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Use of Supplemental Iron for the Enhancement of Physical Performance in Competitive Non-Anemic Female Athletes

Annalese M. Lamke
Bethel University

USE OF SUPPLEMENTAL IRON FOR THE ENHANCEMENT OF PHYSICAL PERFORMANCE IN COMPETITIVE NON-ANEMIC FEMALE ATHLETES

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ANNALESE LAMKE

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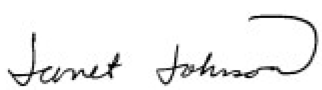
APPROVALS:

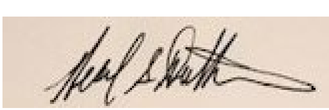
Project Advisor: Janet Johnson, DPT, ATC

Signature: 

Dean of Business, Leadership, Health, and Social Sciences: Chad Osgood, Ed.D., LAT, ATC

Signature: 

Program Director: Neal Dutton, MS, LAT, ATC



Abstract

Background: Iron has been a commonly prescribed supplement for female athletes to take, but there is little evidence to support if iron supplementation can help improve non-anemic female, athlete's performance. There is still a lack of unity to determine whether iron can be beneficial to a female athlete during their competitive season regardless of their blood iron status.

Purpose: The purpose of this literature review is to determine the impact of iron supplementation on physical performance in competitive non-anemic female athletes.

Results: Seventeen articles were selected after following evaluation procedures utilizing the PEDro Scale, CASP, and the Critical Appraisal of a Meta-Analysis or Systematic Review; each of the articles were selected for their respective research types. Ten of the seventeen articles were able to report the benefits of iron supplementation on physical performance. The most common performance improvements were VO_{2max}, energy efficiency, and improved blood lactate levels. Five articles reported no evidence of iron improving performance. The most common outcome supported by the utilized review articles suggested that iron supplementation allowed for iron level maintenance throughout the competitive season.

Conclusion: Iron supplementation is most beneficial to physical performance in patients who have lower iron status. There is evidence to support that iron supplementation maintains blood iron levels throughout a competition which helps patients maintain their aerobic capacity. Iron supplementation was most beneficial to aerobic performance.

Implications for Research and Practice: This research supports using iron supplementation in female athletes regardless of their iron status. The literature encourages athletic trainers and physicians to present athletes with the option for the female athletes to begin supplementation during their competitive season regardless of their iron status. Further research needs to be completed to determine the adverse effects of supplementing iron in patients that currently have normal iron levels as well as research on adequate dosage amounts.

Keywords: female, athlete, iron, supplementation, performance

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Chapter I: Introduction

Iron is one of the most fundamental minerals found to be naturally occurring in an average diet (Haff & Triplett, 2016). Within the human body, iron is a principal component of oxygen transport and energy production, both vital occurrences for athletic performance (Alaunyte, Stojceska, & Plunkett, 2015). Iron's primary function, most importantly, plays a significant role in myoglobin and hemoglobin (Hgb) production and is also stored in the body through ferritin, which is the marker for body iron levels (Bass & McClung, 2011: Silverthorn, 2016). While iron can be absorbed into the body through diet, it can be lost through several body functions; iron can be lost through sweat, urine, menstruation, and other types of physical stress (Woods et al., 2014). Athletes, especially females, are particularly susceptible to being iron deficient (ID) due to the high energy demands they have on their bodies (Woods et al., 2014).

To determine the body's iron levels, transferrin saturation and serum ferritin (sFer) levels can be monitored through a blood sample (Bass & McClung, 2011). These tests are used to determine the amount of ferritin, the iron storage protein, and transferrin, the iron bonding protein, in the patient's bloodstream (Silverthorn, 2016). A healthy level of iron would be a sFer value of $>12\ \mu g \cdot L^{-1}$, anything lower, and the patient may be considered anemic (Crouter, DellaValle, & Haas, 2012). Iron-deficiency anemia (IDA) is the condition where there is an insufficient Hgb synthesis in the blood, caused by an iron loss that is greater than iron intake or by the bone marrow being unable to produce a high enough amount of Hgb (Silverthorn, 2016).

When a patient is anemic, it is important to add additional iron to the diet. This can be done through tablets, iron patches, intravenous solutions, or by having the athlete eat more red meat, beans, and spinach (Silverthorn, 2016). Added incorrectly, there is a risk of hemochromatosis, or iron overload, and oxidative stress, the condition of having an imbalance of oxygen-containing molecules, as well as cellular damage (Bass & McClung, 2011). If added correctly, iron supplementation may provide the benefits of reduced fatigue and increased aerobic endurance (Hinton, 2014). Other studies have shown that iron supplementation can also play a beneficial role in mood disturbances, perceived fatigue, and readiness to train throughout a workout period (Woods et al., 2014). Having a lack of research toward the effect of iron supplementation in health females can lead to uncertainty towards using iron as a primary supplement. This uncertainty is the guiding pathway to the primary purpose and questioning of this Critical Review of Literature. The Critical Review of Research question is: Does iron supplementation increase the physical performance of non-anemic, competitive female athletes?

Statement of Purpose:

The purpose of this literature review is to determine the impact of iron supplementation on the physical performance in non-anemic, competitive female athletes. To do this, iron supplementation will be compared against a placebo and based on physical performance before and after the athletes had gone through a supplementation program. Physical performance includes aerobic capacity, anaerobic performance, muscular strength, blood lactate levels, and recovery time. This research will also be intentional in attempting to find what dosage and type of iron supplementation will provide the greatest impact on physical performance. Preliminary research has found conclusions on the benefit of iron supplementation in anemic athletes; therefore, this research aims to determine if there is evidence to support supplementation in female athletes that are not anemic as well.

Need for Clinical Review:

There is a need for clinical review on this topic because most of the available research on iron supplementation for female athletes only covers supplementing within anemic situations. A further review can help identify if there are benefits for supplementing iron for non-anemic athletes or athletes that have close to normal iron levels. It has been stated that in the general population, nearly 16% of U.S. females are ID, and there is also a prevalence of 3-5% of IDA and even more prevalent within the athletic population (Crouter et al., 2012; Hinton & Sinclair, 2007). According to Parks, Hetzel, Brooks' (2017) study, a range of 16% to 57% of female athletes were iron deficient depending on the parameters of what is considered a deficiency based on the Hgb and sFer tests. With the effects of fatigue, poor performance, and injury, the potential for having more than half of female athletes being iron deficient at a time is a rather alarming number.

Another important reason for the need of a clinical review is the lack of on how ID is defined. Some argue that the ferritin level cutoff should be 20 $ng \cdot mL^{-1}$ but other reports suggest it should be moved to a lower cutoff of 12 $ng \cdot L^{-1}$ (Parks et al., 2017). A change in the ID threshold could potentially impact a result in a decrease in nearly 2/3 of the athletes considered to be ID (Parks et al., 2017). Having a clear and agreed-upon understanding of the cutoff for ID would help improve awareness of when it is appropriate to start the supplementation of iron.

The presence of ID in preparticipation examinations may be enough to place a higher consideration to begin supplementation, but also, there is evidence showing that participation in sports may result in ID. Auersperger et al. (2013) saw a 21% increase of ID in their participants after completing an eight-week endurance running training program. McClung et al., (2009) saw similar results when comparing participants who did and did not receive iron throughout an eight-week training program; however, in this study, they saw a 100% increase in ID in participants who did not receive an iron supplement. These results may be enough to consider iron supplementation, but there is still a need to determine if ID and iron supplementation impacts non-anemic female physical performance.

Understanding this topic and reviewing the impacts of iron supplementation on the healthy athlete may provide insight on whether the entire female athletic population should consider supplementation or just those within the ID standard. A critical review of this issue can provide a better understanding of which female athletes may be best supported with an iron supplement or if iron supplementation should be avoided if not needed. This clinical review will also be designated to determine if there is a dosage or dosage type, such as intramuscular, intravenous, or oral administration, of iron that gives the female athletes the best effect within performance and overall health. This clinical review aims to provide insight on the benefits of iron supplementation, but it will also attempt to provide insight on whether or not there are adverse effects on iron supplementation of the healthy female athlete. A better understanding of this topic could lead to changes in female athletes' diet, performance, and quality of life if there are clear benefits to iron demonstrated in the research. There will be a better understanding of which athletes would be more or less qualified for iron supplementation.

Significance in Athletic Training:

One of the reasons why the topic of iron supplementation within female athletes can be significant for athletic training is because it may provide greater insight into helping female athletes perform at optimal levels. Certain female athletes, especially runners and gymnasts, can be at high risk for ID, which could have a negative effect on their performances (Hinton, 2014). If this Critical Review can determine that there is a benefit of iron supplementation, this may change the way ATs begin their preparticipation exams. Before the athlete even begins practices, it could be beneficial to run tests to determine their Hgb and sFer levels to consider their need for iron supplementation. Even if the athlete's iron levels are remotely low, there may be more of a benefit to adding iron to their diet. While preparticipation examination changes would be necessary to determine the need for iron supplementation before participation, it would also bring awareness to athletes who may be at risk of developing ID during the season. The greatest significance that this review and topic may have for athletic training is that it may lead to healthier blood iron levels in competitive female athletes and providing opportunities for female athletes to compete at their highest physical level.

Chapter II: Methods

The purpose of this chapter is to display the procedures implemented to gather the research articles used for this Critical Review of Literature. This chapter will discuss the search strategies, search terms used, the number of hits received for each search term, inclusion and exclusion criteria, and methods utilized for appraising and evaluating the articles chosen.

Search Strategies:

The primary search database used for this Critical Review of Literature was the CLICsearch, a database provided by Bethel University, MN. Additional databases utilized were PubMed, followed by CINAHL, and then Google Scholar. Finally, articles were obtained through the Reference page of systematic reviews that were credited to be worthy and were included within the review. Keywords in the database search included: “iron,” “female,” “athlete*,” “supplementation,” and “performance.”

The article search process was initiated by utilizing the Bethel University Library CLICsearch page. In the initial search, “Iron supplementation AND female athlete*” resulted in 1,240 results. A search of “Iron supplementation AND athletic performance” was added to the initial search which resulted in 921 hits. Lastly, the two searches were combined to include the search terms of, “Iron supplementation AND female athlete* AND athletic performance,” for a total of 26 hits. From these 26 hits, the researcher was able to evaluate the available articles to find research that fit the inclusion criteria. After reviewing the Bethel University Library CLICsearch page, a literature search was conducted on the Sports Medicine and Education Index Database. A search of “Iron supplementation AND female athlete*” that was limited to peer-reviewed articles and from the years 2010-2020 yielded 13 results. The researcher followed the same inclusion and exclusion criteria to determine if the articles were suitable for this Critical Review of Literature.

Inclusion and Exclusion Criteria:

The inclusion criteria were established so that this Critical Review of Literature would remain focused and intentional in answering the clinical research question. For an article to be included, it needed to possess the following qualities: iron as a lone intervention, females as the majority participant, blood samples taken before and after the intervention, and physical performance obtained as a primary or secondary measure. In this review, the population included adult females (≥18 years of age) who were physically active (in a sport of any nature) and were non-anemic. One article was included where the participants were involved in the military, but not in sport. This study was an exception due to the physical nature of military basic training and how it can be similarly compared to athletic-related practices.

Articles were excluded from the review if they were in languages other than English, if the population was sedentary, and if the study participants were anemic. There were no exclusion criteria based on the type of article, but many articles used were Randomized-Control Trials (RCTs) and Systematic Reviews/Meta-Analyses of RCTs. Articles were also excluded if the subjects were adolescents (≤18) or older adults (≥30); this was done so that the results would be more closely related to the highest level of competitive athletes. There were no inclusion or exclusion criteria based on the date the article was published.

Number of Articles:

A total of 17 articles were selected based on the inclusion and exclusion criteria. Before the articles were included in this review, they went through an appraisal process using several grading tools. The appraisal tools used for the 17 articles were the PEDro Scale for randomized-control studies (The George Institute for Global Health, n.d), the Critical Appraisal Skills Program (CASP) for prospective studies and systematic reviews (Raab & Craig, 2016), and the Critical Appraisal of a Meta-Analysis or Systematic Review (University of Oxford, 2014). After the articles were appraised using the appropriate appraisal worksheet, the level of evidence and quality of evidence were recorded in the matrix. The level of evidence was based on the "Hierarchy of Evidence for Intervention Studies" chart (Fineout-Overholt, Melnyk, Stillwell, & Williamson, 2010). See Appendix A.

Once the articles were appraised and the level of evidence was established, the researcher subjectively determined the quality of the articles as *high, good, fair,* or *poor*. When appraising the article with tools that utilized a numerical score, higher scores typically implied a higher quality. However, some articles were deemed to have a lower quality based on the content of the research itself. For example, if the study used a double-blind, randomized control trial, which would generally score high on a PEDro Scale, but the scientific methods used within the research and the quality of the findings lowered the quality rating of the article because the methods the authors used were not up to the standards of the researcher. This would lead to low quality score in the presence of a high score on the appraisal tool. This method was done on each type of appraisal tool used for the given article and will be reported within the Literature Matrix.

Table 1: Level of Evidence and Quality of Included Articles

Level of Evidence	*High* Quality	*Good* Quality	Fair Quality	Total Number of Articles
I	1	2	1	4
II	4	6	0	10
III	0	1	0	1
IV	1	1	0	2
Total	6	10	1	**17**

Criteria for Evaluating the Studies:

After the appraisal process, the articles were then placed into a Literature Matrix outlined and developed by the Bethel University Graduate Nursing Program. The Literature Matrix was used to summarize the critical topics of the article, using the headings: “Source,” “Design Methodology/Purpose,” “Method,” “Sample Setting,” “Level,” “Quality,” “Design Instruments,” “Results,” and “Recommendation.” See Appendix B. There was no order to how the articles were placed into the Matrix as the articles were entered as they were discovered via the previously discussed search methods. The Matrix was used as a “quick glance” summary of the articles used for the Critical Review of Literature, and they will be used to guide the Literature Review and Analysis in Chapter III. As mentioned in the previous section, articles were evaluated based on their level of evidence and their quality. Articles were objectively identified for their level of evidence using the “Hierarchy of Evidence for Intervention Studies” chart and were then subjectively evaluated by the researcher for the quality of evidence (Fineout-Overholt et al., 2010). The researcher examined each article’s Currency, Relevance, Authority, Accuracy, and Purpose (CRAAP) to assess their subjective values (Raab & Craig, 2016). Those five criteria then allowed the researcher to identify if the article was high- or low-quality.

Summary:

The Bethel University Library CLICsearch and the Sports Medicine and Education Index were the databases used to discover research articles to analyze the effect of iron supplementation on female athletes' performance. While many articles were presented through the initial search results, there are 17 articles that were selected for this review. Once the articles fit the inclusion criteria, they went through an appraisal process to determine the level of evidence and quality of the articles. Finally, the articles were placed into the Bethel University Graduate Nursing Program's literature matrix to summarize the main findings of the article.

Chapter III: Literature Review & Analysis

Synthesis of Matrix:

This chapter's primary purpose is to introduce and summarize the 17 articles that were included in this Literature Review. The summary of each article will be used to complete an answer to the research question of this paper. Each article included in the review was analyzed and placed into a matrix created by the Bethel University Graduate Nursing Program to develop a summary of the findings and the quality of the articles. See Appendix A. There are four different levels of evidence types involved in this review based on the "Hierarchy of Evidence for Intervention Studies" chart (Fineout-Overholt, Melnyk, Stillwell, & Williamson, 2010). In the synthesis, the articles will be summarized according to their level of evidence and alphabetically by name of author.

Synthesis of Major Findings:

Level 1 Evidence: Articles that are conducted as a systematic review and meta-analyses are included as Level 1 Evidence; there are four articles that are included in this category.

Burden et al. (2014) conducted a meta-analysis of randomized-control trials (RCT) to determine whether iron treatments impact the aerobic capacity of IDNA endurance athletes. The study included 17 studies where 443 subjects were included; 363 of the subjects were female and 80 were male (Burden et al., 2014). VO_{2max} was the standard measure for aerobic capacity (Burden et al., 2014).

The results of the analysis revealed that there was a large effect size on the impact of iron treatment on an increase in sFer (Burden et al., 2014). There was only a moderate effect size of the iron supplementation and an increase in VO_{2max} and iron that was supplemented orally rather than intramuscularly (Burden et al., 2014). Supplementation also had a significant effect on endurance performance as well (Burden et al., 2014). Finally, the study concluded that iron supplementation caused improvement of blood iron markers, but there was a diminished effect size after 80 days of using the supplement (Burden et al., 2014). This article shows that when iron is supplemented it can be beneficial to aerobic performance but only for a certain period of time. The benefit of iron supplementation may be more dependent on the patient's initial iron stores as this study only researched IDNA patients and cannot provide evidence to support supplementation for patients with normal iron levels.

Houston et al. (2018) conducted a systematic review of RCT as well, where the purpose of their review was to identify the supplementation of iron in IDNA populations and how it may affect physical performance. There were 18 RCTs and two companion papers that were included in this study, resulting in a combined total of 1170 adult participants (Houston et al., 2018). Iron was supplemented through oral, intramuscular, or intravenous administration but there were no guidelines for iron supplementation (Houston et al., 2018).

For physical performance, iron supplementation was associated with an increase in physical capacity in 19% of the studies (Houston et al., 2018). The most common result in the study showed that iron supplementation was associated with a reduced subjective measurement of fatigue by the participants (Houston et al., 2018). In 14 of the 20 articles reviewed, there was evidence that iron increased sFer and other iron markers in the blood (Houston et al., 2018). Lastly, the study revealed that the most common adverse effects of supplementation included gastrointestinal intolerance, nausea, and constipation (Houston et al., 2018). These findings show that supplementation may only have slight risks, and the benefits of iron could outweigh the small number of adverse events.

Pasricha et al. (2014) conducted a systematic review and meta-analysis to determine the effects of iron supplementation on physical activity in women of reproductive age. In the review, 22 studies were included for a total of 911 participants (Pasricha et al., 2014). Studies included participants aging from 12-50 years old, studies that had an experimental group and a control group, and used VO_{2max}, HR_{max}, V_T, blood lactate, or submaximal exercise performance as an outcome measure (Pasricha et al., 2014).

The most significant finding in Pasricha et al. (2014) was that iron supplementation has a beneficial effect on VO_{2max} and can also improve efficiency in submaximal exercise when compared to no treatment. It was noted in the research that the impact of iron may only be beneficial in well-trained participants and would not be as effective in less active groups (Pasricha et al., 2014). There was no evidence that supported iron supplementation benefiting other aspects of athletic performance (Pasricha et al., 2014). This article provides strong evidence to support the idea that iron supplementation can improve athletic performance.

Rebeor et al. (2018) is the final systematic review to be used in this level of evidence. The goal of this article was to review the literature on iron supplementation in IDNA athletes (Rebeor et al., 2018). A total of 12 studies were included for a total of 283 subjects ranging from the ages of 13-41, the population of the studies were 257 females and 26 males (Rebeor et al., 2018). All the studies included used trials that compared iron supplementation against a placebo (Rebeor et al., 2018).

The research was unable to demonstrate conclusive evidence that supported iron supplementation improved performance. In six of the studies included, iron supplementation showed improvement in athletic performance while the other six articles did not discover improvement (Rebeor et al., 2018). The evidence that was most supported by this article was that iron supplementation could improve performance in patients who are IDNA with sFer levels of 20µg/L or lower (Rebeor et al., 2018). While this article did not give reliable evidence to support the use of iron supplementation for the improvement of performance, it did give valuable information regarding a blood iron level to begin the consideration of using supplements to help the athletes. Iron supplementation may not benefit an entire population, but it may be beneficial to those who are ID but not anemic.

Level 2 Evidence: Randomized-Control Trials are included in Level 2 Evidence; there are 10 articles that are included in this category.

Burden et al. (2015) completed a double-blind, RCT of nine females and six males to determine the effects of iron supplementation on aerobic capacity of marathon runners. All participants were classified as IDNA and were placed into an experimental or placebo group (Burden et al., 2015). The experimental group received 500 mg of iron intravenously (IV) while the placebo group received an injection of saline solution (Burden et al., 2015). Both groups completed three separate treadmill tests to exhaustion during the trial, a test before the injections, 24 hours after the treatment, and four weeks after the treatment (Burden et al., 2015). The treadmill tests were completed to measure VO_{2max}, Submaximal VO_2, and blood lactate levels; blood analysis of sFer, sTf, hepcidin levels, and blood volume were also measured (Burden et al., 2015).

The experimental group received a one-time treatment of a 500 mg iron dosage to test its effects on aerobic performance (Burden et al., 2015). When compared to the placebo, the experimental group saw no significant difference in VO_{2max}, economy, speed, and time to exhaustion (Burden et al., 2015). Although there were no improvements on performance levels, the experimental group saw a significant improvement in blood iron measurements, especially hepcidin levels pre- and post-exercise (Burden et al., 2015). This study showed little to no evidence that supported the claim iron supplementation can improve aerobic performance. It should be noted that this was only a one-time dosage of iron and it may not have been a long enough period to determine if it was effective.

DellaValle and Haas (2014) also conducted a placebo-controlled, double blind RCT to determine the effects of a 100 mg daily dosage of iron on the endurance performance of collegiate rowers. The study consisted of 48 female rowers who were all considered to have normal iron levels or were IDNA; anemic subjects were excluded from the study (DellaValle & Haas, 2014). Participant performance was determined by the completion of a 4-km time trial and a maximal aerobic power test performed on an ergometer (DellaValle & Haas, 2014). These performance tests were completed before the beginning of the study and after the six-week trial (DellaValle & Haas, 2014). Performance measures for this study were maximum aerobic power, blood lactate levels, endurance capacity, energy efficiency, and total body iron stores (DellaValle & Haas, 2014).

Upon the completion of the six-week period, there was a significant improvement in total body iron levels in the experimental group and that participants with the lowest iron stores at baseline benefited the most from supplementation (DellaValle & Haas, 2014). For the physical performance measures, there was a correlation with the supplement and energy efficiency in the time trial as well as a negative correlation between the supplemental iron and maximal lactate levels throughout the time trial (DellaValle & Haas, 2014). The supplemental group also showed a faster 5-minute recovery than the placebo group (DellaValle & Haas, 2014). These findings are significant to answering the research question as it provides evidence supporting that iron can help improve specific aspects of performance. While the overall test results did not differ greatly, participants that received the treatment were more energetically efficient, had lower blood lactate levels, and could recover faster than participants that did not receive the treatment. This is important because it may lead to allowing athletes to participate longer if they are more energetically efficient and have lower maximal lactate levels as they perform.

Garvican et al. (2014) RCT focused on the supplementation of iron in distance runners to determine its effect on VO_{2max} and iron stores throughout the 6-week trial period. This study compared intravenous and oral intake of iron against each other to determine which method of supplementation was most effective (Garvican et al., 2014). The participants of this study were 28 distance runners, 13 females and 14 males, all of whom were considered highly trained (Garvican et al., 2014). The iron status of the participants was measured in weeks 1, 2, 4, 6, and 8 while the treadmill test to determine running economy, VO_{2max}, and lactate threshold was measured before and after the supplementation (Garvican et al., 2014).

At the end of the trial period in Garvican et al.'s (2014) study, both IV and oral supplementation groups were able to increase blood sFer levels; however, it was noted that the IV sFer levels were generally higher throughout the entire study (Garvican et al., 2014). Only two performance measures were different when compared against each other. The IV group was successful at increasing their VO_{2max} as well as their run time to exhaustion compared to the oral group (Garvican et al., 2014). These findings are significant for determining what type of supplementation would be more successful at improving performance. While this information is promising, the study's lack of placebo cannot determine whether this change was caused by the training or the intervention the participants completed.

Hinton and Sinclair (2007) completed a six-week double-blind, randomized-control trial to determine iron supplementation on the endurance performance of IDNA adults. A total of 20 adults, 17 females and 3 males, were used in this study, all of which were considered physically active (Hinton & Sinclair, 2007). The participants were divided into two groups. The experimental group received a 30mg dosage of iron daily or a placebo sugar pill that looked identical to the iron pill ((Hinton & Sinclair, 2007). The participants had their physical endurance tested through a cycle ergometer test for submaximal endurance along with a VO_{2peak} test (Hinton & Sinclair, 2007). Components measured in these tests were ventilatory threshold, respiratory exchange ratio; Hgb, sFer, and sTfR were all measured to determine the participant's iron status (Hinton & Sinclair, 2007). The testing was completed at the beginning of the study and at the end of the six-week period (Hinton & Sinclair, 2007).

After the six weeks, the experimental group saw a significant increase in their sFer levels while the placebo group saw no improvement (Hinton & Sinclair, 2007). Along with the changes in the body iron status, a positive correlation between the change in sFer levels and gross energetic efficiency was found (Hinton & Sinclair, 2007). In other performance measures, the placebo group saw a decrease in their ventilatory threshold while the experimental group was able to maintain theirs (Hinton & Sinclair, 2007). This article showed that not only can iron improve iron status in the body but that the change in iron status can be correlated with a positive change in performance. Hinton and Sinclair (2007) provide evidence that a 30 mg dosage of iron daily can improve endurance performance in IDNA adults over a six-week period.

Kang and Matsuo (2004) completed a single-blind, randomized-control, trial on the supplementation of 40 mg of iron in elite female soccer players who were competing through their national team training camp. A total of 25 participants were included in the study, and all were between the ages of 20-28 years old (Kang & Matsuo, 2004). The participants were split into a control group that received a placebo pill and the experimental group that received 40 mg daily (Kang & Matsuo, 2004). Each participant had blood tests at the beginning of the trial and at the end, four weeks later (Kang & Matsuo, 2004). The blood tests consisted of measuring for WBC count, plasma immunoglobin, sFer, and total iron stores in the body (Kang & Matsuo, 2004).

At the end of the four weeks, the participants receiving the supplementation did not see an increase in blood Hgb levels, but the control group saw a significant decrease in Hgb over the trial period (Kang & Matsuo, 2004). The only blood iron measurement that saw a significant increase in the study was the plasma ferritin levels of the experimental group; the control group saw no change in this statistic (Kang & Matsuo, 2004). While this study did not specifically measure performance, it showed that throughout the study, participants not supplementing iron saw decreases in Hgb levels. This is important as it helps to understand that consistent activity can lead to a decrease in iron stores in the body and that supplementing iron can help prevent the decrease. Even if iron supplementation does not improve performance, Kang and Matsuo's (2007) research supports that iron can help athletes maintain healthy iron levels in the body during a training period.

Klingshirn et al. (1992) conducted RCT to determine the effects of iron supplementation on the endurance capacity of IDNA, female, distance runners. A total of 18 IDNA women ranging in age from 22-39 years old were used in the study (Klingshirn et al., 1992). Participants were split into two groups; the control group received a placebo and the experimental group received 50 mg of iron, each group took their dose twice a day for eight weeks (Klingshirn et al., 1992). Participants were tested on their VO_{2max} test on a treadmill and an endurance capacity test to determine the time to exhaustion, respiratory exchange ratio, rating of perceived exertion, and the blood lactate concentration after the test (Klingshirn et al., 1992).

Klingshirn et al.'s (1992) study found no significant differences in physical performance measures between groups after the eight-week trial. After the trial, both groups showed improvements in their running time to exhaustion, but the changes were not considered to be significant (Klingshirn et al., 1992). No other performance measures showed significant differences as well (Klingshirn et al., 1992). The only significant changes noted in the study were the changes in the experimental group's sFer levels after the trial (Klingshirn et al., 1992). This study is one of the first to report no significant differences in physical performance with iron supplementation. Klingshirn et al. (1992) gives reason to be skeptical about the benefits of iron supplementation on physical performance, but the supplement will still cause improvements to the patient's iron levels.

McClung et al. (2009) conducted a double-blind, randomized-control, trial to determine if iron supplementation would prevent a decrease in body iron status and if it would have an impact on physical performance and mood. This study focused on using 171 female soldiers who were completing their basic combat training (McClung et al., 2009). Participants were divided into two groups; the experimental group received 100 mg capsule of iron daily and the control group received a placebo pill (McClung et al., 2009). Participants had their baseline data recorded one week prior to the beginning of the study (McClung et al., 2009). Measurements at baseline included total body iron, sFer, and Hgb levels; performance measures were a 2-mile run that was required of the participants as part of their combat training (McClung et al., 2009). The participants' mood state was a secondary measure of this study as well (McClung et al., 2009). The trial lasted throughout the 8-week basic combat training that the participants were required to complete (McClung et al., 2009).

At the end of the 8-week training, there was a 100% increase in participants who were now considered anemic based on their Hgb levels, whereas the experimental group only had a 36% increase in anemic participants (McClung et al., 2009). The control group had significantly lower body iron levels than the experimental group; however, the experimental group still reported decreased iron levels (McClung et al., 2009). There were no reports of significant differences in physical performance between the two groups (McClung et al., 2009). The most significant finding regarding performance was that participants that were anemic before the study had a decreased time of 110s during the run if they received the iron treatment (McClung et al., 2009). In the secondary findings, the experimental group tended to show an improvement in mood compared to the control group (McClung et al., 2009). These findings clarify that iron may be most beneficial to improve performance in patients that are deficient or anemic. It may also provide evidence that iron supplementation can help improve a patient's mood.

Mielgo-Ayuso et al.'s (2014) RCT was more unique than the other studies because it looked at markers of strength for physical performance rather than endurance. This study followed 22, non-anemic, professional volleyball players through their 11-week competition season (Mielgo-Ayuso et al., 2014). The experimental group of this study received 105 mg of iron daily throughout the study while the control group received nothing (Mielgo-Ayuso et al., 2014). The participants were monitored for their total body iron stores (Hgb and sFer) as well as their submaximal strength performances on the bench press, military press, half-squat, power clean, clean and jerk, and a pullover (Mielgo-Ayuso et al., 2014).

After completing the 11-week season, the control group saw a significant decrease in iron levels, but the experimental group did not have a decrease in their levels (Mielgo-Ayuso et al., 2014). For the participant's strength performance, the experimental group saw a significantly greater increase of strength in the clean and jerk, power clean, and their total mean strength (Mielgo-Ayuso et al., 2014). It was noted, however, that both groups had a time effect of the improved strength throughout the study (Mielgo-Ayuso et al., 2014). This article was consistent with other articles in their findings that iron supplementation helps prevent the decrease of iron stores throughout a competition season. This article also reveals that iron supplementation may have an impact on strength gains made throughout the season which may help athletes improve performance.

Peeling et al. (2007) double-blind, randomized-control, trial determined the effect of intramuscular (IM) iron injections on VO_{2max}, time to exhaustion, and submaximal exercise economy in IDNA endurance athletes. A total of 16 well-trained adult females who participated in running, cycling, and triathlon clubs were included in this study; all participants were IDNA (Peeling et al., 2007). Participants in the experimental group received five 2 mL IM injections of 100 mg over a 10-day period, and the control group received a 2 mL injection of saline solution (Peeling et al., 2007). Blood tests were performed before the supplementation, 20 days after, and on day 28 of the study; the performance tests were completed at baseline and at the end of the study (Peeling et al., 2007).

Upon the conclusion of the study, there was a significant treatment effect in the experimental groups iron levels as there was a significant increase in their sFer levels (Peeling et al., 2007). There were no significant improvements or differences noted in the study for any of the participant's physical performance measures (Peeling et al., 2007). The only notable changes were that the experimental group did not have a decline in exercise economy like the placebo group experienced, but the changes were not significantly different (Peeling et al., 2007). This did not lead to an answer to the research question, but it did continue to provide further proof that iron supplementation can improve iron status in IDNA patients.

Woods et al. (2014) completed a randomized-control trial to determine the effect of an intravenous (IV) iron supplement on a runner's fatigue, performance, and mood. In this study, 14 highly trained distance runners, eight females and six males, received 2 mL/100 mg dosage of iron or a 2 mL dosage of a saline solution once every two weeks for six weeks (Woods et al., 2014). Participants then completed a 3,000-meter running time trial and a 10x400m workout at baseline and after each supplementation (Woods et al., 2014). The participant's blood samples were taken at baseline and two weeks after the study (8 weeks after baseline) to test for Hgb, iron status, and sFer (Woods et al., 2014). During the running trials, participants were tested for their total time of test, blood lactate levels, and rate of perceived exertion (Woods et al., 2014).

After the six weeks of iron or placebo supplementation, the iron group showed significant improvements in total fatigue scores, decreased 10x400m trial times, decreased blood lactate levels, and improved ratings of exertion and readiness to train (Woods et al., 2014). There were no time changes reported in the iron group's 3,000m time trial, but the placebo group's time was slower than baseline throughout the study (Woods et al., 2014). The iron group also saw significant improvements in their sFer scores throughout the study and the levels remained elevated two weeks after the trial had ended (Woods et al., 2014). This study is beneficial in providing evidence that iron supplemented through IV can improve sFer levels in athletes as well as provide some improvements to physical activity measures. The iron supplementation group had lower levels of lactate and perceived fatigue throughout their trials. This may have an impact on athlete's performance, but there is no evidence to support that it directly improved performance.

Level 3 Evidence: Level 3 Evidence includes articles that are conducted through a Prospective Observational study; only one article included in this review matches these standards.

Auersperger et al. (2013) was designed to determine the markers of iron status in female endurance athletes over a long-term training phase. The sample size included 14 moderately physically active females who were in the normal range of their iron stores (Auersperger et al., 2013). The participants were excluded from the study if they were not moderately physically active, were no longer in reproductive age, did not have a regular menstrual cycle, or if they were anemic (Auersperger et al., 2013). The study was conducted over the participants training for a 10 km or 21 km marathon; the study lasted for eight weeks (Auersperger et al., 2013). The participants were split into two groups, the N group (normal iron stores) and the D group (depleted iron stores) (Auersperger et al., 2013). During the training, body weight, height, body fat percentage, red blood cell concentration, iron stores, and sFer levels were measured before and after the training as well as after a 10-day recovery phase (Auersperger et al., 2013). VO_{2max}, heart rate, and time to recovery were the performance values measured (Auersperger et al., 2013).

Upon the conclusion of the study, it was found that the group with normal iron stores had a larger increase in VO_{2max} (4.8%) than the iron-depleted group (3%) (Auersperger et al., 2013). The study also showed the effects of exercise on the iron stores of the body. At the end of the study, 10 out of 14 participants were iron-depleted; this was an increase of three participants from the beginning of the study (Auersperger et al., 2013). This increase of iron-depleted participants was also maintained throughout the recovery phase (Auersperger et al., 2013). This article did not include a suggestion for iron supplementation; however, the article showed the relationship between exercise and iron stores in the female body. In the study, it showed that physical activity is likely to decrease iron stores and may have an impact on the patient's increase in their VO_{2max} and aerobic performance (Auersperger et al., 2013).

Level 4 Evidence: Level 4 evidence includes Cross-Sectional Studies; two Cross-Sectional studies were included in this review.

Crouter, DellaValle, and Haas (2012) studied 109 women aging from 18-45 to determine the relationship of physical activity, performance, and iron status. Participants were tested through a cycle ergometer test and had their physical activity levels monitored by questionnaires and ActiGraph reports (Crouter et al., 2012). The participants who qualified for the study were moved into two groups: those with normal iron levels and those who were IDNA (Crouter et al., 2012). For the study, participants completed the cycle ergometer test where their Ventilatory threshold (V_T), total wattage, and received blood samples to determine their Hgb, RBC count, sFer and sTfR levels throughout the test (Crouter et al., 2012).

This study found that participants who had normal iron levels were able to achieve a higher wattage than the IDNA participants and the IDNA participants had a significantly lower V_T than the normal level participants (Crouter et al., 2012). An interesting secondary finding of the Crouter et al. (2012) research showed that IDNA participants were significantly more sedentary than those with normal iron levels. This study shows that iron stores in the body can be correlated with performance in maximal aerobic activity and may also play a role in the physical activity behaviors of women. While this study did not directly research iron supplementation, it provided a framework to understand that iron levels that are lower than normal may cause a lessened performance and a likelihood for sedentary activities.

DellaValle and Haas (2012) also conducted a cross-sectional study to determine the relationship between the endurance performance and iron status of collegiate rowers. A total of 149 collegiate rowers participated in this study (DellaValle & Haas, 2012). The rowers were evaluated for their blood iron status before, during, and after training sessions (DellaValle & Haas, 2012). The participants were also evaluated for their Rated Perceived Exertion (RPE), endurance capacity, and aerobic capacity (DellaValle & Haas, 2012). Like the Crouter et al. (2012) research, the participants were split into a normal iron level group and an IDNA group to be compared against each other (DellaValle & Haas, 2012).

This study showed that IDNA rowers had a lower VO_{2peak}, higher lactate concentrations during training periods, and a shortened training time compared to the normal group (DellaValle & Haas, 2012). It was also observed that there was a training effect for participants that were IDNA and that they were able to overcome any iron deficits by being more conditioned and more energetically efficient with their workouts (DellaValle & Haas, 2012). This article did not deal with iron supplementation specifically either, but it, again, shows that there is a relationship with IDNA and a decreased aerobic/endurance performance.

Critique of Strengths and Weaknesses:

Of the 17 articles used, there were many strengths and weaknesses noted. One of the most important strengths of the articles used is that they were all good to high quality except for Rebeor et al.'s (2018) article. Articles that have a higher quality score help provide more credible research and more reliable answers. Another strength of the articles used were that a majority (10 out of 17) of the articles were randomized-control and two of the systematic reviews utilized randomized-control trials to guide the purpose of their studies. This is a strength because it tests the intervention in question against a group that did not receive the treatment. These results may provide more evidence to compare the usage of the treatment to not using it and may allow for generalization of the treatment's effect on the population.

The biggest weakness of the articles used is the overall small population size used for the studies. Apart from the systematic reviews, many of the articles used less than 30 participants in their study. This is a weakness because it makes it difficult to generalize what the effect may be on a larger, less specific, population. Another weakness of the articles used is that there were no uniform methods used across the trials. Each study completed its intervention with a different dosage of supplementation and a different type of physical performance testing. It is difficult to determine if the intervention is beneficial to performance when studies do not use a uniform amount of treatment, as a different amount of treatment could be effective on physical performance.

Summary:

A total of 17 articles were used for this literature review to answer the question: Does iron supplementation increase the performance of non-anemic, competitive, female athletes? The articles were critically appraised using the PEDro Scale, for randomized-control studies (The George Institute for Global Health, n.d), the Critical Appraisal Skills Program (CASP) for prospective studies and systematic reviews (Raab & Craig, 2016), and the Critical Appraisal of a Meta-Analysis or Systematic Review (University of Oxford, 2014). Once each study was appraised, it was categorized into its respective level of evidence according to the "Hierarchy of Evidence for Intervention Studies" chart (Fineout-Overholt, Melnyk, Stillwell, & Williamson, 2010). In the 17 articles summarized, most of the studies found an improvement of iron status when patients were supplemented with iron. Iron supplementation was also determined to help prevent the decline of iron stores throughout a competition/training period. One article supported the use of iron supplementation for the improvement of muscular strength, four articles supported iron decreasing blood lactate levels and improving ventilatory threshold, and two articles supported supplementation improving mood and perceived fatigue. No dosage or time of treatment was reported to be more beneficial than another.

Chapter IV: Discussion, Implications, and Conclusions

The purpose of this literature review was to determine if iron supplementation can increase the physical performance of competitive, non-anemic, female athletes. A critical analysis of 17 articles was conducted to provide an answer to the clinical question. Through the summary of the 17 articles conducted in the previous chapter, this final chapter will address the summary of the literature, the trends and gaps found in the research, the research's implications for the practice of athletic training, and recommendations for future research.

Literature Synthesis:

The primary purpose for this Critical Review of Literature was to answer the question: Does iron supplementation increase the physical performance of non-anemic, competitive, female athletes? To answer this question, 17 articles were reviewed and appraised. The following paragraphs will synthesize the results of the 17 articles for iron supplementations into two categories: iron supplementation improves performance in non-anemic female athletes or iron supplementation does not improve performance in non-anemic females. Finally, the last paragraph of this synthesis will summarize the effects of iron supplementation on non-performance measures. Measures of performance will include: VO_{2max}, energy efficiency, muscular strength, blood lactate during exercise, ventilatory threshold, and recovery. Non-performance measures included in the secondary synthesis will include total body iron stores, Hgb, sFer, and mood.

There were a total of 14 out of the 17 articles that had measures of performance as part of their study. These measures included VO_{2max}, energy efficiency, blood lactate levels during exercise, recovery time, ventilatory threshold, muscular strength, and cardiovascular endurance. Within these performance measures there were 10 articles that were in favor of supporting the use of iron supplementation to improve physical performance in IDNA athletes. Of the 17 articles, 4 articles supported the use of iron to improve VO_{2max}, 3 articles supported benefits to energy efficiency, 3 supported benefiting blood lactate, 2 supported benefiting recovery, 2 supported benefiting ventilatory threshold, and 1 article supported improving muscular strength.

The 4 articles that were of *high* quality in this category; these articles were DellaValle et al. (2012), DellaValle et al. (2014), Hinton and Sinclair (2007), and Woods et al. (2014). The first article of the 4 found that IDNA athletes had lower VO_{2max} values than athletes with a normal iron status. There was a significant positive correlation between sFer levels, VO_{2max} and 4 km performances (DellaValle et al., 2012). In another study using a similar population, DellaValle et al. (2014) found that iron supplementation had a positive impact on energy efficiency, maximal lactate throughout the time trials, and a faster 5-minute recovery then the placebo group. While Hinton and Sinclair (2007) did not explicitly see an improvement in ventilatory threshold in the iron supplemented group, it was noted that the placebo group saw a significant decrease in their ventilatory threshold while the experimental group was able to maintain theirs. Even though there was no evidence of performance improvement, there is evidence of performance maintenance, which could be important considering the non-supplemented group saw a decrease in performance. Lastly, Woods et al. (2014) found that the iron supplemented group had a significant improvement in their fatigue scores, a decreased 10x400m training time, and decreased lactate levels throughout the study.

All other studies included in this section were considered *good* quality. Auersperger et al. (2013), Garvican et al. (2014), Pasricha et al. (2014), and Crouter et al. (2012) all had results that were in favor of supporting iron supplementation improving VO_{2max} in participants of the study. Auersperger et al. (2013) saw some of the biggest increases in VO_{2max}, as their participants had a

4.8% increase in VO_{2max} while the placebo group saw a smaller improvement. In Pasricha et al. (2014), it was noted that VO_{2max} was most improved when highly trained or anemic women received the supplementation. This information may provide evidence that supplementation is more beneficial for more competitive females or females who are deficient of iron. DellaValle and Haas (2012), DellaValle and Haas (2014), Hinton and Sinclair (2007), Peeling et al. (2007), and Woods et al. (2014) all found evidence that iron supplementation positively affected blood lactate levels during performance. In Peeling et al. (2007), participants were able to achieve higher blood lactate levels in their maximal endurance testing while Woods et al. (2014) found that experimental participants had lower blood lactate levels throughout their time trials. While this evidence may appear contradictory to each other, Peeling et al.'s (2007) evidence would suggest that participants could work longer until fatigue and Wood et al.'s (2014) would suggest that lactate accumulation occurs slower with supplementation and would prevent the participant from fatiguing as quickly. Both results would be considered an improvement to performance. Mielgo-Ayuso et al. (2014) was the only article of this group to measure muscular strength. In their study, there was evidence to support that the experimental group saw an increase in strength throughout the competitive volleyball season in the clean and jerk, power clean, and total mean strength in comparison to the placebo group (Mielgo-Ayuso et al., 2014). This is the only claim of iron supplementation affecting muscular strength in this Review of Literature.

A total of 5 out of the 17 articles did not support the claim that iron supplementation improves the performance of IDNA female athletes. Of those 5 articles, only 1 article is considered *high* quality. Burden et al.'s (2014) meta-analysis saw no significant effect on iron supplementation on VO_{2max} or any other aerobic performance measure. The study also noted that iron supplementation was only effective within the first 80 days of treatment and would then have a diminished effect (Burden et al., 2014). The remaining 4 articles were all considered *good* quality. Burden et al. (2015) saw similar results in their study as well; there was no significant difference between groups for VO_{2max}, economy, speed, or time to exhaustion. These results showed that iron supplementation had little to no effect on aerobic capacity (Burden et al., 2015). Both Klingshirn et al. (1992) and Woods et al. (2014) determined that iron supplementation had little to no effect on VO_{2max} or endurance capacity.

Lastly, it is important to note the effects of iron supplementation on the iron status of IDNA females. While it does not explicitly answer the question, most of the articles supported evidence that iron supplementation improved iron status in the patients that received the treatment. A total of 10 out of the 17 articles received results that supported the usage of iron to improve iron status, especially sFer, in patients. Out of those 10 articles, 4 were *high* quality and all the remaining were *good* quality. There were no articles found that did not support the claim iron supplementation improving iron status. Most notably, in McClung et al. (2009) the experimental group was able to better maintain their iron status throughout the trial while the placebo group had a 100% increase in participants becoming iron-deficient by the end of the trial. Not only did the participants have a large change in iron status categorization, their sFer levels were at 66% of their baseline values, whereas the experimental group was able to maintain their levels at 87% of their baseline (McClung et al., 2009). It was supported by the remaining 9 articles that iron supplementation significantly increases sFer levels in participants when compared to a placebo (Burden et al., 2012; Burden et al., 2014; DellaValle & Haas, 2012; Garvican et al., 2014; Hinton & Sinclair, 2007; Houston et al., 2018; Kang & Matsuo, 2004; Klingshirn et al., 1992; Peeling et al., 2007).

Current Trends and Gaps in Literature:

In the current literature, there were multiple trends that were seen across the 17 articles used in this Critical Review of Literature. The first, and most common, trend was that iron supplementation helps maintain iron status throughout a competitive season. This trend is found in 8 of the articles reviewed. McClung et al. (2009) was a leader in this trend, as their RCT study found that the iron receiving group were more likely to maintain their iron status while the placebo group saw a 100% increase in participants that were iron-deficient by the end of the eight-week study. Hinton and Sinclair (2007) had also shown that in a six-week supplementation period, the iron receiving group had significant improvements in sFer levels while the control group did not. Auersperger et al. (2013), Burden et al. (2015), Houston et al. 2018), Klingshirn et al. (1992), and Mielgo-Ayuso et al. (2014) all had similar results that supported the findings of both McClung et al. (2009) and Hinton and Sinclair (2007).

A second trend in the research was that females that are more iron-deficient have more to gain with iron supplementation. This means, females with a lower iron status were more likely to see an increase in iron levels and performance with supplementation than patients who had higher iron levels. Rebeor et al. (2018) study found that patients with sFer levels less than 20 µg/L had a higher likelihood of improving performance with iron supplementation than patients with higher sFer levels. Patients with lower levels and who received supplementation saw improvements in aerobic/endurance performances when compared to a placebo or patients with higher sFer levels (Rebeor et al., 2018). This supported McClung et al.'s (2009) research as well, where participants that were iron-deficient anemic had a mean decrease in their 2-mile run time by 110s after the eight weeks of supplementation. In Pasricha et al. (2014) similar results were found, where iron supplementation had the most effect on VO_{2max} when iron was supplemented to iron-deficient women.

The most significant gap surrounding this topic is the lack of research on the long-term and adverse effects of iron supplementation on the female athlete. Only 2 articles reported adverse events that occurred throughout the supplementation of iron (Houston et al., 2018; Woods et al., 2014). This is an important gap to close. There needs to be a cost-benefit analysis of whether the iron supplementation will do more to help or harm to the athlete and their performance. It is also important to close the gap on the length of effectiveness of the supplementation. Burden et al. (2014) was the only article to report diminished returns after 80 days of supplementation. This should be researched since the competitive seasons typically last longer than 80 days. If supplementation does not provide benefits for the entire season, it may not be as necessary to administer.

Implications for Athletic Training:

The athletic trainer has a responsibility to their patients to care for them through mental, physical, and nutritional health. Due to this responsibility, it is important to understand the supplements and their effects on a patient's performance. Having a better understanding of how supplementing iron to iron-deficient female athletes can have an impact in their performance would be beneficial to many athletic trainers, especially in competitive sports settings. One implication from this Literature Review is the need for blood testing of female athletes throughout the competitive season. Female athletes, especially endurance athletes, are more likely to enter the competitive season with an iron-deficiency; these athletes may have a 42% risk of becoming iron-deficient throughout the season (Auersperger et al., 2013). This statistic may lead to better screening of female athlete's iron stores and possible prescriptions for supplementing iron. This may also lead to athletic trainers spending more time educating patients and athletes on the benefits or adverse effects of iron supplementation.

Recommendations for Future Research:

After the synthesis of the 17 articles, there was still inconclusive evidence towards the benefits of iron supplementation in female athletes. Many of the current research studies female populations that are already iron-deficient. More research should be done to determine the effects of iron supplementation on patients with normal iron status. This research may determine if there is any additional effect of iron supplementation when it is not nutritionally needed. Lastly, research should be done to determine a standard dosage of iron to supplement. None of the 17 articles utilized in the Critical Review of Literature used the same amount of iron supplemented to their patients. In the RCTs of this study, all were compared against a placebo. If the research conducted a RCT utilizing several dosage types of iron more evidence may be provided to whether iron can or cannot impact performance.

Conclusion:

The findings of this Critical Review of Literature cannot validate or invalidate the use of iron supplementation to improve competitive, non-anemic, female athletes' physical performance as a whole, but can support that iron supplementation can benefit aerobic performance. The conclusions can validate that iron supplementation improves the total iron stores in females, especially their sFer levels. A total of 10 articles were in support of iron supplementation for improving sFer levels. Several performance measures that supported iron supplementation to produce improvements; 4 articles supported iron improving VO_{2max}, 3 articles supported improvements to energy efficiency, 3 supported positively impacting blood lactate, 2 supported iron benefiting recovery, and 1 article supported iron benefiting muscular strength. While the results of this Critical Review of Literature do not fully support the iron supplements concretely improving performance, it provides an opportunity to discuss utilizing iron for patients with lower iron status. If applied and monitored correctly, iron may be an impactful addition to female's athlete's dietary regimen.

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Appendix A: Hierarchy of Evidence

Hierarchy of Evidence for Intervention Studies

Type of evidence	Level of evidence	Description
Systematic review or meta-analysis	I	A synthesis of evidence from all relevant randomized controlled trials.
Randomized controlled trial	II	An experiment in which subjects are randomized to a treatment group or control group.
Controlled trial without randomization	III	An experiment in which subjects are nonrandomly assigned to a treatment group or control group.
Case-control or cohort study	IV	Case-control study: a comparison of subjects with a condition (case) with those who don't have the condition (control) to determine characteristics that might predict the condition. Cohort study: an observation of a group(s) (cohort[s]) to determine the development of an outcome(s) such as a disease.
Systematic review of qualitative or descriptive studies	V	A synthesis of evidence from qualitative or descriptive studies to answer a clinical question.
Qualitative or descriptive study	VI	Qualitative study: gathers data on human behavior to understand *why* and *how* decisions are made. Descriptive study: provides background information on the *what*, *where*, and *when* of a topic of interest.
Expert opinion or consensus	VII	Authoritative opinion of expert committee.

Adapted with permission from Melnyk BM, Fineout-Overholt E, editors. Evidence-based practice in nursing and healthcare: a guide to best practice [forthcoming]. 2nd ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins.

Appendix B: Literature Review Matrix

<table>
<tr><td colspan="4">Source: Auersperger, I., Skof, B., Leskosek, B., Knap, B., Jerin, A., & Lainscak, M. (2013). Exercise-induced changes in iron status and hepcidin response in female runners. PLOSOne, 8(3), 1-8.</td></tr>
<tr><td>Design Methodology/ Purpose
Prospective observational study
Purpose: Investigate iron status markers throughout long-term exercise training in female runners
Method:
Participants completed 8 weeks of a physical training program with two 3-week phases of 3-4 training days a week. Blood samples were taken before training, after training, and after a 10-day recovery phase. Patients performed 2400m time trials for baseline testing.</td><td>Sample/ Setting
14 moderately physically active females

Level: III

Quality: Good</td><td>Design Instruments
Body weight, height, body fat percentage, lean mass.
Blood tests for RBC concentration and distribution, iron stores, and sFer levels</td><td>Results
Group with normal iron stores had a VO_{2max} increase of 4.8% where the iron deficient group only saw increase of +3%.
10/14 participants had depleted iron stores after the training phase and remained 9/14 after the recovery phase. (50% of participants were iron depleted at the end)</td></tr>
<tr><td colspan="4">Recommendation: There may be a correlation with iron stores and performance. Patients who were at a more normal iron store before the training showed a greater group improvement, however there is no way to be completely certain that these results are concrete. This study also shows how intense exercise causes iron stores in females to drop greatly over time. The normal iron storage group had 3/7 participants move from normal stores to deficient stores over 8 weeks. Overall, this study shows that exercise can be a cause of iron deficiency even in women with normal levels at baseline. There is also small evidence that having normal iron stores could lead to better improvement of performance.</td></tr>
</table>

Source: Burden, R.J., Pollock, N., Whyte, G.P., Richards, T., Moore, B., Busbridge, M., Srai, S., Otto, J., & Pedlar, C.R. (2015). Effect of intravenous iron on aerobic capacity and iron metabolism in elite athletes. *Medicine & Science in Sports & Exercise, 47*(7), 1399-1407.			
Design Methodology/ Purpose Double-blind, randomized control **Purpose:** Determine response of iron metabolism to IV iron supplementation and to test if the supplementation would enhance aerobic capacity. **Method:** Participants were randomized into an experimental group (EG) or a placebo group (PG) and were all similar at baseline. Patients completed 3 treadmill tests until exhaustion. Test 1 performed before experimental group received 500 mg supplement, test 2 was performed 7 d later and within 24 hours of the patients receiving their second treatment. Test 3 was taken 4 weeks after treatment.	**Sample/ Setting** 9 females/6 males from the London Marathon endurance performance group. Classified as iron-deficient nonanemic (IDNA) **Level:** II **Quality:** Good	**Design Instruments** Blood analysis for SFe, sFer, and sTf as well as blood volume were assessed. Submaximal VO_2, VO_{2max}, and blood lactate were measured throughout the treadmill testing and analyzed through a one-way ANOVA.	**Results** sFer increased within 24 hours of the injection, EG had hepicidin values were significantly higher at all time points. No significant difference between groups VO_{2max}, economy, speed, and time to exhaustion. The significant increase in sFer results in postexercise increase in hepcidin.
Recommendation: IV supplementation of 500mg of iron did not have an increase in aerobic capacity in comparison to a placebo. There was an increase in overall iron stores 24 hours after supplementation and can be maintained for 4 weeks after treatment. IV iron treatments can increase iron levels for 4 weeks but may not have an impact on aerobic performance.			

<table>
<tr><td colspan="4">Source: Crouter, S.E., DellaValle, D.M., & Haas, J.D. (2012). Relationship between physical activity, physical performance, and iron status in adult women. Applied Physiology Nutrition and Metabolism, 37(4), 697-705.</td></tr>
<tr>
<td>Design Methodology/ Purpose Cohort Study
Purpose: examine the relationship of physical activity, performance, and iron status in females
Method: Participants completed cycle ergometry testing and were screened for their blood iron levels. Participants also monitored their weekly physical activity reports through and ActiGraph.</td>
<td>Sample/ Setting
109 women from Cornell University and surrounding area (age 18-45)
Considered either IDNA or at healthy iron levels.
Level: IV

Quality: good</td>
<td>Design Instruments
Blood collections for Hgb, hematocrit, RBC count, sFer, and sTfR. Maximal cycle test to determine Ventilatory threshold (V_T), endurance (time to exhaustion). ActiGraph to determine normal activity levels.

IDNA were compared to the activity levels of females with similar daily physical activity reports but had normal iron levels.</td>
<td>Results
There were no significant differences between the iron groups except for V_T. Participants with normal iron levels reached higher maximal watts that IDNA groups. There was a significant difference between groups in comparison to physical activity, normal group spent 68.4 min less being sedentary than IDNA.</td>
</tr>
<tr><td colspan="4">Recommendation: IDNA patients are more likely to be sedentary than patients with normal iron levels. IDNA also have a significantly lower V_T threshold than those who have normal iron levels. Study did not cover how iron supplementation would impact performance but does show promising insight that iron deficiency could negatively impact physical performance as well as lifestyle behaviors.</td></tr>
</table>

Source: DellaValle, D.M. & Haas, J.D. (2012). Iron status is associated with endurance performance and training in female rowers. *Medicine & Science in Sports & Exercise, 44*(8), 1552-1559.			
Design Methodology/ Purpose Cross-sectional study **Purpose:** To examine the relationship between endurance performance and iron status of collegiate rowers **Method:** Iron levels were monitored before, during, and after training sessions. RPE of the workout, endurance capacity, and aerobic power were all measured and compared against IDNA rowers and normal iron rowers.	**Sample/ Setting** 149 collegiate female rowers **Level:** IV **Quality:** High	**Design Instruments** Hgb, hematocrit, RBC count, total body iron, and sFer. Eating habits menstrual status, and rowing regimen. VO_2, energy expenditure, lactate concentration.	**Results** Rowers with IDNA had lower VO_{2peak} compared to normal status athletes. Also had higher lactate concentrations, trained 11min less than normal rowers. Significant positive correlation between sFer and VO_{2peak} and 4-km performance. Iron status and endurance performance depended on training load.
Recommendation: IDNA athletes may be quicker to fatigue or have a lower VO_{2peak} potential in comparison to normal iron status athletes. The study does suggest that more highly trained rowers are able to overcome any deficits that may be caused by iron deficiency because of their better trained iron efficiency. The positive correlation of sFer and endurance performance may suggest that iron supplementation to increase sFer would help an athlete with their aerobic performance.			

Source: Hinton, P.S. & Sinclair, L.M. (2007). Iron supplementation maintains ventilatory threshold and improves energetic efficiency in iron-deficient nonanemic athletes. *European Journal of Clinical Nutrition, 61*, 30-39.			
Design Methodology/ Purpose Double-blind Randomized control **Purpose:** To examine the effects of supplementing iron on endurance performance of IDNA, physically trained, adults **Method:** A 6-week supplementation program where participants ingested 30mg iron or a placebo daily. Participants completed VO_{2peak} tests, and submaximal exercise performance tests on a cycle ergometer for measurements. Blood samples were taken to test for the blood iron levels.	**Sample/ Setting** 20 IDNA physically active adults (17F, 3M) **Level:** II **Quality:** High	**Design Instruments** Blood was collected at baseline and after the 6-week trial. Cycle ergometer tests were used to measure, VT, VO_{2peak}, and RER. Measurement of the blood samples included Hb, sFer, and sTfR. Patients had daily nutritional intake monitored to ensure that participants were not eating more the the DRI.	**Results** Experimental group saw a significant increase in sFer levels, where placebo group did not. The placebo group showed a significant decrease in VT after the treatment, E-group showed no change. Significant negative correlation of change in RER and change in logsFer (increase in sFer correlated with RER reduction). Iron supplementation had no change on optimal oxygen consumption. There was an improvement of gross energetic efficiency to the participants ability to do work.
Recommendation: Iron supplementation is able to increase sFer level in participants and is capable of helping IDNA patients return to 'normal' iron levels. A 30mg dosage is able to increase endurance capacity and energetic efficiency as well as preserve VT during maximal exercise over a 6-week period. A larger dose or longer supplemental period may need to be studied to determine if there is an even greater impact of supplementation.			

<table>
<tr><td colspan="4">Source: Houston, B.L., Hurrie, D., Graham, J., Perija, B., Rimmer, E., Rabbani, R., Bernstein, C.N., Turgeon, A.F., Fergusson, D.A., Houston, D.S., Abou-Setta, A.M., & Zarychanski, R. (2018). Efficacy of iron supplementation on fatigue and physical capacity in non-anemic iron-deficient adults: A systematic review of randomized controlled trials. BMJ Open, 8(4), 1-9.</td></tr>
<tr><td>Design Methodology/ Purpose Systematic review of randomized-control trials
Purpose: To identify and appraise data from randomized-control trials on research about iron supplementation in IDNA populations
Method: Collection and analysis of studies that conducted randomized-control trials where iron was supplemented. Use of systematic and meta-analysis reviews.</td><td>Sample/ Setting
18 trials and 2 companion papers. 1170 adult subjects

Level: I

Quality: Good</td><td>Design Instruments
Studies included used iron interventions of oral, intramuscular, or intravenously administered iron. The primary outcomes of the studies needed to be fatigue, physical capacity, and contained sub-group analysis. Secondary outcomes included blood iron concentrations and any adverse effects that may have been caused by the supplementation.</td><td>Results
Supplementing iron was associated with reduced subjective measures of fatigue. There was no significant impact on objective measures of physical capacity across the researched articles. Only 19% of studies showed significant increases in physical capacity. 14/20 Trials showed that iron supplementation increased sFer after the trial. Most common adverse events were GI intolerance, nausea, and constipation.</td></tr>
<tr><td colspan="4">Recommendation: There is some small evidence that iron supplementation increases performance capacity, but the majority of evidence says that it does not. However, there was not enough adverse events reported in the trials to consider that the supplementation causes more harm than it does good. Iron supplementation is associated with perceived fatigue levels, which may help athletes perform longer, but does not have a direct impact on their performance alone.</td></tr>
</table>

Source: Kang, H.S. & Matsuo, T. (2004). Effects of 4 weeks iron supplementation on hematological and immunological status in elite female soccer players. *Asia Pacific Journal of Clinical Nutrition, 13*(4), 353-358.			
Design Methodology/ Purpose Randomized-Control Trial (Single Blind) **Purpose:** To determine if 4 weeks of iron supplementation would improve hematological parameters in nonanemic elite female athletes **Method:** Subjects were placed in either an experimental (E) group or a control (C) group. The E group received 40mg/day iron supplementation and the C group received a placebo Patients had their daily food intake tracked as well as body composition. Patients underwent blood and plasma tests to determine hematological composition.	**Sample/ Setting** 25 elite female soccer players (a= 20-28) **Level:** II **Quality:** Good	**Design Instruments** Blood tests were taken before start of trial and after the 4 weeks. Measurements were taken for hematological and iron-related measurements, WBC counts, leucocyte differential, and plasma immunoglobin. Measurements were compared across groups and then compared. Food logs were also taken into consideration to determine how much of the RDA the subjects were getting of each nutrient source.	**Results** Groups were similar at baseline. All subjects ingested 100% of their energy RDA, but were insufficient in calcium, iron, and vitamin A. Blood hemoglobin did not change in E group, but C group saw a significant decrease over the 4 weeks. Plasma ferritin increased significantly in E group but there was no change in C group.
Recommendation: 40mg/day of iron supplementation may help female athletes maintain a “healthy” iron level that may be lost during exercise. Iron supplementation may also cause a rise of plasma ferritin, which causes an increase in total body iron stores. There was no evidence that iron supplementation improves performance, but it does help prevent the loss of iron levels caused by exercise.			

Source: McClung, J.P., Karl, J.P., Cable, S.J., Williams, K.W., Nindl, B.C., Young, A.J., & Lieberman, H.R. (2009). Randomized, double-blind, placebo-controlled trial of iron supplementation in female soldiers during military training: Effects on iron status, physical performance, and mood. *American Journal of Clinical Nutrition, 90*(1), 124-131.			
Design Methodology/ Purpose RCT, double-blind **Purpose:** To determine if iron supplementation can prevent decrement of iron status after basic training, and to also determine the effects on physical performance and mood. **Method:** Blinding of both subjects and examiners. E group received 100mg capsules of ferrous sulfate to take daily, C group received capsules containing cellulose. Baseline tests were taken prior to initial dosage and then after the 8-week basic combat training (BCT) military training. Training included a 2-mile timed run, road marching, sprinting, and muscle strengthening activities.	**Sample/ Setting** 85/107 volunteers completed the study. Female soldiers **Level:** II **Quality:** High	**Design Instruments** Patients were watched to ensure that they complied to the supplementation. Blood samples were collected before and after the training, looking for assessment of Hg, RBC count, and iron status indicators (sFer, serum iron, and iron-binding capacity). A two-mile run was assessed for physical performance. Subjects also completed the Profile of Mood States questionnaire to determine mood state.	**Results** sFer had declined a significant amount in the C group but not in the E group. C group sFer values were 66% lower than starting values, and the E group was 87% of the beginning values. The C group saw a 100% increase in subjects with ID, but the E group only had a 36% increase. There was no difference in physical performance between groups for subjects that were not ID or IDA at the beginning of the trial. However, subjects that were IDA at the beginning of the trial that received the supplement had an increase mean run time of 110s faster. E group also showed a significant improvement in mood state, E group showed higher rates of vigor that improved in training unlike the C group.

Recommendation: Iron supplementation was not shown to improve performance in already healthy participants of this study. However, there was nearly a two-minute improvement from patients that were iron-deficient anemic. More studies may need to be done to determine effects on healthy athletes. Iron supplementation also helped the subjects maintain their iron status over an 8-week period in comparison to a control group that saw an increase in subjects who became ID. Iron supplementation may also be associated with mood improvements, which may also have an impact on performance. 100mg/day was highest dose seen yet in this review, may have the greatest results (no adverse effects reported).

Source: Mielgo-Ayuso, J., Zourdos, M.C., Calleja, Gonzálex, J., Urdampilleta, A., & Ostojic, S. (2014). Iron supplementation prevents a decline in iron stores and enhances strength performance in elite female volleyball players during the competitice season. *Applied Physiology, Nutrition, and Metabolism, 40*(6), 615-622.			
Design Methodology/ Purpose Randomized-Control Trial (No placebo) **Purpose:** To find the effect of supplementation of iron on hematological profiles and strength performance of volleyball players during the competitive season. **Method:** Patients were randomly selected to be in the experimental group or the control group. The E group received 325mg of time-released ferrus sulphate (105mg elemental iron) tablets daily for 11 weeks, C group did not receive a placebo. Patients had blood tested for hematological parameters at baseline and after 11 weeks. Patients were also tested on submaximal strength tests for bench press, military press, half-squat, power clean, clean and jerk, and pullover. A dietary assessment also occurred to determine if there were any between group differences in diets.	**Sample/ Setting** 22 non-anemic, professional, female volleyball players (a= 27 ±5.6) **Level:** II **Quality:** Good	**Design Instruments** Blood tests for hematological parameters included sFer, FER, TSI, and Hb levels. A submaximal strength test of 7-10 RM for examination of strength. Food Frequency Questionnaire and a 7-day dietary recall at the first and last weeks of the trial.	**Results** The control group saw a significant decrease in iron level categorization or patients, but the E group did not see a similar decrease. While the C group saw significant decreases in their blood iron parameters, the E group did not see much change. When compared to the C group, the E group saw significantly greater increases of strength in the clean and jerk, power clean, and total mean strength. However, both groups did have a time effect increase in bench, military press, and half-squat.
Recommendation: This research supports other articles in their findings that iron supplementation helps prevent the decrease of iron stores that occur over time with sport/training. This study also suggests that iron supplementation has an impact on muscular strength as well. 325mg of ferrous sulfate is beneficial in helping prevent female athletes from becoming ID over the course of a season and may also play a role in muscular strength.			

Source: Rebeor, A., Goojha, C., Manning, J., & White, J. (2018). Does iron supplementation improve performance in iron-deficient nonanemic athletes? *Sports Health, 10*(5), 400-405.			
Design Methodology/ Purpose Systematic Review **Purpose:** To complete a review of literature of iron supplementation of IDNA athletes **Method:** Conduct a literature search with terms: athletic performance, resistance training, physical endurance, iron, iron dietary, ferritin, supplement, non-anemic, low ferritin, and iron storage.	**Sample/ Setting** 12 studies with 283 subjects, ages 13-41, 257 females and 26 males. **Level:** I **Quality:** Fair	**Design Instruments** PubMed, CINAHL, ERIC, and Cochrane databases were used to search for articles. Articles were excluded on the basis of if performance was measured objectively, studies included participants with and without ID, unconfirmed athletes, and studies that did not use a placebo.	**Results** There was no conclusive evidence from the systematic review. In 6 studies, it was found that supplementation improved performance, but the other 6 did not improve performance. Reasonable evidence was given that says that iron supplementation may increase performance of athletes who have IDNA, or sFer levels of 20µg/L or lower.
Recommendation: There is no consistent evidence on whether or not iron supplementation improves performance across studies. There were also inconsistencies on dosage of iron used across studies. Evidence may be available showing that iron supplementation can increase performance of female athletes with IDNA.			

Source: Klingshirn, L.A., Pate, R.R., Bourque, S.P., Davis, M., & Sargent, R.G. (1992). Effect of iron supplementation on endurance capacity in iron-depleted female runners. *Medicine & Science in Sports & Exercise, 24*(7), 819-824			
Design Methodology/ Purpose RCT **Purpose:** To examine the effects of iron supplementation on endurance capacity in iron-depleted nonanemic female distance runners. **Method:** Iron supplementation for 8 weeks while a control group takes a placebo. Runners tested on their VO_{2max} as well as their blood lactate and time to exhaustion on treadmill tests. Experimental group took a daily dosage of 50mg elemental iron daily.	**Sample/ Setting** 18 IDNA endurance runners (age 22-39) **Level:** II **Quality:** Good	**Design Instruments** Whole blood collects for Hb and sFer concentrations. VO_{2max} treadmill testing and Endurance capacity treadmill testing. RER and RPE were also collected after the submaximal testing.	**Results** There was no significant difference between groups in VO_{2max} testing or endurance capacity. The experimental group saw an increase in mean sFer after the supplementation.
Recommendation: Iron supplementation of 50mg of iron did not provide any improvements to performance when compared to a control group. Experimental group did see an improvement of mean iron concentration however.			

Source: Woods, A., Garvican-Lewis, L.A., Saunders, P.U., Lovell, G., Hughes, D., Fazakerley, R., Anderson, B., Gore, C.J., & Thompson, K.G. (2014). Four weeks of IV iron supplementation reduces perceived fatigue and mood disturbance in distance runners. *PLOS ONE, 9*(9), 1-11.			
Design Methodology/ Purpose RCT **Purpose:** To determine the impact of IV iron supplementation on runner's fatigue, performance, and mood. **Method:** Iron and Placebo groups received treatment every two weeks for 6 weeks. Received 2ml (100mg) of ferric carboxymaltose solution or 2ml of saline solution every two weeks. Runners completed 3,000m time trials and 10x400m workouts at baseline and after each additional supplementation. Blood samples were taken at baseline and 2 weeks after the study. Participants also completed fatigue and mood questionnaires every 2 weeks and were also asked to complete a training log throughout the study period.	**Sample/ Setting** 14 highly trained distance runners: 8 Females, 6 Males **Level:** II **Quality:** High	**Design Instruments** Hb mass, Hct, iron status, and percent transferrin saturation were all measured through blood samples. Brief Fatigue Inventory, Brunel Mood Scales, and Total Mood Disturbance were all measured every 2 weeks. Time of 3000m trial, and 10x400m training were all measured along with blood lactate and RPE were used as performance measures.	**Results** The Iron group showed significant improvements on Total fatigue scores when compared to the Placebo, and also had a significant improvement on Total mood Disturbance. The Iron group saw no change in the 3000m run trials, but the Placebo were slower than baseline at week 4. No significant difference between groups RPE. Iron group participants were also able to decrease their 10x400m training times and had improved perceptions of fatigue and readiness to train. There was a decrease in blood lactate in the Iron group throughout the run trials and the Placebo group saw an increase.
Recommendation: There may be an acute improvement in performance due to IV iron supplementation. Iron supplementation does seem to have an impact on perceived fatigue and mood, as well as blood lactate levels during exercise. It is noted that one patient withdrew from the trial due to adverse effects of the IV supplementation (GI distress). Small, and not significant, improvements to performance, but significant improvements in fatigue, mood, and perceived readiness were associated with IV iron supplementation.			

Source: Garvican, L.A., Saunders, P.U., Cardoso, T., MacDougall, I.C., Lobigs, L.M., Fazakerley, R., Fallon, K.E., Anderson, B., Anson, J.M., Thompson, k.G., & Gore, C.J. (2014). Intravenous iron supplementation in distance runners with low or suboptimal ferritin. *Medicine & Science in Sports & Exercise, 46*(2), 376-385.

Design Methodology/ Purpose	**Sample/ Setting**	**Design Instruments**	**Results**
Randomized Trial **Purpose:** To determine the impacts of IV and oral supplementation on iron status, Hb mass, and running performance in distance runners. **Method:** 6-week supplementation period. Participants were placed into an Oral supplement group or an IV group. Oral groups took 105mg of elemental iron daily, while IV group received supplements every two weeks. Runners then completed a VO_{2max} treadmill test before and after the 6 weeks of supplementation. All training and lifestyle practices were recorded for the study as well. Hb mass was measured at baseline and at weeks 1, 2, 4, 6, and 2 weeks after the completion of the supplementation.	28 distance runners 13 Females, 14 Males. **Level:** II **Quality:** Good	Hb mass was measured through blood samples, sTfR and sFer were also measured. Blood lactate concentration was taken in the recovery period of the VO_{2max} testing.	Both supplementation types were an increase in sFer levels, IV sFer levels were higher throughout the entire study in comparison of the Oral groups. Oral supplementation had a small impact on Hb_{mass} yet there were significant increases in Hb_{mass} for the IV groups. VO_{2max} and running time were faster in the IV group in comparison to the Oral groups. IV group did see an improvement in VO_{2max}.

Recommendation: When compared to oral supplements, IV iron supplementation may have a greater impact on performance. IV supplementation also only needs to be done every two weeks, which may be a benefit as well. There were no significant differences between groups for blood iron levels. IV supplementation can be maintained for up to two weeks after supplementation, unlike oral supplementation.

<table>
<tr><td colspan="4">Source: Burden, R.J., Morton, K., Richards, T., Whyte, G.P., & Pedlar, C.R. (2014). Is iron treatment beneficial in, iron-deficient but non-anemic (IDNA) endurance athletes? A meta-analysis. British Journal of Sports Medicine, 49(21), 1389-1397.</td></tr>
<tr><td>Design Methodology/ Purpose
Meta-Analysis
Purpose: To determine if iron treatments help iron status and aerobic capacity of IDNA endurance athletes
Method: Literature search using the guidelines of the International Prospective Register for Systematic Reviews. Oral and parenteral administration methods were both included in the study.</td><td>Sample/ Setting
17 studies
443 participants (363 Female, 80 Male)
Level:
I
Quality:
High</td><td>Design Instruments
Inclusion Criteria: RCT of non-randomized control trials, participants were endurance athletes and were considered IDNA, participants were either in an iron group or a control group, iron was the sole intervention used, and VO_{2max} was aerobic capacity measure.</td><td>Results
There was a large effect size on iron treatment and an increase in sFer by both administration types. Oral iron treatment was effective in increasing sFer for up to 8 weeks. There was a moderate effect size on iron and Hb status, larger effect size in women then in men. Iron had a moderate effect on VO_{2max}, but there was a significant effect from oral treatments, and a significant effect at all time points. Treatments that lasted over 80 days had a diminished effect size over time.</td></tr>
<tr><td colspan="4">Recommendation: There is a moderate to significant effect size on the use of oral iron supplementation on aerobic capacity in IDNA endurance athletes. The study does suggest that the impact depends on the athlete’s initial iron stores, and athletes that have less stores are more likely to benefit from the treatment. Parenteral and oral supplementation are both impactful on blood iron store levels, but oral supplementation is more likely to improve aerobic capacity. This article is also the first to mention diminished effects after a certain amount of time, 80 days the average time before supplementation effects began to diminish.</td></tr>
</table>

Source: Peeling, P., Blee, T., Goodman, C., Dawson, B., Claydon, G., Beilby, J., & Prins, A. (2007). Effect of iron injections on aerobic-exercise performance of iron-depleted female athletes. *International Journal of Sport Nutrition and Exercise Metabolism, 17*(3), 221-231.			
Design Methodology/ Purpose Double-Blind RCT **Purpose:** To determine the effect of IM iron supplementation on VO_{2max}, time to exhaustion, and submaximal exercise economy on IDNA endurance athletes. **Method:** Patients were randomly placed into either the Iron group (IG) or a Placebo group (PG). IG received 5 x 2ml IM injection over a 10-day period of Ferrum H (100mg elemental iron). PG received 2 ml of saline solution. After the injections, both groups underwent 3 exercise tests for steady-state submaximal economy test, an incremental VO_{2max} until exhaustion, and a time to exhaustion test. The subjects performed this testing before the initial injection and 20 days after. The third and final blood sample was taken 28 days after the first injection.	**Sample/ Setting** 16 IDNA endurance athletes (all adult females) **Level:** II **Quality:** Good	**Design Instruments** Collection of blood iron levels, sFer, Hb, etc. Blood lactate was measured one minute after exercise testing. Oxygen consumption, heart rate, and a 7-day physical activity log was also taken.	**Results** After the 5 injections, there was a significant treatment by time effect on sFer in the IG. The IG had a significant increase of sFer than the PG on days 20 and 28. There was no significant differences or improvements on exercise economy between the IG and the PG. IG group did not see a decline in economy that the PG saw. No significant improvements of VO_{2max}. The IG group had an increased blood lactate level after the exercises compared to the PG group.
Recommendation: IM iron supplementation was not beneficial in increasing VO_{2max}, but it did help prevent a decline of the test scores that was seen in the PG. IM injections is also beneficial in increasing blood iron stores. The increase in blood lactate of the IG may mean that iron supplementation is beneficial in helping athletes work at greater intensities or for longer durations that the PG could not.			

Source: Dellavalle, D.M., & Haas, J.D. (2014). Iron supplementation improves energetic efficiency in iron-depleted female rowers. *Medicine & Science in Sports & Exercise, 46*(6), 1204-1215			
Design Methodology/ Purpose Randomized Double-Blind, placebo controlled. **Purpose:** To examine the effects of iron supplementation on changes in body iron status and endurance performance in nonanemic female rowers. **Method:** Participants were randomized into an iron supplementation or placebo group. Pre-test and and baseline measurements were taken. The supplementation occurred over a 6-week period. Testing was done before and after the 6-week period.	**Sample/ Setting** Female, Collegiate Rowers **Level:** II **Quality:** High	**Design Instruments** Anthropometric and body measurements were taken before and after. Iron status variables were measured though blood samples. Physical performance measures were energy expenditure, blood lactate concentrations, and a 4-km Time trial where O_2 and CO_2 was measured, endurance capacity was also measured.	**Results** There was a significant time effect on Hgb levels in the treatment group than the placebo. There was also a moderate relationship between the supplemental iron consumed and change in total body iron. Total energy efficiency was significantly lower in the experimental group and there was a significant interaction within the treatment group and dose consumption for efficiency. Significant negative correlation between the supplemental iron and maximal lactate at the 1000m mark. Supplemental group also showed a faster 5 min recovery than the placebo group.
Recommendation: Iron supplementation can produce benefits in prolonging blood lactate levels in the initial segments of exercise as well as provide a quicker recovery post-exercise. Iron supplementation may also play a role in total energy efficiency in exercising. This article also provided evidence that athletes with lower blood iron levels have greater chance of improvement with iron supplementation.			

Source: Pasricha, S.R., Low, M., Thompson, J., Farrell, A., & De-Refil, L.M. (2014). Iron supplementation benefits physical performance in women of reproductive age: A systematic review and meta-analysis. *The Journal of Nutrition, 144*(6), 906-914.			
Design Methodology/ Purpose Systematic Review and Meta-Analysis **Purpose:** To determine the effects of daily iron supplementation on physical activity in women of reproductive age (WRA). **Method:** Search for RCT lasting for longer than 5 weeks where iron went against a control. Studies contained the age range of 12-50. Outcomes of the study needed to have results for VO_{2max}, HR_{max}, VT, blood lactate, and submaximal exercise performance.	**Sample/ Setting** 22 Studies 911 participants **Level:** I **Quality:** Good	**Design Instruments** Studies were included if they were RCT that gave iron as the sole intervention with a placebo control. The articles found were then analyzed by the authors of the study. Risk of bias was also assessed. The studies were then synthesized using the mean difference and standardized mean difference to determine the CI of the articles results. 22 Studies were accepted based on the inclusion criteria and through the assessment of bias.	**Results** There was a significant beneficial effect of iron on VO_{2max}, however, this effect may only be seen in trained or anemic women. There was no difference for other exercise variables (RER and TTE). Iron also improved the efficiency of submaximal exercise.
Recommendation: It is seen that iron supplementation may be most beneficial for trained individuals in both maximal exercise and submaximal exercises. There was also evidence that iron supplementation is more beneficial for patients who are iron-deficient or anemic. Iron supplement is not shown to be greatly beneficial for untrained patients.			