particles and converting it from the less absorbable ferrous form to the more easily absorbed ferric form. Hence, PPIs and histamine-2-receptor antagonists that suppress gastric acid production can impair iron absorption.[102] Other medicines that may interact with iron are tetracyclines, where there is a pharmacokinetic interaction (decreased oral absorption of both iron and tetracyclines), and thyroid agents where there is possible pharmacokinetic interaction (decreased thyroxine absorption).[92]

Numerous underlying medical and surgical conditions can lead to impaired iron absorption. These include inflammatory bowel disease, coeliac disease, chronic pancreatitis, *Helicobacter pylori* infection, gastrectomy, gastric bypass and small bowel resection. Patients with persistent gastrointestinal or gynaecologic bleeding or other forms of blood loss might find it challenging to absorb adequate enteral iron to counterbalance these losses, even when absorption is not impaired. In situations where oral iron therapy alone proves insufficient or ineffective, exploring alternative approaches is crucial.[78]

Side effects of oral iron

Common side effects that pharmacists should communicate to patients include:[104,105]

- **Gastrointestinal issues** — Gastrointestinal side effects associated with oral iron repletion therapy are very common, often leading to non-adherence in up to 50% of patients. This can result in treatment discontinuation and, consequently, inadequate therapeutic outcomes.[106,107] The issues can include constipation, diarrhoea and stomach upset, such as stomach cramps, nausea or vomiting. While it is better to take oral iron on an empty stomach, with the presence of gastrointestinal side effects, it is sometimes recommended to take oral iron with meals.
- **Dark stools** — Iron supplements can make the stool black or dark green. This is generally harmless and should not be a cause for concern.[104,105]
- **Metallic taste** — Some people may experience a metallic taste after taking iron supplements.[104,105]
- **Teeth staining** — Liquid iron formulations, such as ferrous sulfate drops, syrups, elixirs and suspensions, may cause teeth staining.[108]
- **Other side effects** — Less common side effects can include fainting, dizziness, chest pain and fast heartbeat.[104,105]

Treatment duration and monitoring parameters

The goal of oral iron treatment is to increase haemoglobin levels by 2 g/dl within four weeks.[109] An increase of 1 g/dl in haemoglobin levels following one month of treatment is considered an adequate response to therapy.[110] For adults, treatment should be continued for three months after the anaemia is corrected to ensure the replenishment of iron stores.[111] The correction of anaemia should be confirmed by normalisation of ferritin levels or TSAT.

3.2.1.2 Parenteral iron

Parenteral iron can be administered intravenously, intramuscularly or intradialytically.

IV iron is a rapid and effective treatment for IDA, offering advantages over oral therapy and blood transfusion.[78] The main advantage of IV iron lies in its capacity to bypass the gastrointestinal tract, reducing mucosal irritation and related side effects.[112] Additionally, healthcare providers have confidence in patient adherence. IV iron has demonstrated higher efficacy than oral iron and is generally better tolerated. However, its widespread use is constrained by availability and cost considerations.[113] Funder institutions normally requires 3 month of oral iron therapy before they are willing to cover the cost of IV iron therapy.

The use of intramuscular (IM) iron therapy for iron repletion is generally discouraged in current recommendations.[114] This is because IM iron is poorly absorbed, no safer than IV iron therapy, and can result in local side effects such as pain and skin discolouration at the injection site.[115,116] However, it is important to note that there are specific clinical scenarios where IM iron therapy might still be appropriate, and these decisions should be made based on clinical judgement.

Intradyalitic treatment refers to administering iron therapy during haemodialysis sessions. Intradialytic iron supplementation using ferric pyrophosphate citrate was demonstrated to maintain haemoglobin levels safely, reduce the need for erythropoiesis-stimulating agents, and to help manage anaemia in patients with chronic kidney disease who are undergoing haemodialysis.[117]

When to treat patients with IV iron

IV iron administration should be considered for patients with one or more of the following:[64,118,119]

- Demonstrated intolerance, poor adherence or lack of efficacy with oral iron due to gastrointestinal side effects despite modification of dose, timing and frequency.
- Pregnancy beyond the first trimester with haemoglobin levels below 10.5 g/dl, at which oral iron is unlikely to provide sufficient iron for fetal development.
- Iron deficiency with severe anaemia (e.g. Hb < 7 g/dl) and stable haemodynamics, while severe anaemia with organ ischaemia is treated with transfusion.
- Presence of comorbidities interfering with oral iron absorption (e.g., inflammatory bowel disease, chronic renal impairment).
- There is inadequate time for oral iron to achieve a suitable response when surgery is imminent.
- Ongoing blood loss surpassing the capacity of oral iron absorptive to meet needs (heavy menstrual bleeding, mucosal telangiectasias).
- Malabsorption syndromes (coeliac disease, Whipple's disease, bacterial overgrowth), which potentially compromise iron absorption.

Studies suggested that IV iron is not necessarily associated with acute and chronic infection risk.[120-122] A prospective study

Table II: Parenteral iron formulations available in the market[63]

Compound	Concentration of elemental iron	Recommended amount per dose[a]	Infusion time[b]
Low-molecular-weight iron dextran (LMW ID)[c]	50 mg/ml	Single dose of 1 000 mg (diluted in 250 ml normal saline) or multiple doses of 100 mg.	2–6 h
Ferrous gluconate (FG)	12.5 mg/ml	Multiple doses of 125 to 250 mg.	12.5 mg/ min
Iron sucrose (also referred to as iron saccharate)	20 mg/ml	Multiple doses of 200 to 300 mg. Typically ranging from 1 to 3 weeks.[126]	100 mg/30 min
Ferumoxytol	30 mg/ml	Single dose of 1 020 mg or 2 doses of 510 mg, given 3 to 8 days apart.	15 min
Ferric carboxymaltose[d]	50 mg/ml	For weight ≥ 50 kg: 1 or 2 doses of 750 mg, administered at least 7 days apart. For weight < 50 kg: 1 or 2 doses of 15mg/kg, administered at least 7 days apart.	15 min
Ferric derisomaltose (previously called iron isomaltoside)	100 mg/ml	For weight ≥ 50 kg: A single 1 000 mg dose or up to 3 doses of 500 mg, administered over 7 days For weight < 50 kg: A single dose of 20 mg/kg	Infusion time ranges between > 15min and ≥ 30min

[a] A 25 mg test dose before infusion of a full dose of iron dextran is required; test doses are not required with the other agents but are often recommended in patients with multiple drug allergies or a history of prior reactions to IV iron.[127]

[b] The infusion time depends on the dose and whether it is being administered in a diluted or undiluted form. Refer to the updated drug product inserts for specific guidance.

[c] High molecular weight iron dextran (HMW ID) is no longer available. LMW ID can be administered intramuscularly; however, it is considered painful and less effective than intravenously.

[d] There are some advantages of this iron preparation compared to other available iron formulations; however, this preparation is the most expensive preparation and inaccessible for many patients. Pharmacists need to consider cost-effectiveness in advising the treatment.

involving 988 patients undergoing haemodialysis across 19 European centres, followed over six months with 51 episodes of bacteraemia, revealed no association between IV iron and the risk of infection.[123] Infection should not be seen as a contraindication to intravenous iron repletion therapy if a careful evaluation of the risk/benefit supports the treatment of the anaemia.

Dosing regimen and IV iron preparations

A range of IV iron preparations is available, and the selection of which formulation to use depends on several factors, including cost considerations, the preference of the patient and physician, and the product's availability.[124] Older IV iron formulation, such as high-molecular-weight dextran iron, has been withdrawn due to their unfavourable safety records, characterised by a relatively high incidence of anaphylactic reactions.[125]

Concerning the dosing regimen, a formulation with a smaller dose would be more suitable for patients who have frequent hospital visits, such as individuals undergoing haemodialysis due to chronic kidney disease. On the other hand, larger-dose preparations are more convenient for patients who require rapid iron replenishment. Furthermore, there can be variations in how well different patients tolerate certain formulations.[63] Table II provides a list of parenteral iron formulations.

All these preparations, as listed in Table II, are equally effective in managing iron deficiency and share a similar safety profile.[105,128,129] Some key differences include cost, formulary agreements, procurement agreements, the frequency of visits or time needed to administer the full dose.[64] Healthcare professionals are advised to refer to the product monographs, as certain formulations recommend weight-based dosing.[63,64]

Pharmacokinetic properties

Iron is administered intravenously as iron carbohydrate complexes, composed of polynuclear iron(III)-hydroxide surrounded by the carbohydrate ligand. The ligand aims to stabilise the complex and protect it against further polynuclearisation. Some pharmacokinetics parameters for intravenous iron preparations are set out in Table III.

Side effects of IV iron

Newer intravenous iron preparations rarely lead to infusion-related reactions. However, hypersensitivity-type and infusion reactions (approximate incidence 0.5%) are more common than for oral iron or placebo.[120] Severe hypersensitivity reactions and serious adverse events, such as anaphylaxis, are rare. Identification and management of these reactions have been extensively documented in the literature.[120,121,136]

Hypophosphataemia has been identified as one of the side effects of all types of IV iron preparations. This incidence appears to be linked to the molecules complexed to the iron rather than the iron itself.[60] Hypophosphataemia is more commonly observed with ferric carboxymaltose than with other formulations.[137-139] The rates of hypophosphataemia among various preparations are as follows: ferric carboxymaltose (58%), iron derisomaltose (4%) and iron sucrose (1%). However, the clinical importance of these rates has not been determined. Most cases involved are biochemically moderate (serum phosphate in the range 0.32–0.64 mmol/l) and asymptomatic, resolving without any intervention.[140,141] Nonetheless, due to the rare association with hypophosphataemic osteomalacia, the Medicines and Healthcare Products Regulatory Agency (United Kingdom) issued a recommendation in 2020 suggesting monitoring serum phosphate levels in patients with risk factors for hypophosphataemia. This recommendation also extends to those who receive prolonged or multiple high-dose infusions of ferric carboxymaltose.[142]

Skin staining due to iron deposition, also referred to as cutaneous siderosis or haemosiderin staining, is a rare side effect associated with IV iron infusions.[143] Siderosis is characterised by iron accumulation in various tissues, leading to brownish-grey skin discolouration. Skin discolouration or extravasation at the infusion site occurs in approximately 1.6% of cases.[144] There have been a

Table III: Pharmacokinetics parameters for some iron preparations[130]

Parameters	Sodium ferric gluconate	Iron sucrose	Ferric carboxymaltose	Iron dextran USP/BP	Ferumoxytol
Reactivity with transferrin	High	Medium	Low	Low	Low
Dosage used for the pharmacokinetics characteristics (mg Fe)	125[a]	100[b]	100/1 000[c]	500–2 000[d]	316[e]
terminal k_{el} — first-order rate constant for elimination (h^{-1})	0.488	0.145	0.094/0.074	0.024[d]	0.048
terminal $t_{1/2}$ — half-life (h)	1.42	5.3	7.4/9.4	27–30[f]	14.7
C_{max} — peak concentration (mg Fe/L)	20.6	35.3	37/331	-	130
AUC — area under the curve (mg Fe/L*h)	43.7	83.3	333/6 277	6,853[g]	2,912
CL — clearance (L/h)	2.99	1.23	0.26/0.16	-	0.11
V_c — Initial distribution volume (L)	2	3.2	2.7/2.1	3.0	2.3

[a] Study in iron deficient subjects[131]
[b] Study in healthy volunteers[132]
[c] Study in volunteers with mild iron deficiency anaemia[133]
[d] Study in iron deficient patients[134]
[e] Study in normal subjects and hemodialysis patients[135]
[f] Calculated from a study conducted by Henderson et al. (1969)[134]
[g] Calculated for a dose of 500 mg iron by using t1/2 (terminal kel) and Vd

limited number of reported skin staining associated with IV iron, primarily involving ferric carboxymaltose,[145-147] iron sucrose[148] and iron polymaltose infusions.[149-152] This adverse effect can be concerning for patients from an aesthetic standpoint and may cause emotional distress.

IV iron administration demonstrates no increase in adverse events leading to treatment discontinuation and no increase in mortality. Additionally, there was no increased risk of severe adverse events related to cardiovascular, respiratory, neurological, thromboembolic, constitutional or gastrointestinal effects with IV iron administration.[120]

Treatment duration and monitoring parameters

The treatment goal of IV iron is to increase haemoglobin levels by at least 2 g/dl within four to eight weeks.[153] It is recommended to conduct a follow-up assessment of haemoglobin and ferritin levels after at least four weeks following IV iron administration.[64] This four- to eight-week window also allows sufficient time for erythropoiesis and iron utilisation.[154] In cases of chronic ongoing blood loss, as seen in conditions such as hereditary abnormal uterine bleeding or haemorrhagic telangiectasia, more frequent follow-up appointments may be necessary to assess the treatment response and establish the appropriate dosing regimen.[64,154] If haemoglobin and iron status fail to return to normal range, it is essential to carefully identify the underlying causes of this lack of improvement.[155]

3.2.2 Blood transfusion for severe IDA

Red blood cell transfusion leads to an immediate and transient increase in haemoglobin levels, delivering around 200–250 mg of iron per blood unit.[78] However, red blood cell transfusion is not the recommended approach for treating IDA, except when urgent oxygen delivery elevation is needed, such as when patients have angina pectoris or cardiac failure, or when IDA is complicated by severe, ongoing acute bleeding.[118]

Patients with severe IDA, which is characterised by Hb levels below 7 g/dl, with symptoms of insufficient oxygen delivery (e.g., syncope, chest pain) are likely to gain benefit from transfusion. However, most patients with severe anaemia generally experience fatigue and do not require transfusion. If the decision is made to transfuse a patient for IDA, a single unit of red blood cells is often sufficient. Further increases in Hb can be facilitated through oral or intravenous iron.[156]

The Choosing Wisely campaigns, operating across different jurisdictions and medical specialties, have underscored the importance of restricting red blood cell transfusions. They encourage the selection of alternative therapeutic approaches when they are appropriate and accessible.[156-159] The risks linked to transfusion include transmitting infectious diseases, transfusion-associated lung injury, haemolytic transfusion reactions, cardiac overload due to transfusion, and alloimmunisation.[160] Red blood cell transfusion as a treatment option for patients with IDA is not only unfavourable from a diagnostic perspective but also in terms of cost-effectiveness.[160] Transfusions' financial and ethical implications can vary based on how they are calculated.[161] Healthcare professionals are advised to refrain from transfusing red blood cells for individuals with iron deficiency, regardless of their haemoglobin levels, unless there is a lack of haemodynamic stability.[156,162]

3.3 Non-pharmacological interventions

3.3.1 Dietary modification

Pharmacists can empower individuals to make informed dietary choices through their role in nutritional education in collaboration with dietitians.[163] The optimal approach to improving iron levels involves a combination of strategies such as introducing iron-rich foods into the diet, food fortification,[124,164] using "enhancers" to improve micronutrient absorption, avoiding substances that hinder micronutrient absorption ("inhibitors"), and harnessing beneficial food processing techniques.[124,163]

3.3.1.1 Iron-rich foods

Incorporating various iron-rich foods into the diet is essential, and it is equally important to consider how the body can effectively absorb iron from dietary sources.[165,166] It depends on the type of iron consumed from different food sources with different absorption levels in the body.[167,168]

Iron-rich foods encompass animal and plant sources.[124] Haem iron is the most common in daily diets and is present solely in animal-based products. It demonstrates a high bioavailability, approximately between 25% and 30%. On the other hand, non-haem iron, found in plant- and animal-based products, shows a bioavailability range of around 1% to 10%.[169,170] Incorporating haem iron derived from animal-based sources (particularly beef, lamb, pork and chicken) into non-haem iron meals will further enhance the overall bioavailability and absorption of iron from a meal.[171] Some foods containing haem iron and non-haem iron can be seen in Figure 8 and Figure 9, respectively.

Improving dietary diversity is important; however, the expense and accessibility of animal products and fruits and vegetables frequently constrain patients in their efforts to get more nutritious food.[124,164] It is essential for pharmacists to consider their patients' socio-economic conditions when advising an increase in the intake of iron-rich foods.

3.3.1.2 Food fortification

Food fortification refers to adding micronutrients to food and beverages, thereby enriching their nutritional content, using, for example, meal ingredients or condiments.[172] This can include using isolated iron compounds, such as iron salts or chelates, or ingredients naturally rich in iron, such as meat and its derivatives. The selection of these compounds is determined by the intended characteristics of the final product, such as taste and colour, and may be influenced by costs.[172] Iron is most commonly fortified in wheat and maize flour, infant formula and cereals.[164,173]

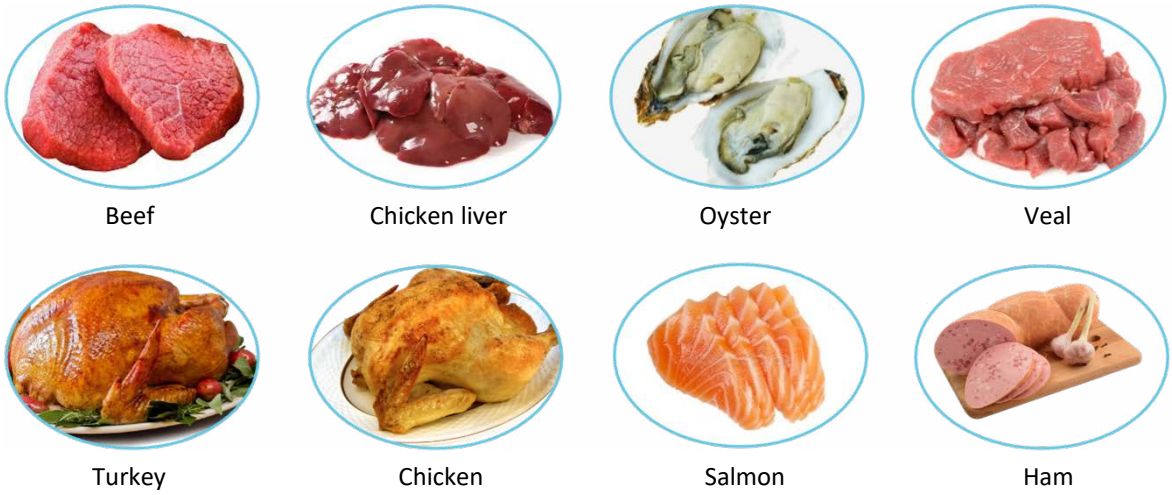

Figure 8: Foods containing haem iron

Figure 9: Food containing non-haem iron

According to the WHO, several iron compounds are used for fortification in food.[164] They are divided into three types based on their solubility properties, namely, freely soluble (usually the preferred option), poorly water-soluble but soluble in dilute acids, and water-insoluble and poorly soluble in dilute acids. These three types of iron compounds are as follows:

- **Iron compounds that are water-soluble** — Ferrous sulfate, ferrous gluconate, ferrous lactate and ferric ammonium citrate[166] are used to fortify products such as pasta, edible salt, flour and infant foods.[174] They can change the colour and taste of food products.[166]
- **Iron compounds that are poorly water-soluble but soluble in dilute acids** — Ferrous fumarate is commonly used to fortify infant cereals, and ferric saccharate is utilised in chocolate drink powders.[164] They induce fewer alterations in the taste and colour of the final product.[166]
- **Iron compounds that are water-insoluble and poorly soluble in dilute acids** — Ferric phosphate compounds, such as ferric orthophosphate and ferric pyrophosphate, are used to fortify rice, certain infant cereals and foods containing chocolate.[164] They have lower absorbability, but they do not affect the organoleptic characteristics of the food product, making them a viable choice.[166] They are also more cost-effective than the other types. However, they are generally considered a last-resort option, particularly when the target population's diet contains inhibiting factors for iron absorption.

Encapsulated forms of several iron compounds are readily available in the market. These include ferrous sulfate and ferrous fumarate, coated with hydrogenated oil, such as soybean, cottonseed or ethyl cellulose and Ferric Pyrophosphate coated with a lecithin layer.[164,166] The encapsulated coatings in iron compounds play a role in preventing oxidative damage, thereby mitigating sensory changes to fortified food products.[164] Encapsulation of micronised particles with a lecithin layer allows for endosomal absorption and better bioavailability without expected side effects.

3.3.1.3 Enhancing iron absorption

Adding "enhancers" such as citric acid, malic acid or vitamin C may enhance iron absorption from plant-based foods.[175] For example, consuming foods rich in vitamin C, such as citrus fruits,

strawberries and bell peppers, can enhance absorption of non-haem iron.

3.3.1.4 Avoiding iron inhibitors

Reducing the intake of certain foods and beverages, such as tea and coffee, which contain compounds that can hinder iron absorption, can be advantageous.[171] Moreover, the bioavailability of iron compounds is not solely determined by their solubility properties but is also influenced by dietary composition. This includes the proportion of iron-inhibiting factors in the diet, notably iron-binding phytates found in cereals and other staple foods like sorghum and pulses, as well as polyphenolic compounds in fruits and vegetables.[172]

3.3.1.5 Harnessing beneficial food processing techniques

Food processing methods, such as soaking, fermentation, germination and thermal or mechanical processes, can also improve iron bioavailability and absorption from non-animal sources.[176] For example, soaking and sprouting cereal and pulse grains results in a decrease in phytate content and an increase in iron absorption.

3.3.2 Lifestyle modification

Lifestyle modifications play a role in the comprehensive management and treatment of IDA. Patients are encouraged to adopt various general practices to improve their condition. Lifestyle recommendations that pharmacists can advise include:

- It is important patients follow recommendations from healthcare professionals regarding supplementation and dietary changes to manage their iron levels effectively.
- Patients can be encouraged to have a diet rich in iron-containing foods, such as lean meats, beans and dark leafy greens, and pair them with vitamin C-rich foods, such as citrus fruits, to enhance absorption. Limiting the consumption of substances inhibiting iron absorption, such as excessive tea or coffee, can also be beneficial.
- Staying well-hydrated aids in the optimal absorption of dietary iron.
- Regular health check-ups are important for monitoring iron status and overall well-being.
- Patients who regularly donate blood should remain vigilant by monitoring their iron levels and adhering to responsible blood donation guidelines to ensure it does not compromise their health.
- Treating the underlying cause is crucial in managing IDA. There could be a possibility where healthcare professionals recommend additional tests or treatment to address the root issue.

3.4 Supporting pharmacists' roles in IDA treatment and management

3.4.1 Patient counselling guide steps

Patient adherence and treatment compliance can enhance haematological indices in patients with IDA, which can be done through patient counselling over time.[177,178] Creating a comfortable and conducive environment for patient counselling is important as it fosters open engagement and understanding.[178]

Figure 10 illustrates patient counselling guide steps to optimise patient outcomes and improve patient adherence and treatment compliance.

3.4.1.1 Establishing open-ended communication[178]

Communication is a tool that is needed to establish a connection with the patient.[179] An open-ended communication can be established through the following:[178]

- Creating a safe communication environment by initiating an introduction as the attending healthcare provider.[178] To ensure effective communication, it is important to confirm the patient's preferred language and communicate using it. In cases of a language barrier, use an interpreter to facilitate the discussion.
- Obtaining patient's consent to continue the conversation and confirm if the patient has ever been diagnosed with IDA.

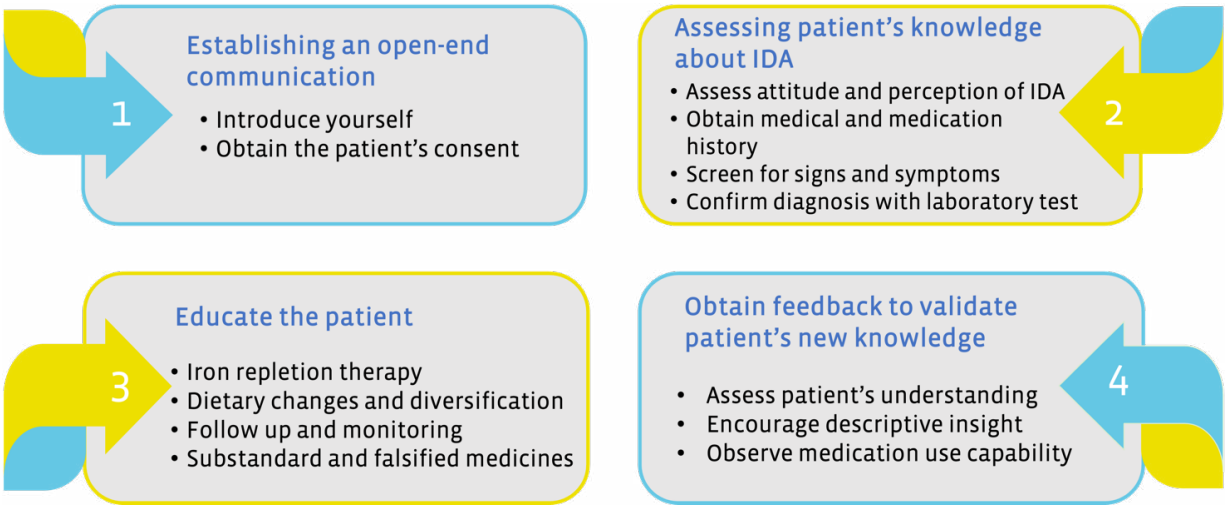

Figure 10: Patient counselling guide point

3.4.1.2 Assessing patient's knowledge about IDA[178]

Patients' health literacy is important as it links to medication adherence, and pharmacists are recommended to assess patients' knowledge about IDA.[180] Patients should be asked open-ended questions to evaluate their knowledge.[178]

1. **For patients not diagnosed with IDA, assess their knowledge by:[178]**
    a. Gathering their medical and medication histories, including their dietary habits and other risk factors (see Section 3.1.2: Medical and medication histories for details).
    b. Identifying their signs and symptoms, such as fatigue, pallor and shortness of breath (see Section 3.1.1: Signs and symptoms for details).
    c. Confirming IDA diagnosis through test results in collaboration with other healthcare professionals (see Section 3.1.3: Examination and investigation for details).
    d. Continue to the steps under point 2 (patient diagnosed with IDA) below.
2. **For patients diagnosed with IDA, to avoid misconception and promote adherence to medication, their knowledge should be assessed by:[178]**
    a. Understanding their attitude towards and perception of IDA. This is through acknowledging and confirming patients' symptoms and asking about their treatment goals so the approach will be patient-centred by building on their goals.
    b. Gathering their complete medication history, which relates to any prior health conditions they may have experienced.
    c. Providing them with non-pharmacological advice, which includes dietary change advice.

3.4.1.3 Educating patients[178]

Some points that could be considered in educating patients are as follows:

- **Iron repletion therapy —** Dosage, Results, Underlying issues, and General information (DRUG) method can be used to educate patients on iron repletion therapy and cover important aspects of medication counselling.[178]
    a. D (Dosage) — Ensure that patients know the proper dosage and administration instructions by directing them to the prescription information of specific iron therapy.
    b. R (Results) — Discuss that the treatment duration may extend up to six months, aligning with the time needed to improve clinical blood parameters during regular treatment. Additionally, explore the potential consequences of not adhering to the prescribed regimen.
    c. U (Underlying Issues) — Discuss all possible side effects and difficulties patients may experience with iron therapy. Also, discuss possible drug interactions that may affect the effectiveness of these treatments and potential gastrointestinal issues that patients may encounter, particularly with oral iron therapy. Patients can also be advised on how to manage or minimise side effects, such as by (i) drinking sufficient fluid if medically appropriate to minimise constipation; (ii) switching to every other day dosing or taking with food if intolerable gastrointestinal side effects; (iii) switching to formulation which has evidence for lower incidence of constipation due to incorporation of ingredient such as sorbitol[181]; and (iv) drinking water or chewing gum to possibly help reduce the metallic taste.
    d. G (General Information) — Broaden the discussion to encompass all aspects of blood health. Elaborate on how various micronutrients, including folic acid (particularly vital for expectant mothers), vitamin C, vitamins B_{12} and B_6, copper and manganese, play essential roles in maintaining overall blood health. Additionally, provide guidance on the correct usage and storage of medicines and ensure that patients are informed about whom to contact for any inquiries or concerns.
- **Dietary changes** — Dietary changes and food diversification can boost iron intake. Pharmacists play an important role in promoting healthy lifestyles and can educate patients on various food sources (see Section 3.3: Non-pharmacological).[43,178,182]
- **Follow up** — Appropriate therapy follow-up should also be communicated with patients. A 30-day follow-up is recommended to determine parameters such as haemoglobin, blood cell indices and iron status to assess treatment response. If therapy is continued, subsequent follow-ups at six-month intervals should be conducted to monitor response status.
- **Substandard and falsified medicines** — Substandard and falsified medicines cause harm to patients and affect all regions of the world.[183] Educating patients on the importance of getting medicines from registered pharmacy outlets and not from unregulated platforms online or illegal street markets is important.

3.4.1.4 Obtaining feedback to validate patients' new knowledge[178]

Pharmacists can do the following to obtain feedback from patients:

- **Assess patient's understanding —** Devote time to verify patients' understanding of IDA and lifestyle changes needed to manage their condition.[178]
- **Encourage descriptive insight —** Ask patients to describe how they will use the medicines that have been prescribed.[178] Leverage this opportunity to address any concerns or questions they might have.[178]

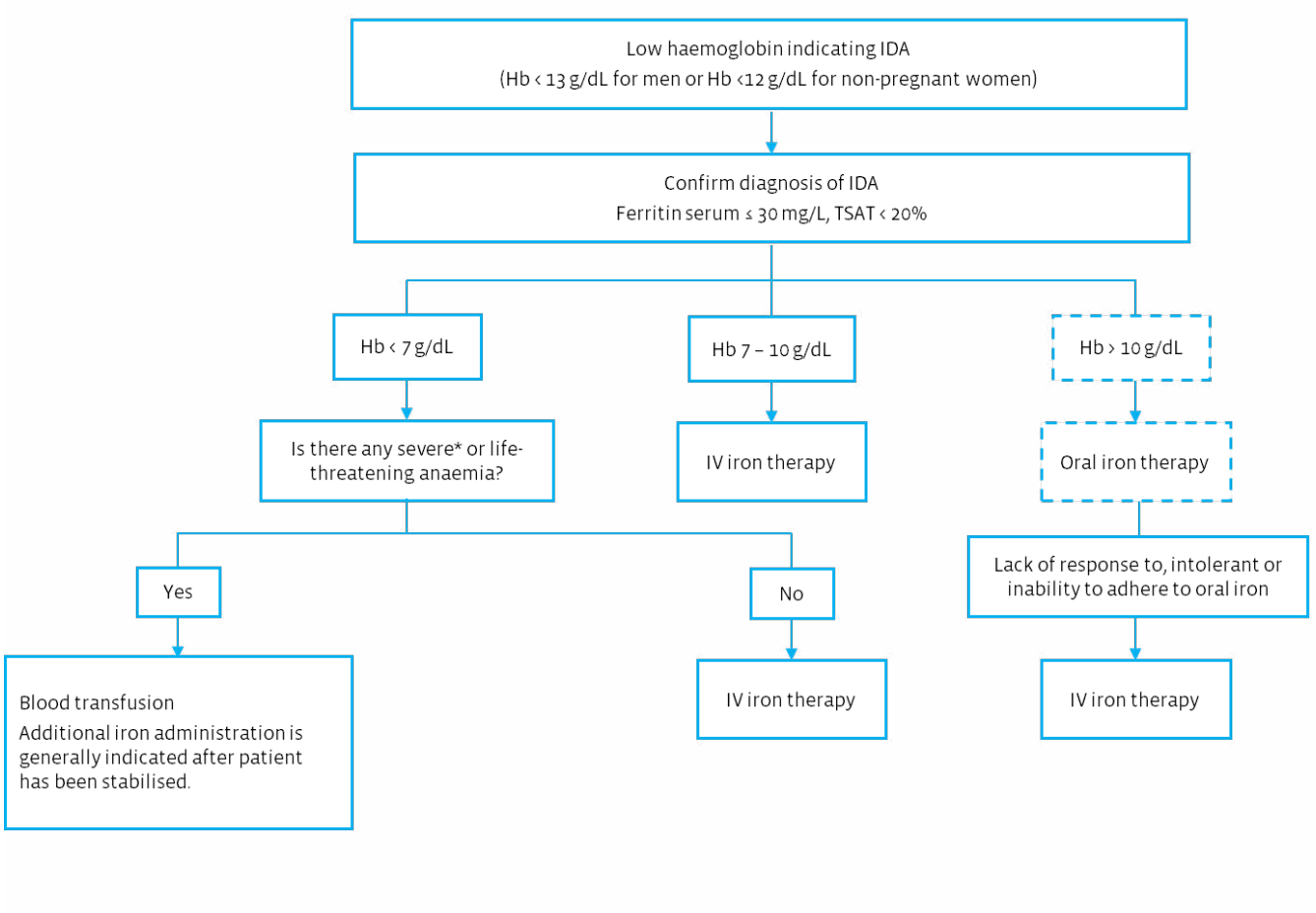

Figure 11: Treatment and management of IDA in adults[64, 77, 184-186]

- **Observe medicines use capability** Identify any potential barriers to adherence by observing the patient's attitude and providing more necessary information to address any concerns.[178]

Flowchart of IDA treatment and management in primary and secondary care settings

Early intervention of IDA enhances physical and mental well-being, reduces fatigue and cognitive impairment, alleviates other symptoms and complications and improves quality of life.[153] Collaborative approaches among health professionals are essential in effectively managing IDA. Figure 11 illustrates IDA treatment and management for adults in primary and secondary care settings.

References available on request.

https://www.fip.org/file/5751