# IRON DEFICIENCY BEST PRACTICE GUIDELINES

This document is intended for sport physicians, sports dietitians and physiologists in the Australian high performance sport system. It outlines best practice for managing iron deficiency (ID) in athletes.

## Background

Iron is important for several key functions in the body including, oxygen transport, energy metabolism, cognitive function and optimal immune function. These functions are important to athletes, since they can impact endurance (aerobic) capacity, mood, perceived fatigue levels, training adaptation and performance, plus overall health status. Fatigue and lethargy may present as the initial symptoms relevant to ID. In such circumstances, or when risk factors for ID are present, a sports physician will determine whether the athlete requires a blood test to confirm their iron status.

Compromised iron stores are common in athlete populations because athletes have a greater iron turnover. Although ID is most common in female athletes (~15-35% athlete cohorts deficient), ~5-11% of male athlete cohorts also present with compromised iron stores. Three groups are considered to be at particularly high-risk of ID:

- Female athletes
- Endurance athletes (in part due to greater iron losses via training)
- Vegetarian/ vegan athletes (since iron is harder to absorb from vegetable sources)
- Athletes with lower energy intakes/requirements (achieving recommended iron intakes is more difficult on a lower energy budget)

The recommended daily iron intake for adult males is 8 mg per day, and 18 mg daily for (pre-menopausal) females. Daily iron requirements can only be met from dietary or supplemental sources. Meat, fish, poultry, wholegrain cereals and iron-enriched cereals are major contributors to iron intakes in Australia. Iron exists in food in haem and non-haem forms. Both types of iron occur in animal food (~40% haem, 60% non-haem iron) sources whereas plant sources provide only non-haem iron. The haem form of iron is better absorbed than the non-haem form (~5-35% vs. ~2-20%), yet despite this, most iron in the Australian diet comes from plant food rather than meat. The amount of iron absorbed from a meal is determined by factors such as body iron status, the type of iron in the food, and the balance between dietary factors that enhance and inhibit the absorption of iron. Dietary factors such as vitamin C (50mg) and a component in meat can enhance iron absorption, whereas phytates, present in legumes, nuts, wholegrain cereals and unprocessed bran, is the main inhibitor of non-haem iron absorption. Other inhibitors of non-haem iron absorption include polyphenol containing beverages such as tea, coffee, cocoa and red wine (Hurrell et al., 1999). High dose calcium and zinc supplements should also be avoided with meals when attempting to enhance iron status.

Recently, the hormone hepcidin has been identified as a key regulator of iron metabolism. It has been suggested that increases in hepcidin (peaking 3-6 hours after exercise) could reduce the absorption of iron consumed in meals post-exercise. Accordingly, new research (McCormick et al., 2019) suggests iron should be consumed in the morning (to avoid the diurnal increase in hepcidin), and before, or as close to exercise completion as possible, in order to avoid the peak periods of post-exercise hepcidin elevation. While this coincides with athletes' typical higher breakfast calcium intake, non-supplemental calcium intake has less effect on iron absorption (Saunders et al., 2013).

## Risk Factors

- Poorly considered vegetarian/ vegan diets, chronic low-energy diets, and other dietary patterns which see infrequent intake of red meat combined with inadequate substitution of other foods providing bioavailable iron
- High intakes of food combinations that reduce the bioavailability of dietary iron, particularly when it comes from plant sources. This includes high intakes of tannins (tea/ coffee), supplemental calcium and phytates at meals in which iron-rich foods are eaten

August 2022



ASC36846

- Recently diagnosed or poorly managed clinical disorders such as coeliac disease and Crohn's disease
- Other gastrointestinal disturbances e.g. athletes with spinal cord injuries, with increased transit and digestions times
- Increased iron requirements such as female athletes (iron losses associated with menses), adolescent athletes undergoing growth, pregnancy and periods of accelerated erythropoiesis such as exposure to altitude and high intensity endurance training
- Increased iron losses due to gastrointestinal bleeding (e.g. ulcers, including those associated with use of non-steroidal anti-inflammatory drugs), excessive haemolysis due to increased training stress (e.g. footstrike haemolysis in runners), sweat losses and other blood losses (e.g. surgery, nosebleeds, contact sports)

A combination of these factors often occurs in endurance athletes in impact, high repetition activities (e.g. runners, triathletes, race walkers).

## Assessment

The following table provides considerations for various performance support team members that may indicate iron screening is warranted.

| Sports Medicine | Sports Nutrition | Physiology |
|---|---|---|
| **History:**<br>• Blood loss<br>• Illness/ infection<br>• NSAID use<br>• Other symptoms specific to haematological disorders<br>**Clinical examination:**<br>• Signs of anaemia<br>• Malabsorption syndromes<br>**Haematology tests:**<br>• Full blood count<br>• Iron studies<br>**Other clinically indicated tests:**<br>• Coeliac screen<br>• Micronutrient assays (e.g. vitamin B & folate) | **Dietary assessment:**<br>• Total energy intake/ energy availability<br>• Total dietary iron intake<br>• Sources of iron (haem vs. non-haem)<br>• Co-ingestion with iron inhibitors/ enhancers<br>• Timing of high iron meals relative to key exercise sessions<br>• Iron supplementation, including daily dose and distribution over the day | **History:**<br>• Fatigue<br>• Change in mood/ motivation<br>• Overreaching/ under recovery<br>• Underperformance (training, competition)<br>**Haematology:**<br>• Decrease in haemoglobin mass<br>**Changes in training:**<br>• Large change in training load (volume and intensity)<br>• Altitude training |

Note: It is essential to investigate the underlying cause of the deficiency and particularly to exclude significant underlying pathology.

Athletes with insufficient or deficient iron stores are typically asymptomatic and only identified via screening. However, iron deplete athletes may present with some, or all, of the following symptoms, particularly as they regress towards stage 3 ID; frequent illness, lethargy and fatigue, underperformance, loss of power, "jelly legs", "light headedness", restless legs when sleeping, loss of endurance, decreased motivation to train, poor mood.

In such instances, a blood test may reveal low ferritin and/or haemoglobin concentrations. However, it is important to take current health and training status into account, as acute phase reactions may artificially increase ferritin levels, which can vary within a wide range due to both biological and analytical factors, including:

- Menstrual cycle phase
- Acute phase reactions
- Pre-iron assessment training completed and hydration status
- Growth phases
- Type and precisions of analyser (note: typical within laboratory variation ranges from 5-10%)

Additionally, haemoglobin levels can be affected by changes in plasma volume, and therefore, if serial measures of haemoglobin mass are available, a decrease in haemoglobin mass may also be present, providing a more reliable indicator of haemoglobin status. On the basis of the above considerations, sports physicians are guided to the following framework when contemplating the standardisation and frequency of iron blood screening for athletes (from Sim et al., 2019):

## Considerations and frequency of iron blood screening for athletes

### Variables to be considered

- Minimum: Serum ferritin, hemoglobin concentration, transferrin saturation
- Desirable: Serum soluble transferrin receptor, hemoglobin mass, C-reactive protein

### Standardisation of blood collection

- Time of day: Preferably in the morning
- Hydration state: hydrated preferably assessed by waking urinary specific gravity (<1.025)
- Low to moderate activity in the preceeding 24 hours, including no muscle-damaging exercise (e.g. eccentric) in the 2-3 days prior
- No signs of sickness or infection

### Annually

- No history of iron deficiency
- No history of irregular/excessive menses or amenorrhea
- No reports of fatigue after extended rest
- Strength/power-based sports with minimal endurance component
- No iron-related dietary restrictions
- No evidence of low energy availability
- No intention to undertake hypoxic training in the next 12 months
- No underlying pathology (e.g. coeliac or Crohn's disease)

### Biannually

- Female
- Previous history (>24 months) of iron depletion (e.g. Stage 1*)
- Previous history (>24 months) of irregular/excessive menses
- Intention to undertake high training loads especially in endurance and team-based sports
- Minimal (or zero) reports of prolonged fatigue after extended rest
- No iron-related dietary restrictions (e.g. non-vegetarian, non-vegan)
- No evidence of low energy availability
- Intention to undertake hypoxic training in the next 12 months

### Quarterly

- Any recent history (<24 months) of iron depletion/deficiency (Stage 1, 2 or 3*) irrespective of sex
- Any evidence of irregular/ excessive menses or amenorrhea
- High training loads in team and endurance-based sports
- Reporting prolonged fatigue/ lethargy even after extended rest
- Reduced work capacity during training
- Unexplained poor athletic performance
- Individuals restricting sources of dietary iron (e.g. vegetarian and vegan) or overall calorie intake
- Any evidence of low energy availability
- Intention to undertake hypoxic training in the next 6 months

The current routine clinical assessment of ID requires analysis of blood markers, including ferritin, haemoglobin concentration and transferrin saturation. Additionally, serum-soluble transferrin receptor levels are considered a reasonable threshold for identification of ID. Details on these iron studies follow below.

- **Full Blood Count (FBC):** Low haemoglobin (Hb) occurs later in the course of iron deficiency and Hb can initially be in the normal range. Mean Corpuscular Volume (MCV) is usually low in iron deficiency. Red Cell Distribution (RDW) is usually increased in iron deficiency. The film may be reported as showing microchromic, microcytic red cells with elliptocytes (elongated red cells) and pencil cells (elongated cells with tapered ends). The FBC is usually normal in iron overload.
- **Serum Iron:** Serum iron is a measure of iron content in serum. It is affected by diurnal variation, recent iron intake and acute phase responses. It is therefore of limited utility in assessment of overall iron status, however is used in the calculation of transferrin saturation.
- **Ferritin:** In steady state, ferritin levels are generally a good indicator of total body iron stores. Very low levels are diagnostic of ID. However, a ferritin level within normal range but <100 µg/L does not exclude ID as ferritin is an acute phase reactant that can be increased in inflammatory states, liver disease and malignancy. Elevated levels may reflect iron overload, but again ferritin level alone can be misleading as it can be increased in all the above conditions. High transferrin saturation is required for the diagnosis of iron overload.
- **Transferrin:** Transferrin is the iron transport protein. Total Iron Binding Capacity (TIBC) is an indirect measure of transferrin levels. Transferrin levels are increased in the setting of ID, as well as in pregnancy and with oestrogen administration. It is decreased in states of inflammation, chronic liver disease and malnutrition.
- **Transferrin Saturation:** Percentage of transferrin's carrying capacity that is saturated with iron. This is a calculated measurement (serum iron/TIBC x 100). Decreased saturation is suggestive of ID or inflammation. Transferrin saturation is useful in the assessment of high ferritin. A high ferritin with a Tsat below 45% in women or below 50% in men is more likely to be secondary to another cause. Testing should be repeated and if the Tsat remains elevated genetic testing should be performed to investigate for haemochromatosis (Ideally measured on fasting sample as it may be falsely elevated by recent iron ingestion).
- **Soluble Transferrin Receptor:** Transferrin receptor is up-regulated in states of increased iron demand, such as ID, or dysregulated erythropoiesis (e.g. haemolysis, thalassaemia, B12 or folate deficiency etc.) and is thus inversely related to body iron stores. Unlike ferritin it is not an acute phase reactant and therefore may be useful to demonstrate ID in the presence of an acute phase response and to distinguish ID from anaemia of chronic disease.

## Stages of Iron Deficiency

Iron deficiency in athletes can be a progressive issue and is categorised with various levels of severity. Initial stages of iron deficiency, namely iron deficiency non-anaemia (IDNA), occur when ferritin stores are depleted (<35 µg/L) before there is significant impact on haemoglobin concentrations. Iron deficiency anaemia (IDA) presents when both iron stores and haemoglobin are depleted. Provided athlete iron screens are tightly controlled as described in the previous section (i.e. blood sample is done in the morning in a rested state), **a low ferritin (serum ferritin <35 µg/L) is typically used to identify the presence of an ID**. Further blood markers, namely haemoglobin and transferrin saturation, can then be used to classify the stage of ID (as per below). Soluble transferrin receptor has also more recently been identified as a reasonable threshold for IDA. All stages of ID can affect performance and thus should be treated.

| Stage | Typical Laboratory Profile |
|---|---|
| Stage I: Iron Deficient Non-anaemia<br>(Stage 1 IDNA) | **Serum Ferritin <35µg/L**<br>Soluble Transferrin Receptor (sTfR) <2.5mg/L<br>Transferrin Saturation >16%<br>Haemoglobin (Hb) – women >120g/L<br>Haemoglobin (Hb) – men >135g/L |
| Stage II: Iron Deficient Non-anaemia<br>(Stage 2 IDNA) | Serum Ferritin <20µg/L<br>Soluble Transferrin Receptor (sTfR) <2.5mg/L<br>Transferrin Saturation <16%<br>Haemoglobin (Hb) – women >120g/L<br>Haemoglobin (Hb) – men >135g/L |
| Stage III: Iron Deficiency Anaemia<br>(IDA) | Serum Ferritin <12µg/L<br>Soluble Transferrin Receptor (sTfR) >2.5mg/L<br>Transferrin Saturation <16%<br>Haemoglobin (Hb) – women <120g/L<br>Haemoglobin (Hb) – men <135g/L |

Early identification of compromised iron stores is important since it allows athletes to consider nutritional and supplementation options to prevent progression to IDA. Furthermore, there is evidence that training capacity may be compromised, or feelings of fatigue may be exaggerated, when iron deficiency non-anaemia (IDNA) is present.

### Further Reading:


- Sim M, Garvican-Lewis LA, Cox GR, Govus A, McKay AKA, Stellingwerff T, Peeling P. (2019). Iron considerations for the athlete: a narrative review. Eur J Appl Physiol, 119(7), 1463-1478.
- Clenin GE, Cordes M, Huber A, Schumacher YO, Noack P, Scales J, Kriemler S. (2015). Iron deficiency in sports – definition, influence on performance and therapy. Swiss Medical Weekly. 145, w14196.


## Treatment

Treatments for an ID include nutritional support, oral iron supplementation, and intravenous iron approaches, depending on the severity of the issue and the athlete's history. The treatment approach should be directed by a sports physician in consultation with a sports dietitian. As a guide, the following approaches might be considered:

| Treatment | Indication | Considerations |
|---|---|---|
| Food Approach | Ferritin: 35-50 ug/L<br>Normal haemoglobin | In consultation with a sports dietitian, increase iron intake via food choices, verify energy and carbohydrate availability, and avoid "iron inhibitors" while consuming high-iron foods to maximise iron intake |
| Oral Iron Supplement | Ferritin: 20-35 ug/L<br>Normal haemoglobin | Supplementation for 8-12 weeks with ~100 mg elemental iron provided in the morning, daily, or every second day if gastrointestinal upset occurs with the supplement |
| Intravenous Iron Approach | Ferritin: <20 ug/L<br>Compromised haemoglobin | Intravenous iron should only be considered in consultation with a sports physician and abide by the organisation's injection policy as outlined in the AIS Sports Science and Sports Medicine Best Practice Principles. Note: efficacy of this approach appears best when IDA is present i.e. low ferritin stores and compromised haemoglobin mass. Iron is not prohibited by WADA but if the amount of fluid used to give the infusion is >100ml then a Therapeutic Use Exemption is required. If less than 100ml is used then no Therapeutic Use Exemption is required. |

## What does Treatment look like?

A framework to guide practitioners towards optimal treatment protocols for ID can be found in the **AIS Sports Supplement Framework**.

### Food approach

- An accredited sports dietitian should consider increases in meat and/or vegetable sources of dietary iron. Note: the absorption of iron from meat sources is more efficient than non-meat sources, hence the greater risk of ID in vegetarian athletes.
- A dietary assessment of iron absorption enhancers and inhibitors should be conducted, and recommendations made on how to use/avoid certain foods for optimised iron absorption e.g. avoid coffee/tea/calcium but include vitamin C with high iron meals.
- Planning high-iron meals in the morning may result in a greater level of iron absorption (McCormick et al., 2019b).
- The favourable impact of co-ingesting vitamin C with meals/ snacks on non-haem iron absorption is presented in **Appendix 1**.

## Oral iron supplements

- Oral iron supplements are usually provided as ferrous salts: ferrous fumarate, ferrous sulphate or ferrous gluconate.
- Ferrous sulphate preparations (e.g. Ferro-gradumet) containing ~100 mg elemental iron are the established and standard treatment for depleted iron stores. The total amount of elemental iron contained in the supplement should be checked to ensure that the specific target dose is achieved. These are generally AUST-R registered medicines and thus have a very low contaminant risk, but nevertheless, always check your supplements in accordance with **Sports Integrity Australia**.
- Current research suggests that a daily dose of 100 mg of elemental iron (or every second day if GI upset is present) for 8-12 weeks can significantly improve ferritin stores (Dawson et al. 2006; Garvican et al. 2014; McCormick et al., 2019a, McCormick et al 2020).
- Consuming the oral iron supplement in the morning, as close to exercise as possible, may result in a greater level of iron absorption (McCormick et al., 2019b).
- The absorption of oral iron supplements is enhanced by consuming it with a source of vitamin C (~50-100 mg). This can be achieved by choosing a supplement in which Vitamin C is also provided, or by consuming it with an appropriate (e.g. citrus) fruit or juice. Factors that interfere with iron absorption such as calcium (dairy) and tannins (tea and coffee) should be avoided for an hour each side of the time of consumption of the supplement.
- Iron supplements should only be taken under medical supervision as part of an integrated iron management program which includes dietary assessment. Athletes should be discouraged from taking iron supplements "just in case". Excess iron intake may lead to iron overload.
- Iron supplementation does not address dietary issues. Dietary counselling in the early investigation phase of treatment should be provided via a referral to an accredited sports dietitian.

## Intravenous iron supplements

- Intravenous iron should only be considered in consultation with a sports physician and abide by the organisation's injection policy as outlined in the AIS Sports Science and Sports Medicine Best Practice Principles. Note: efficacy of this approach appears best when IDA is present – i.e. low ferritin stores and compromised haemoglobin mass.
- Parenteral iron therapy (intravenous injection of ferric carboxymaltose*) may be prescribed following complete medical review in the following circumstances:
  - Severe IDA
  - When documented long term oral supplementation has been deemed to be ineffective in raising iron stores. i.e. if 100mg daily oral iron supplementation has not raised ferritin to >35 ug/l over 6 months.
  - Where low iron stores are detected in close proximity to major sporting events and haemoglobin mass is deemed compromised

* Note: Ferric carboxymaltose is macromolecular ferric hydroxide carbohydrate complex, which allows for controlled delivery of iron with minimal risk of release of large amounts of ionic iron in the serum. This preparation is suitable for out-patient use. The use of Iron Dextran is NOT suitable.

## Further Reading:


- McCormick R, Sim M, Dawson B, Peeling P. (2020). Refining treatment strategies for iron deficient athletes. Sports Med, 50(12), 2111-2123.
- Stoffel NU, van Siebenthal HK, Moretti D, Zimmermann MB. (2020). Oral iron supplementation in iron-deficient women: How much and how often? Mol Aspects Med, 105(5), 1232-1239.

# References


Berglund B. [1992]. High-altitude training. Aspects of haematological adaptation. Sports Med, 14(5), 289303.

Clenin GE, Cordes M, Huber A, Schumacher YO, Noack P, Scales J, Kriemler S. [2015]. Iron deficiency in sports – definition, influence on performance and therapy. Swiss Medical Weekly. 145, w14196.

Dawson B, Goodman C, Blee T, Claydon G, Peeling P, Beilby J, Prins A. [2006]. Iron supplementation: oral tablets versus intramuscular injection. Int J Sport Nutr Exerc Metab, 16(2), 180-186.

Fallon, K.E. [2001]. The acute phase response and exercise: the ultramarathon as prototype exercise. Clin J Sport Med, 11(1), 38-43.

Garvican LA, Saunders PU, Cardoso T, Macdougall IC, Lobigs LM, Fazakerley R, Fallon KE, Anderson B, Anson JM, Thompson KG, Gore CJ. [2014]. Intravenous iron supplementation in distance runners with low or suboptimal ferritin. Med Sci Sports Exerc, 46(2), 376-385.

Garvican-Lewis LA, Govus AD, Peeling P, Abbiss CR, Gore CJ. [2016]. Iron supplementation and altitude: decision making using a regression tree. J Sports Sci Med, 15(1), 204–205.

Garvican LA, Lobigs L, Telford R, Fallon K, Gore CJ. [2011]. Haemoglobin mass in an anaemic female endurance runner before and after iron supplementation. Int J Sports Physiol Perform, 6(1):137-140

Govus AD, Garvican-Lewis LA, Abbiss CR, Peeling P, Gore CJ. [2015]. Pre-altitude serum ferritin levels and daily oral iron supplement dose mediate iron parameter and hemoglobin mass responses to altitude exposure. PLoS One, 10(8), e0135120.

Kim I, Yetley EA, Calvo MS. [1993]. Variations in iron-status measures during the menstrual cycle. Am J Clin Nutr, 58(5), 705-709.

Lyseng-Williamson K.A, Keating GM. [2009]. Ferric carboxymaltose: a review of its use in iron-deficiency anaemia. Drugs, 69(6), 739-756.

McCormick R, Moretti D, McKay AKA, Laarakkers CM, Vanswelm R, Trinder D, Cox GR, Zimmerman MB, Sim M, Goodman C, Dawson B, Peeling P. [2019]. The impact of morning versus afternoon exercise on iron absorption in athletes. Med Sci Sports Exerc, 51(10), 2147-2155.

McCormick R, Dreyer A, Lester L, Sim M, Goodman C, Dawson B, Peeling P. [2020]. The efficacy of daily and alternate day oral iron supplementation in iron deplete athletes. Int J Sports Nutr Exerc Metab, 30(3), 191-196.

Nemeth E, Tuttle MS, Powelson J, Vaughn MB, Donovan A, Ward DM, Ganz T, Kaplan J. [2004]. Hepcidin regulates cellular iron efflux by binding to ferroportin and inducing its internalization. Science, 306(5704), 2090-2093.

Peeling, P. [2010]. Exercise as a mediator of hepcidin activity in athletes. Eur J Appl Physiol, 110(5), 877-883.

Peeling P, Dawson B, Goodman C, Landers G, Wiegerinck ET, Swinkels DW, Trinder D. [2009]. Effects of exercise on hepcidin response and iron metabolism during recovery. Int J Sport Nutr Exerc Metab, 19(6), 583-597.

Pitsis GC, Fallon KE, Fallon SK, Fazakerley R. [2004]. Response of soluble transferrin receptor and iron-related parameters to iron supplementation in elite, iron-depleted, nonanemic female athletes. Clin J Sport Med, 14(5), 300-4.

Saunders AV, Craig WJ, Baines SK, Posen JS. [2013]. Iron and vegetarian diets. Med J Aus Open, 1:11-16.

Sim M, Garvican-Lewis LA, Cox GR, Govus A, McKay AKA, Stellingwerff T, Peeling P. [2019]. Iron considerations for the athlete: a narrative review. Eur J Appl Physiol, 119(7), 1463-1478.

Stoffel NU, van Siebenthal HK, Moretti D, Zimmermann MB. [2020]. Oral iron supplementation in iron-deficient women: How much and how often? Mol Aspects Med, 105(5), 1232-1239.

Suominen P, Punnonen K, Rajamäki A, Irjala K. [1998]. Serum transferrin receptor and transferrin receptor-ferritin index identify healthy subjects with subclinical iron deficits. Blood, 92(8), 2934-2939.


August 2022

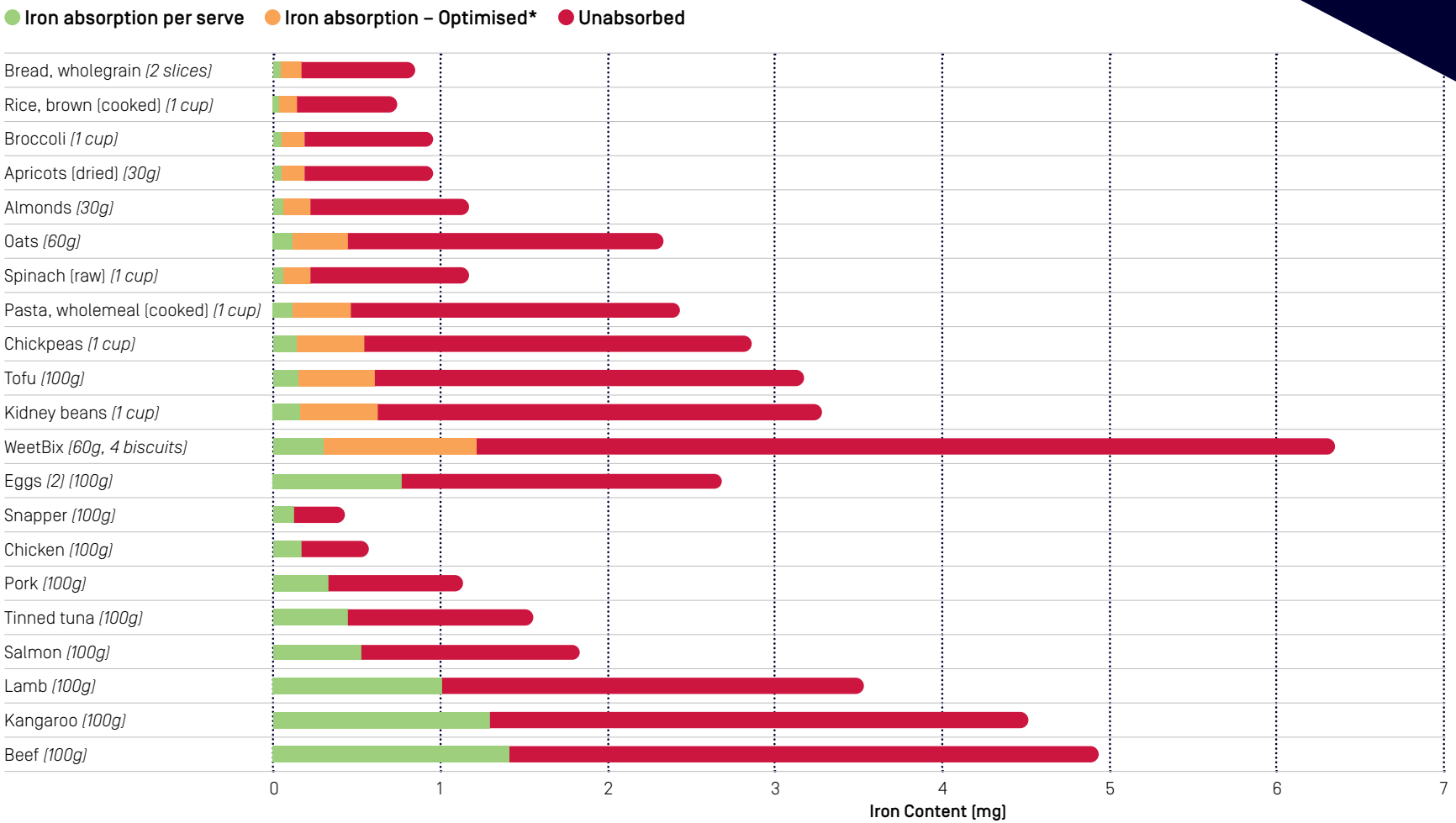


ASC36846

## Appendix 1

# DIETARY IRON

### INGESTED VS ABSORBED




*The absorption of non-haem iron (plant derived) is enhanced when co-ingested with 50-100mg of vitamin C. Benefits of Vit. C co-ingestion on non-haem iron absorption is impacted by a wide range of variables, including (but not limited to) Vit. C dose, iron inhibitors contained in the meal and the iron status of the athlete. For illustrative purposes, a 200% enhancement is shown but may range from 40-400%. Haem iron contributes 10-15% of total iron intake in meat eating populations, but because of its higher absorption, it likely contributes >40% of total absorbed iron.