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TRANSFUSION

ORIGINAL RESEARCH

Blood Donors and Blood Collection

Impact of iron supplementation among anemic voluntary first-time blood donors: Results from the BLOODSAFE pilot trial in Ghana

Yvonne Dei-Adomakoh[1] | **Edeghonghon Olayemi**[1] | **Susan Telke**[2] | **Lucy Asamoah-Akuoko**[3] | **Bernard Appiah**[4] | **Catherine Segbefia**[5] | **Caitlin Ward**[2] | **Tara Tancred**[6] | **Alfred Edwin Yawson**[7] | **Seth Adu-Afarwuah**[8] | **Amma Benneh Akwasi-Kuma**[1] | **Solomon Fiifi Ofori-Acquah**[9] | **Philip Baba Adongo**[10] | **Michael Ebo Acquah**[1] | **Reena Ametorwo**[1] | **Imelda Bates**[11] | **Francis Agyei**[12] | **Meghan Delaney**[13] | **Cavan Reilly**[2] | **for the BLOODSAFE investigators**

[1]Department of Haematology, University of Ghana Medical School, Accra, Ghana

[2]Coordinating Centers for Biometric Research, Division of Biostatistics, University of Minnesota Research, City-Twin cities, minnesota, USA

[3]Planning Monitoring & Evaluation Department, National Blood Service, Accra, Ghana

[4]Department of Public Health, Syracuse University, Syracuse, New York, USA

[5]Department of Child Health, University of Ghana Medical School, Accra, Ghana

[6]Department of International Public Health, Liverpool School of Tropical Medicine, Liverpool, UK

[7]Department of Community Health, University of Ghana Medical School, Accra, Ghana

[8]Department of Nutrition and Food Science, University of Ghana, Accra, Ghana

[9]School of Biomedical & Allied Health Sciences, College of Health Sciences, University of Ghana, Accra, Ghana

[10]Department of Social & Behavioural Sciences, School of Public Health, University of Ghana, Accra, Ghana

[11]The Centre for Capacity Research, Liverpool School of Tropical Medicine, Liverpool, UK

[12]Department of Family and Community Health, University of Health and Allied Sciences, Hohoe, Ghana

[13]Division of Pathology & Laboratory Medicine, Children's National Hospital, Washington, DC, USA

Correspondence
Yvonne Dei-Adomakoh, Department of Haematology, University of Ghana Medical School, Accra, Ghana.
Email: yadei-adomakoh@ug.edu.gh

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Abstract

Introduction: In sub-Saharan Africa (SSA), an adequate supply of safe blood for transfusion is a major developmental challenge. In Ghana, deferral from blood donation for anemia accounts for nearly half of the ineligible blood donors. We conducted a longitudinal two-arm parallel-group non-inferiority trial to test if iron supplementation among blood donors with iron deficiency (ID) or anemia could increase their hemoglobin levels to near those without ID or anemia.

Materials and Methods: A structured questionnaire was used to collect participants' sociodemographic and medical information after written informed consent was obtained. Blood samples were analyzed for full blood count (FBC), serum ferritin, malaria rapid test, and a peripheral blood smear. The

primary outcome was hemoglobin level after 4 months comparing anemic donors who received iron supplementation to the standard of care participants, nonanemic donors who did not receive iron supplementation. All donors received nutritional counseling.

Results: Adherence to low-dose iron supplementation three times a week was poor. Hemoglobin levels in the iron supplementation arm were not close enough to those in the control group after 4 months of iron supplementation to declare non-inferiority. However, non-inferiority was met when the 4 month hemoglobin comparison was restricted to female donors.

Conclusion: After 4 months of iron supplementation, hemoglobin levels in the iron supplementation group did not sufficiently match those in the control group to declare non-inferiority. Data from this pilot trial informed and shaped the design of a larger randomized control type 1 pragmatic effectiveness implementation hybrid trial which is currently ongoing.

KEYWORDS

first-time blood donors, Ghana, iron supplementation, nutritional counseling, voluntary

1 | INTRODUCTION

Blood services in sub-Saharan Africa (SSA) struggle to meet the worldwide blood collection target of 10–20 units of whole blood for every 1000 inhabitants.[1,2] However, blood donation poses a risk for the development of iron deficiency (ID) and iron deficiency anemia (IDA) among successful donors because of the significant loss of iron (200–250 mg) following a donation of 450 mL of whole blood.[1–3] Anytime a person donates blood, there is mobilization of iron from body stores[4] with a decrease in iron stores and increased iron absorption from the duodenum and jejunum.[5] With ongoing iron loss, the donor eventually reaches a state of equilibrium at a reduced level of iron stores or even a negative iron balance. Once stores are depleted, ID and, ultimately, IDA occur if there is no compensation for the lost iron.[6,7] The probability of donating blood devoid of the development of IDA depends on factors like dietary iron intake, the prevalence of ID in that particular populace, iron loss via menstruation in women of reproductive age, frequency of blood donation, use of supplemental iron and how much iron is absorbed.[8,9]

The BLIS (Bloodsafe Ghana—Iron and Nutritional Counseling Strategy) pilot study tested the hypothesis that low-dose iron supplementation will increase hemoglobin (Hb) levels sufficiently among anemic individuals to make them eligible to donate blood. Data from this pilot trial were further used to inform and shape the design of a larger randomized control type 1 pragmatic effectiveness implementation hybrid trial.

2 | MATERIALS AND METHODS

This was a two-arm parallel-group non-inferiority trial, designed to test if iron supplementation among those with ID or anemia could increase Hb levels to near those seen among Ghanaian blood donors who do not have ID or anemia at 4 months after donating. Participant recruitment took place at donation events in the greater Accra area. The trial was restricted to first-time, voluntary blood donors aged 18–60 years who passed all donor screening criteria except Hb screening. Potential donors who had recently taken iron supplements, had malaria or helminthic infections at screening, or who donated and tested positive for syphilis, HIV 1 and 2, hepatitis B or C were excluded. After consenting, a full blood count (FBC) was conducted, and serum ferritin (SF) was measured. If a participant had Hb below 10 g/dL at screening the participant was withdrawn and referred for medical care, otherwise, the participant was assigned to the iron supplementation group if the participant had ID (SF < 15 μg/L) or anemic (Hb < 11.5 g/dL for women and <13 g/dL for men) using values for women which were more stringent than World Health Organization (WHO) cutoff values.[10–12] Those who consented and did not have ID or anemia at the time of screening were followed as part of the control group. Participants in the iron supplementation arm (mostly females) were given low-dose iron (65 mg elemental iron) three times weekly for 4 months while the control arm only received standard nutritional counseling.

The primary endpoint was the Hb level measured after 4 months of supplementation (Clinical trial registration information: NCT04949165; ClinicalTrials.gov).

The non-inferiority margin was selected so that those with ID or anemia at screening would be likely to have Hb levels high enough to donate after 4 months of treatment. In Ghana, one can donate if Hb levels exceed 12 g/dL for women and 13 g/dL for men. For the margin calculation, preliminary data on Hb levels in West Africa were used to estimate the standard deviation (SD) of Hb levels in the trial population: this estimate was 1.89 g/dL. Assuming Hb levels are normally distributed with this SD, the mean Hb level among men with a level that leads to deferral is 11.5 g/dL while the mean among men who would not be deferred is 14.5 g/dL. If the Hb level does not change in the group who is qualified to donate, then a margin of 1 g/dL implies a mean Hb of 13.5 g/dL among those who were deferred so that the majority of these individuals would qualify to donate. A similar calculation for women arrives at the same conclusion.

Participants were followed with biweekly phone calls and bimonthly in-person visits. At screening and follow-up visits, a structured questionnaire was used to collect participants' sociodemographic and medical information, and blood samples were taken for an FBC, SF, malaria rapid test, and a peripheral blood smear. Control participants who became anemic or developed ID over the 6 months of follow-up were prescribed low-dose iron (ferrous sulphate 65 mg elemental iron) by the study hematologist.

2.1 | Statistical methods

Continuous data were summarized with means and SDs. Confidence intervals (CIs) were used to summarize evidence for differences and *p*-values less than .05 were deemed statistically significant. Tests of associations between dichotomous variables used Fisher's exact test and the measure of association used odds ratios (OR) which were estimated using conditional maximum likelihood. Tests of the difference in mean hemoglobin from baseline to Month 4 within each treatment arm and by subgroup used a complete-case paired *t*-test. One-sided 97.5% confidence intervals based on the *t*-distribution were used to test for non-inferiority overall and by subgroups of gender, age group (<21 years, 21+ years) and comparing participants assigned iron at screening and the subset of control participants who did not receive iron over follow-up. All statistical analysis was conducted using R version 3.6.0.

2.2 | Ethics statement

Approval was obtained from the College of Health Sciences, Ethical and Protocol Review Committee, University of Ghana (protocol ID: CHS-Et/M.5-P4.14/2021) and oversight was provided by the BLOODSAFE data coordinating center at the University of Minnesota and also by a Data and Safety Management Board (DSMB).

3 | RESULTS

3.1 | Demographics and baseline characteristics

Two hundred and twenty-three first-time voluntary blood donors consented and passed pre-screening donation requirements (105 in the iron supplementation arm vs. 118 in the control arm) between September 2021 and February 2023. As this was not a randomized trial, there were important differences between the two groups at baseline. As seen in Table 1, ages were similar between the iron supplementation and control groups (mean 19.7 and SD 2.5 vs. mean 20.1 and SD 3.1 years respectively). In both groups, there were more females than males; however, there were significantly more women in the iron supplementation group (iron: 75.2%; control: 51.7%, OR of 2.33, $p = .004$, 95% CI: 1.29, 4.25) (Table 1). Most participants in both arms donated; however, the percentage was significantly higher in the control arm (iron: 61.0%; control: 97.5%, OR of 24.2, $p < .001$, 95% CI: 6.43, 166.4).

In the iron supplementation group at screening, 6.7% (7/105) had ID but were not anemic, 14.3% (15/105) had IDA, and 79% (83/105) were anemic but not ID. Among the 43 participants who were deferred, 39 (90.7%) were anemic while among the 180 that were not deferred, 59 (32.8%) were anemic. Of the 22 participants who were ID, 15 (68.2%) were deferred. Of the 98 participants who were anemic, 39 (39.8%) were deferred (Table 2).

3.2 | Follow-up

The primary analysis of Hb levels at 4 months failed to reject the null hypothesis of inferiority in the iron supplementation group. The difference was −0.93 g/dL and the lower limit of the one-sided 97.5 confidence interval was −1.41 which included the non-inferiority margin of −1.0 (Table 3). Differences at other time points were also consistent with lower Hb levels in the iron supplementation group (Table 3, Figure 1).

TABLE 1 Characteristics among enrolled donors.

		Overall	Treatment arm	
			Control	Iron supplementation
		N (%)	*N* (%)	*N* (%)
Donors enrolled[a,b]		223	118 (52.9)	105 (47.1)
Age (years); mean (SD)		19.93 (2.83)	20.14 (3.09)	19.70 (2.51)
Sex	Female	140 (62.8)	61 (43.6)	79 (56.4)
	Male	83 (37.2)	57 (68.7)	26 (31.3)
Current student	No	5 (2.2)	2 (40.0)	3 (60.0)
	Yes	218 (97.8)	116 (53.2)	102 (46.8)
NBSG deferral decision[c]	Deferred	43 (19.3)	3 (7.0)	40 (93.0)
	Not deferred	180 (80.7)	115 (63.9)	65 (36.1)
NBSG deferral assessments categories				
Passed by $CuSO_4$ (8 with confirmatory HemoCue)		153 (68.6)	96 (62.7)	57 (37.3)
Passed by HemoCue ($CuSO_4$ not performed)		27 (12.1)	19 (70.4)	8 (29.6)
False pass by $CuSO_4$ (failed by follow-up HemoCue)		1 (0.4)	0 (0.0)	1 (100.0)
Failed by $CuSO_4$ (5 with confirmatory HemoCue)		32 (14.3)	2 (6.2)	30 (93.8)
Failed by HemoCue ($CuSO_4$ not performed)		10 (4.5)	1 (10.0)	9 (90.0)
Hemoglobin from FBC (g/dL)[d]; mean (SD)		12.38 (1.54)	13.39 (1.26)	11.25 (0.91)
Ferritin (log (ferritin +1))[d]; mean (SD)		3.89 (0.84)	4.21 (0.67)	3.54 (0.87)
Successfully donated at screening[e]	No	1 (0.6)	0 (0.0)	1 (100.0)
	Yes	179 (99.4)	115 (64.2)	64 (35.8)
History of blood loss in the last 3 months[f]	No	156 (70.0)	78 (50.0)	78 (50.0)
	Yes	67 (30.0)	40 (59.7)	27 (40.3)
Sibling(s) with known repeated anemia	No	221 (99.1)	117 (52.9)	104 (47.1)
	Yes	2 (0.9)	1 (50.0)	1 (50.0)
Heavy, frequent, or long duration periods among menstruating women[g]	No	77 (55.4)	37 (48.1)	40 (51.9)
	Yes	62 (44.6)	25 (40.3)	37 (59.7)
Body mass index (kg/m^2); mean (SD)		23.57 (6.53)	23.07 (3.31)	24.12 (8.83)
Systolic blood pressure (mm Hg); mean (SD)		117.17 (10.93)	117.89 (11.08)	116.35 (10.76)
Diastolic blood pressure (mm Hg); mean (SD)		76.57 (8.58)	76.92 (9.13)	76.17 (7.94)
Number of meals yesterday	0 (fasting)	1 (0.4)	0 (0.0)	1 (100.0)
	1 meal	16 (7.2)	6 (37.5)	10 (62.5)
	2 meals	87 (39.0)	47 (54.0)	40 (46.0)
	3 or more meals	119 (53.4)	65 (54.6)	54 (45.4)

Note: Percentages overall are among enrolled participants and are within each characteristic for treatment arm.

Abbreviations: $CuSO_4$, copper sulphate; FBC, full blood count; NBSG, National Blood Service Ghana; SD, standard deviation; TTI, transfusion transmissible infection.

[a]The enrollment visit was scheduled approximately 2 weeks after the screening visit to allow processing of blood specimens that were obtained at screening.

[b]Participants were consenting first-time voluntary donors who passed all other pre-screening donation requirements (e.g., medical history), reported not taking iron supplementation (including turkey berries) in the last month, had hemoglobin ≥10 g/dL at screening, and had no evidence of malaria, helminthic infection, or TTI. TTI was only assessed among donors who successfully donated at screening.

[c]NBSG deferral was based on $CuSO_4$ or HemoCue result at the time of donation. Donors deferred by $CuSO_4$ or HemoCue result were preferentially approached for study consent.

[d]Analysis results from blood specimens obtained at screening.

[e]One venous access failure resulted in a single failure to donate. One adverse event was reported among successful donors and was described as painful arm.

[f]Defined as donor reporting any of the following within the last 3 months: bleeding piles, stomach ulcer, bled from injury, surgery, or treatment for malaria.

[g]Defined as self-report of heavy periods, periods every 3 weeks or periods lasting longer than 10 days.

TABLE 2 Iron and anemia status among participants at enrollment.[a]

	Overall	Control SF ≥ 15 ug/L not anemic	Iron supplementation SF ≥ 15 ug/L anemic	Iron supplementation SF < 15 ug/L not anemic	Iron supplementation SF < 15 ug/L anemic
	N (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)
Donors enrolled[b,c]	223 (100.0)	118 (52.91)	83 (37.22)	7 (3.14)	15 (6.73)
NBSG deferral decision[d]					
Deferred	43 (19.3)	3 (2.5)	25 (30.1)	1 (14.3)	14 (93.3)
Not deferred	180 (80.7)	115 (97.5)	58 (69.9)	6 (85.7)	1 (6.7)

Abbreviations: $CuSO_4$, Copper Sulphate; Hb, hemoglobin; NBSG, National Blood Service Ghana; SF, serum ferritin; TTI = transfusion transmissible infection.
[a]Iron deficiency (ferritin <15 ug/L); Anemia (males: Hb 13 ≤ g/dL; females: Hb 11.5 ≤ g/dL).
[b]Participants were consenting first-time voluntary donors who passed all other pre-screening donation requirements (e.g., medical history), reported not taking iron supplementation (including turkey berries) in the last month, had hemoglobin ≥10 g/dL at screening, and had no evidence of malaria, helminthic infection or TTI. TTI was only assessed among donors who successfully donated at screening.
[c]Donors deferred by $CuSO_4$ or HemoCue result were preferentially approached for study consent.
[d]NBSG deferral was based on $CuSO_4$ or HemoCue result at the time of donation.

TABLE 3 Hemoglobin levels of participants at screening and follow-up visits.

	Screening	Interim visit 1 (8 weeks)	Interim visit 2 (16 weeks)	Final visit (26 weeks)
Iron supplementation Mean Hb (SD), g/dL	*N* = 105 11.25 (0.91)	*N* = 89 11.42 (1.08)	*N* = 56 11.35 (1.27)	*N* = 58 11.41 (1.03)
Control Mean Hb (SD), g/dL	*N* = 118 13.39 (1.26)	*N* = 92 12.55 (1.52)	*N* = 74 12.28 (1.46)	*N* = 70 12.42 (1.44)
Iron supplementation minus control Mean Hb difference (97.5% CI_{low}), g/dL	−2.14 (−2.43)	−1.13 (−1.52)	−0.93 (−1.41)	−1.01 (−1.46)
Subset control[a] Mean Hb (SD), g/dL	*N* = 67 13.82 (1.24)	*N* = 47 13.56 (1.24)	*N* = 36 13.36 (1.17)	*N* = 40 12.88 (1.41)
Iron supplementation[b] minus subset control[a] Mean Hb difference (97.5% CI_{low}), g/dL	−2.89 (−2.90)	−2.14 (−2.54)	−2.01 (−2.53)	−1.47 (−1.96)

Abbreviations: CI, confidence interval; SD, standard deviation.
[a]Control participants who did not receive study prescribed iron supplementation over follow-up.
[b]*N* = 1 iron supplementation participant was advised to stop taking iron supplementation by study medical personnel. Hemoglobin values for this individual are included in the analysis.

The mean Hb values decreased over time from baseline to the fourth month in the control group (screening: $N = 118$, 13.4 ± 1.3 g/dL; interim visit 2: $N = 74$, 12.3 ± 1.5 g/dL; p-value <.001) and increased in the iron supplementation group, although the increase was not statistically significant (screening: $N = 105$, 11.3 ± 0.9 g/dL; interim visit 2: $N = 56$, 11.4 ± 1.3 g/dL; p-value = .15). However, the primary comparison, mean hemoglobin difference between the iron supplementation and control arm at 4 months, did not meet the prespecified threshold of −1 g/dL to reject the inferiority hypothesis. Results were similar for analyses excluding control participants who were prescribed iron during follow-up due to anemia or iron deficiency.

Among controls assessed at 2 months post-donation, that is, interim visit 1, 23.4% (11/47) and 42.6% (20/47) of females had developed ID and anemia, respectively, while 20.9% (9/43) of males were anemic with none ID. Among participants assigned to iron supplementation who were anemic at screening, 31.7% (20/63) of females and 28.6% (6/21) of males were no longer anemic at interim visit 1. Among iron supplementation participants who were ID at screening 53.3% (8/15) of females and no males (0/2) were found to be iron replete at interim visit 1.

Only half of the participants receiving iron supplementation self-reported perfect adherence at the first and second interim visits (end of iron supplementation;

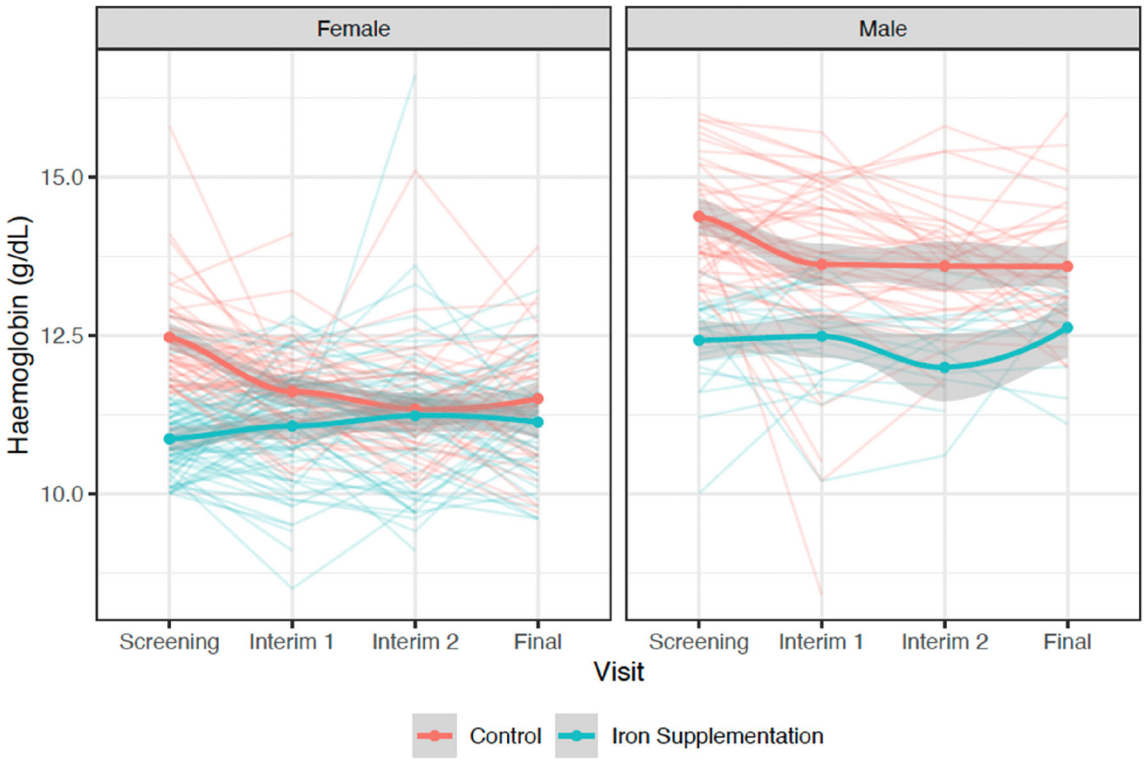


FIGURE 1 Hemoglobin levels by gender at screening and follow-up visits shown with 95% loess curve. [Color figure can be viewed at wileyonlinelibrary.com]

Table 4). A small proportion of participants reported side effects of dark stools and abdominal pain. We did not observe bacterial infections or increased malaria incidence. There were no serious adverse events reported. None of the adverse events related to iron supplementation or study procedures resulted in an adverse clinical outcome. Most events were of mild intensity and infrequently led to a change in treatment. The most frequently reported adverse side effects were dark stools and abdominal pain (Table 5). Dark stools were common in the iron supplementation arm and expected. Surprisingly, abdominal pain was common in the control arm. Treatment discontinuation was study clinician directed for only one iron supplementation participant.

Subgroup analyses by gender met the non-inferiority threshold for women with a mean hemoglobin difference of −0.10 g/dL, 97.5 $CI_{low} = -0.57$ (Table 6). The treatment effect on 4-month hemoglobin differed by gender (p-value = .017) and not by age group (p-value = .50) (Table 5). Among female controls, Hb decreased over 1 g/dL from screening to 4-month follow-up (screening: $N = 61$, 12.5 ± 0.8 g/dL; interim visit 2: $N = 43$, 11.3 ± 0.9 g/dL; p-value <.001) and increased 0.3 g/dL in the iron supplementation group, although this was not significant (screening: $N = 79$, 10.9 ± 0.6 g/dL; interim visit 2: $N = 47$, 11.2 ± 1.3 g/dL; p-value = .09). Among males, Hb decreased 0.8 g/dL in the control group from screening to 4-month follow-up (screening: $N = 57$, 14.4 ± 0.8 g/dL; interim visit 2: $N = 31$, 13.6 ± 1.0 g/dL; p-value <.001) and decreased 0.4 g/dL in the iron supplementation group, although this difference was not statistically significant (screening: $N = 26$, 12.4 ± 0.7 g/dL; interim visit 2: $N = 9$, 11.9 ± 0.8 g/dL; p-value = .72) (Figure 1).

Participants with evidence of a transfusion transmissible infection (TTI) in donated blood or very low hemoglobin (<10 g/dL) were referred to a clinic for appropriate follow-up care. These participants remained in the study unless they actively withdrew consent. A total of 8 participants actively withdrew consent during follow-up.

4 | DISCUSSION

The primary goal was to evaluate the Hb level of first-time blood donors with ID or IDA after 4 months of low-dose iron supplementation. We found a slight increase in the hemoglobin level of first-time blood donors on iron supplementation and a decline in the hemoglobin level of the control group. Similar studies from high-income countries have shown the benefit of low-dose iron supplementation in improving the Hb levels of blood donors deferred due to anemia.[9,13,14] In Ghana, the copper sulphate test is primarily used to screen for anemia among

TABLE 4 Self-reported adherence to iron supplementation at first and second interim visits.

	Interim visit 1 (8 weeks) *N* (%)	Interim visit 2 (16 weeks) *N* (%)
Forms submitted among Iron Supplementation participants	90	56
Number of remaining pills; mean (SD)	5.34 (6.81)	6.32 (6.88)
Do you ever forget to take your medicine?[a]	52 (57.8)	34 (60.7)
Are you careless at times about taking your study medicine?[a]	21 (23.3)	10 (17.9)
Sometimes if you feel worse, do you stop taking your study medicine?[a]	7 (7.8)	6 (10.7)
Thinking about last week, how often have you not taken your study medicine?		
0 (participant reports taking pills every required day)	45 (50.0)	28 (50.0)
1 day	9 (10.0)	6 (10.7)
2 days	11 (12.2)	7 (12.5)
3 days	25 (27.8)	15 (26.8)
How many days did you miss taking your iron pills in the last 2 weeks? mean (SD)	1.82 (2.22)	1.82 (2.32)

Abbreviation: SD, standard deviation.
[a]Count and percentage of "Yes" responses.

potential blood donors. However, this semiquantitative method has been reported to pass anemic donors while excluding eligible donors[15] erroneously. This was observed in our study, where 59/180 (32%) of participants qualified to donate by the copper sulphate test but were anemic by an FBC. Therefore, Hb screening should be verified using a standard diagnostic or reference technique as the International Committee for Standardization in Hematology recommends. This poses several questions: Is this feasible at blood banks in SSA? What is the cost implication of introducing a FBC automated analyzer at our blood banks? Will the HemoCue test be more feasible for hb determination in SSA?

Adherence to oral iron supplementation has been reported as 88–92.5% in some studies.[16,17] In our study, adherence was significantly lower, with only 50% of iron supplementation participants reporting taking pills every required day among 90/105 (85.7%) participants with a 4-month visit and 56/105 (53.3%) with an 8-month visit. However, it is important to note that our study participants were young adults and mostly females with a mean age of approximately 20 years. Adherence in this age group faces several challenges, including fear of weight gain, forgetfulness, and lack of awareness. One approach to improve adherence is through ongoing education on anemia and its preventive measures. It is however not surprising to have higher rates of ID or IDA in females of reproductive age.[18]

Some of this study's findings were consistent with similar trials, with no indication of increased risk for clinically significant adverse events.[9,12,13] Because compliance was low it was difficult to determine the proportion of participants who would have had to discontinue treatment due to adverse events. Notably, patients treated with iron did not demonstrate an increased risk of malaria or bacterial infections, underscoring the safety profile of the iron preparation (ferrous sulfate) used in this trial. Ferrous Sulfate is well tolerated and well absorbed. The potential risks associated with iron supplementation are related to excessive intake of iron at much higher doses than we used in this pilot trial.[19]

Further studies are warranted since even after 4 months of oral iron supplementation, the donors on iron supplementation did not reach the iron status of the control group. We used 65 mg of elemental iron three times a week. It is well known that approximately 10%–20% of an oral iron dose will be absorbed upon initiation of therapy.[20]

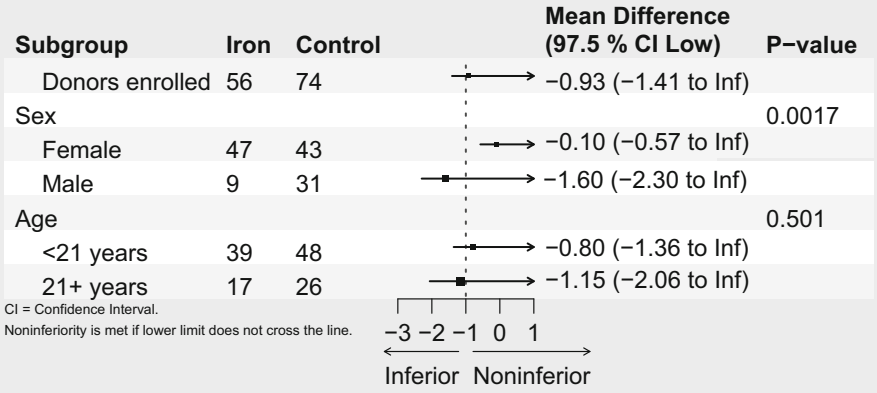
Additionally, the study experienced higher than anticipated loss to follow-up, poor adherence, and uncertainty with regard to the length of time required to increase iron levels among those who are ID or IDA. We have designed and recently initiated a study that addresses these weaknesses. We have modified the endpoint to not rely on a marker that requires a blood draw during follow-up. The primary endpoint in the follow-on study is blood donation, which can be ascertained by phone call and is the motivation for providing iron supplementation to potential donors. We have altered the dosing schedule to be every day to simplify adherence. Finally, we have required 6 months of iron supplementation to increase the chances that iron levels will be increased to a level that allows donation.

The current pilot study is one of the few iron supplementation trials conducted in SSA, where there is a high prevalence of malaria and bacterial infections in the general population. Nevertheless, it is imperative to recognize the limitations of our pilot trial, which include loss to follow-up and early discontinuation, the short duration of the intervention, and poor adherence. Furthermore, extended duration of intervention and improved adherence strategies such as frequent follow-up visits are imperative to ascertain the long-term safety and improved hemoglobin levels of deferred blood donors in SSA.

TABLE 5 Adverse side effects over follow-up for interim and final visits.

	Interim 1		Interim 2		Final	
	Control	Iron supplementation	Control	Iron supplementation	Control	Iron supplementation
	N (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)
Forms submitted	96	90	74	56	70	58
Unpleasant taste	0 (0.0)	6 (6.7)	1 (1.4)	4 (7.1)	3 (4.3)	3 (5.2)
Constipation	9 (9.4)	2 (2.2)	2 (2.7)	3 (5.4)	5 (7.1)	1 (1.7)
Dark stools	0 (0.0)	14 (15.6)	0 (0.0)	3 (5.4)	4 (5.7)	6 (10.3)
Nausea	2 (2.1)	7 (7.8)	3 (4.1)	0 (0.0)	6 (8.6)	0 (0.0)
Vomiting	2 (2.1)	2 (2.2)	1 (1.4)	1 (1.8)	7 (10.0)	2 (3.4)
Abdominal pain	10 (10.4)	3 (3.3)	5 (6.8)	6 (10.7)	4 (5.7)	6 (10.3)
Diarrhea	2 (2.1)	6 (6.7)	1 (1.4)	4 (7.1)	2 (2.9)	4 (6.9)
Other	6 (6.2)	3 (3.3)	4 (5.4)	3 (5.4)	0 (0.0)	2 (3.4)
Any	24 (25.0)	31 (34.4)	13 (17.6)	19 (33.9)	20 (28.6)	18 (31.0)

TABLE 6 Subgroup analyses for the mean difference in hemoglobin level at 4 months for iron supplementation compared with control with the lower 97.5% confidence limit for the non-inferiority hypothesis and the test of the interaction between subgroup and hemoglobin value at interim visit 2.



5 | CONCLUSION

After 4 months of iron supplementation, hemoglobin levels in the iron supplementation group did not sufficiently match those in the control group to declare non-inferiority. To effectively reduce anemia and iron deficiency, additional strategies such as extending the duration of iron supplementation are necessary. This is crucial for making iron supplementation a viable approach to increasing donations among individuals deferred for low hemoglobin in SSA.

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CONFLICT OF INTEREST STATEMENT

The authors have disclosed no conflicts of interest.

ORCID

Imelda Bates https://orcid.org/0000-0002-0862-8199
Meghan Delaney https://orcid.org/0000-0003-1089-5787

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