MENSTRUAL BLOOD LOSS AND THE DURABILITY OF IRON REPLETION IN ENDURANCE ATHLETES A CRITICAL REVIEW OF ATHLETE FOLLOW-UP, ORAL DOSING AND BLEEDING TREATMENT

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ABSTRACT

To assess the duration of biochemical correction after iron treatment in menstruating endurance athletes and distinguish it from improvement in exercise function. Population, treatment, assessment interval, laboratory outcome, exercise outcome and follow-up completeness were examined. A retrospective cohort of 22 female athletes documented considerable variation in ferritin decline after intravenous iron. IRONWOMAN randomised 26 recreationally active women and identified better running economy at four weeks, without between-group differences in peak oxygen uptake, lactate threshold or haemoglobin mass; its three-month blood assessments followed unblinding and an offer of iron to placebo participants. In 150 iron-depleted women, daily and alternate-day oral treatment produced end-of-course ferritin medians of 43.8 and 44.8 $\mu g/L$, respectively, after different treatment durations. In a separate bleeding-treatment trial of 165 women, six-cycle ferritin medians increased from 19 to 34 $\mu g/L$ with a levonorgestrel-releasing intrauterine system and from 19 to 21 $\mu g/L$ with cyclic medroxyprogesterone acetate. End-of-course ferritin, ferritin during continued supplementation and ferritin after treatment cessation describe different treatment conditions. Athlete trials support selected short-term functional benefits, while bleeding-treatment trials demonstrate improvements in iron indices in non-athlete populations. These findings do not establish a reduction in recurrent iron deficiency among endurance athletes through a particular bleeding-treatment regimen.

Keywords: endurance athletes; heavy menstrual bleeding; ferritin; iron treatment; running economy; treatment follow-up.

INTRODUCTION

Iron depletion in endurance sport arises when dietary absorption and available stores cannot meet physiological demand and continuing losses. Menstrual bleeding adds to exercise-related and other losses, while dietary intake, illness, training and altitude alter the interpretation of laboratory measurements. A rise in serum ferritin after treatment therefore answers a narrower question than whether sufficient stores remain after the course ends. The distinction matters when

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an athlete continues to bleed, modifies training or changes the prescribed iron regimen (Sim et al., 2019; Pedlar et al., 2018).

The frequency of heavy menstrual bleeding (HMB) in exercising populations makes this distinction clinically relevant. Bruinvels and colleagues identified HMB in 54% of 789 online respondents and 36% of 1073 marathon respondents (Bruinvels et al., 2016). Dugan and colleagues subsequently identified anaemia in 94 of 887 recreationally active women who underwent fingerprick testing, and ferritin below 30 $\mu g/L$ in 51 of 104 selected participants undergoing further iron tests (Dugan et al., 2024). The latter proportion describes the retested subgroup, not every woman recruited into the screening study.

Longer observation after replacement is already present in the athlete literature. McKay and colleagues examined ferritin decline after intravenous iron in 22 female athletes, with marked differences between individuals (McKay et al., 2020). Performance studies address a separate question: whether replacement improves oxygen uptake, exercise economy, time-trial performance or symptoms. Pengelly and colleagues reviewed 23 studies involving 669 female athletes across 16 sports and found considerable variation in the endpoints and treatment responses (Pengelly et al., 2025). A laboratory response and an exercise response cannot be treated as interchangeable measures of recovery.

This review examines three linked questions: how menstrual bleeding is measured, how iron delivery influences correction, and what the available follow-up establishes about retention of that correction. The clinical focus is adult endurance athletes with menstrual or treatment-associated uterine bleeding. Non-athlete trials are included for oral dosing, bleeding treatment and intravenous formulation safety; their results are distinguished from athlete-specific evidence throughout.

BLEEDING EXPOSURE AND BIOCHEMICAL ASSESSMENT

WHAT THE ATHLETE SURVEYS ESTABLISH

The Bruinvels survey combined online recruitment with recruitment at the London Marathon. Its differing HMB proportions reflect two recruitment routes, and the 37% proportion among elite respondents remains a subgroup observation. Neither menstrual blood volume nor an individual's iron loss can be calculated from these percentages. Self-selection, recalled anaemia and perceived exercise interference restrict causal interpretation (Bruinvels et al., 2016).

The Australian screening study recruited 1042 active women aged 18–65 years; 887 supplied a haemoglobin sample. Further iron testing was requested for women with haemoglobin below 120 g/L or values between 120 and 130 g/L, which the investigators used to identify possible deficiency. Of 104 women retested, 51 had ferritin below 30 $\mu g/L$ (Dugan et al., 2024). This selective testing preferentially examined women with lower haemoglobin and could miss depleted stores in women with higher haemoglobin. It cannot yield a ferritin-defined prevalence for the complete recruitment group. The abstract pairs 274 HMB classifications with 30.9%; that percentage corresponds numerically to the 887 haemoglobin-tested participants rather than all 1042 recruits. Interpretation of bleeding prevalence therefore requires attention to the tested denominator.

In the Strava-based study of 6812 exercising women, menstrual symptoms were associated with availability to train and compete (Bruinvels et al., 2021). Such participation outcomes describe symptom burden rather than a biochemical diagnosis. Fatigue and missed training can also accompany pain, sleep disturbance, illness or inadequate energy intake. Assessing bleeding, laboratory status and symptoms separately prevents an iron-related explanation from being assigned to every menstrual complaint.

BLEEDING MEASUREMENT

Clinical assessment includes bleeding duration, flooding, clots, nocturnal disruption, unscheduled bleeding and interference with daily activity. A hormonal regimen needs documentation alongside the actual bleeding pattern, because contraceptive use alone does not quantify uterine blood loss. A pictorial blood-loss assessment chart (PBAC) can provide repeated estimates when its chart version, scoring rules and sanitary products match a validated method. Magnay and colleagues found variation in chart design, product validation and diagnostic cutoffs (Magnay et al., 2020). Product counts cannot be converted universally into blood volume or iron loss.

ACOG guidance on adolescents with HMB emphasizes evaluation for anaemia and possible endocrine or bleeding disorders (American College of Obstetricians and Gynecologists, 2019). Its relevance to younger athletes is investigation and referral; it is not validation of an adult endurance-athlete monitoring schedule. Substantial or atypical bleeding warrants evaluation even when a contemporaneous ferritin concentration is adequate.

LABORATORY CONTEXT AND OTHER CAUSES OF DEPLETION

Ferritin estimates iron stores but can rise during inflammation. Haemoglobin concentration depends on circulating haemoglobin and plasma volume, so a training-associated change in blood volume may affect the measured concentration. Clénin and colleagues identify ferritin below 30 $\mu g/L$ as low stores in athletes older than 15 years, with further distinction between low and empty stores (Clénin et al., 2015). This classification does not identify a universal ferritin concentration for maximal sporting performance.

Follow-up interpretation requires collection time, recent strenuous exercise, illness, hydration, altitude and timing relative to an oral dose or infusion. Where clinically appropriate, haemoglobin, ferritin, transferrin saturation and an inflammatory marker are considered together. McKay and colleagues' methodological review emphasizes sampling consistency, training load, diet and actual supplement intake in exercise studies (McKay et al., 2022). A high ferritin concentration soon after intravenous treatment does not by itself establish long-term retention.

Menstrual loss is one possible explanation for depletion. Dietary inadequacy, gastrointestinal bleeding or malabsorption, other bleeding and the individual's clinical history remain relevant when deficiency persists or returns (Sim et al., 2019; Pedlar et al., 2018). Low energy availability can coexist with iron depletion, but HMB does not diagnose relative energy deficiency in sport. Heavy bleeding and menstrual suppression associated with problematic low energy availability also require distinct clinical interpretation (Mountjoy et al., 2023).

ORAL IRON: DOSE SPACING, TOLERABILITY AND TREATMENT DURATION

ABSORPTION STUDIES

Hepcidin regulates intestinal absorption and iron recycling through ferroportin. Peeling and colleagues examined pooled observations from 54 athletes and found that pre-exercise iron stores modified the post-exercise hepcidin response; the response was attenuated when stores were low (Peeling et al., 2014). A uniform restriction of absorption after every exercise session is therefore an inadequate description of the physiology.

McCormick and colleagues used a crossover design in 16 endurance-trained runners, including six women. Participants completed 90 minutes of running at 65% of the velocity associated with maximal oxygen uptake in morning and afternoon conditions. Isotope-labelled iron was administered with a standardized meal 30 minutes after exercise, and erythrocyte incorporation was measured 14 days later. Fractional absorption was greater after the morning run than in the corresponding rested condition (McCormick et al., 2019). This experiment addresses meal timing and absorption, not recurrence of deficiency over a training season.

Moretti and colleagues studied 54 non-anaemic women with ferritin at or below 20 $\mu g/L$. Twenty-four hours after oral doses of at least 60 mg, hepcidin increased and fractional absorption of a subsequent dose fell by 35–45% (Moretti et al., 2015). Stoffel and colleagues then randomised 40 iron-depleted women to 60 mg on consecutive days for 14 days or alternate days for 28 days. Geometric mean cumulative fractional absorption was 16.3% and 21.8%, respectively, and cumulative absorbed iron was 131.0 and 175.3 mg. A separate 20-woman comparison found no significant absorption advantage from splitting a 120-mg dose into two daily administrations (Stoffel et al., 2017). The dosing intervals and treatment lengths were integral to these results; the findings do not supply an athlete-specific performance effect.

FERRITIN AFTER EQUAL CUMULATIVE DOSES

Von Siebenthal and colleagues randomised 150 women with ferritin at or below 30 $\mu g/L$ to 100 mg daily for 90 days followed by placebo, or 100 mg on alternate days for 180 days. End-of-course ferritin medians were 43.8 and 44.8 $\mu g/L$, respectively ($p = 0.98$). Gastrointestinal symptoms on iron-intake days were more frequent with consecutive-day dosing: longitudinal prevalence ratio 1.56, 95% confidence interval (CI) 1.38–1.77 (von Siebenthal et al., 2023). Similar end-of-course medians do not demonstrate statistical equivalence, and equal cumulative doses were achieved over different calendar periods.

At six months, the consecutive-day group had completed approximately three months without active iron, whereas the alternate-day group had just completed treatment. Ferritin after the daily course was 27.0 $\mu g/L$ (interquartile range [IQR] 18.4–42.0) at three months after cessation. The later alternate-day assessment was 39.4 $\mu g/L$ (IQR 23.6–58.7) at approximately four months after cessation (von Siebenthal et al., 2023). These observations are useful for the timing of biochemical assessment, but their unequal post-course intervals and non-athlete participants preclude a direct comparison of sporting benefit or menstrual-loss-related recurrence.

EXERCISE FUNCTION AND FOLLOW-UP AFTER INTRAVENOUS TREATMENT

ENERGETIC EFFICIENCY AND MAXIMAL OXYGEN UPTAKE

The observational study in collegiate rowers associated depleted stores with slower self-assessed simulated 2-km performance (DellaValle and Haas, 2011). The subsequent double-blind trial randomised 40 rowers to iron or placebo and retained 31 at six weeks: 15 of 21 allocated iron and 16 of 19 allocated placebo. Both groups improved peak oxygen uptake. Group-by-time tests favoured iron for energy expenditure ($p = 0.01$) and energetic efficiency ($p = 0.03$), while the adjusted ferritin test had $p = 0.07$ (DellaValle and Haas, 2014). Completion loss was 9/40, or 22.5%, calculated from these counts. The primary abstract specifies 100 mg/day of $FeSO_4$; its compound-dose notation is not converted here into an elemental-iron prescription. Missing-outcome handling and confidence intervals for the efficiency contrast could not be assessed from the abstract.

Rubeor and colleagues reviewed 12 studies with 283 participants; six identified performance improvement and six did not (Rubeor et al., 2018). These counts are not a pooled treatment effect. In Pengelly's 23-study review, 18 studies had group sizes of 20 or fewer, and the literature search ended in July 2023 (Pengelly et al., 2025). Small groups, differing deficiency thresholds and separate performance endpoints restrict precision and prevent the assignment of one expected benefit to all athletes with low ferritin.

IRONWOMAN: FOUR-WEEK FUNCTION AND THREE-MONTH BLOOD TESTS

IRONWOMAN randomised 26 recreationally active women to 1000 mg intravenous iron isomaltoside or saline. Assessments occurred before treatment, at four days and at four weeks. Running economy improved in the iron group and differed from placebo at four weeks; peak oxygen uptake, lactate threshold and haemoglobin mass did not differ between groups. Fatigue improved within the iron group, whereas mood and quality of life did not change (Dugan et al., 2025). The abstract's fatigue significance test does not supply a numerical between-group effect or CI, so the magnitude of fatigue benefit cannot be quantified from that test alone.

At four weeks the trial was unblinded and placebo participants were offered iron. Both groups were asked to undergo blood assessments three months after intervention, with 89% follow-up adherence. Ferritin remained elevated relative to pretreatment values in the publisher's follow-up account (Dugan et al., 2025). Subsequent treatment in the placebo group prevents that assessment from being interpreted as a continued randomised comparison. The three-month observation also concerns blood indices rather than a three-month exercise-economy test.

FEMALE-ATHLETE FERRITIN DECLINE OVER SIX MONTHS

McKay and colleagues retrospectively modelled post-infusion ferritin in 22 female athletes. The abstract gives one- and six-month ferritin estimates of 154 and 107 $\mu g/L$, with considerable between-athlete variation, and recommends blood assessments at those intervals (McKay et al., 2020). These estimates describe the course of ferritin in the cohort; they are not a rate of recurrent deficiency. The absence of randomised treatment allocation and limited characterization of menstrual exposure prevent attribution of the decline to uterine bleeding. An individual's decline must also be distinguished from crossing a clinically applicable deficiency threshold after documented correction.

BLEEDING TREATMENT, IRON INDICES AND FORMULATION SAFETY

SIX-CYCLE CHANGES IN FERRITIN AND HAEMOGLOBIN

Kaunitz and colleagues randomised 165 women with HMB to a levonorgestrel-releasing intrauterine system (LNG-IUS; $n = 82$) or medroxyprogesterone acetate ($n = 83$), 10 mg/day for 10 days per treatment cycle. Median ferritin increased from 19.0 to 34.0 $\mu g/L$ with LNG-IUS and from 19.0 to 21.0 $\mu g/L$ with oral treatment after six cycles. Median haemoglobin increased from 12.4 to 13.4 g/dL and from 12.2 to 12.6 g/dL, respectively (Kaunitz et al., 2012). The relative increases in ferritin and haemoglobin favoured LNG-IUS ($p < 0.001$). The participants were not selected as endurance athletes, and the study did not assess whether iron deficiency returned after replacement ceased.

The ECLIPSE trial compared LNG-IUS with usual medical treatment in 571 primary-care women. Usual treatment included tranexamic acid, mefenamic acid, combined oestrogen–progestogen or progesterone alone. At six months, mean improvements on the 0–100 MMAS were 32.7 and 21.4 points, respectively. Over two years, the mean between-group difference in improvement was 13.4 points (95% CI 9.9–16.9) (Gupta et al., 2013). This establishes an advantage for bleeding-related quality of life under those trial conditions, without quantifying an athlete's exercise response or post-treatment iron stores.

These trials support attention to continuing blood loss when deficiency accompanies HMB. They do not establish a contraceptive prescription for performance enhancement. Treatment depends on the cause of bleeding, contraindications, reproductive goals and patient preferences. Menstrual-health or haematology assessment may be necessary when the pattern suggests a bleeding disorder or another underlying cause (American College of Obstetricians and Gynecologists, 2019). Replacing iron and investigating substantial bleeding address different components of the clinical problem.

INTRAVENOUS IRON AND PHOSPHATE RISK

Intravenous formulations differ in adverse-event risk. Wolf and colleagues conducted two trials in 245 adults with iron-deficiency anaemia and intolerance or inadequate response to oral iron. Participants received iron isomaltoside 1000 mg once, or ferric carboxymaltose 750 mg on days 0 and 7. Hypophosphataemia, defined as serum phosphate below 2.0 mg/dL during 35 days, occurred in 7.9% versus 75.0% in trial A and 8.1% versus 73.7% in trial B (Wolf et al., 2020). The populations, doses and formulations must accompany these percentages. They are not estimates of risk in endurance athletes, but they demonstrate why ferritin response alone is insufficient for comparing intravenous treatment options.

INTERPRETING CORRECTION DURING AND AFTER TREATMENT

A measurement during continued supplementation establishes iron status under continuing replacement. A measurement after cessation addresses how much correction remains after the course. Von Siebenthal's daily and alternate-day groups illustrate the distinction: at the same six-month calendar point, one group had been off active treatment for approximately three months and the other had just completed it (von Siebenthal et al., 2023). The comparison cannot be described simply as a difference between two dosing schedules without its treatment history.

The same principle applies to intravenous follow-up. IRONWOMAN's four-week exercise result arose during a randomised comparison; its later blood result followed unblinding and a treatment offer. McKay's one- and six-month ferritin estimates arose from retrospective athlete follow-up (Dugan et al., 2025; McKay et al., 2020). Neither observation yields a randomised estimate of recurrent deficiency prevented by menstrual treatment. Ferritin decline after an infusion also cannot be equated with recurrence when the athlete remains above a clinically applicable deficiency threshold.

For clinical interpretation, the useful information is therefore the dated laboratory result, the dose actually taken or infused, time since treatment cessation, current bleeding, symptoms and relevant sampling conditions (Pedlar et al., 2018; McKay et al., 2022). Continued treatment can maintain sufficient stores when loss remains substantial; clinically indicated maintenance should not be judged a failure merely because replacement has not stopped. Conversely, an end-of-course increase does not establish that later stores will remain sufficient.

Exercise function requires its own assessment. The rower and IRONWOMAN trials demonstrate that energetic efficiency or running economy can improve without a parallel between-group increase in peak oxygen uptake (DellaValle and Haas, 2014; Dugan et al., 2025). Fatigue, economy, maximal uptake and training participation answer different questions. Their interpretation should retain the test conditions and treatment interval instead of combining them into an unvalidated recovery score.

CONCLUSION

The duration of iron correction cannot be inferred from an isolated ferritin rise. Existing athlete studies document variation in post-infusion ferritin and selective four- to six-week exercise benefits. Oral dosing studies distinguish treatment completion from later observations without active iron. Bleeding-treatment trials demonstrate six-cycle improvements in ferritin and haemoglobin and a two-year improvement in bleeding-related quality of life in non-athlete women. In menstruating endurance athletes, these findings support joint assessment of iron status, actual replacement exposure, continuing bleeding and exercise symptoms. They do not establish that one bleeding-treatment regimen prevents recurrent deficiency or sustains performance after iron withdrawal. A clinically meaningful account of treatment response must state when correction was measured, whether replacement continued, and which laboratory or functional outcome improved.

DECLARATIONS

AUTHOR CONTRIBUTIONS

All authors contributed equally and all authors read and approved the final version of this manuscript.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest related to this study.

DATA AVAILABILITY

Data required for this research is included within the manuscript.

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