PROTOCOL TITLE:

Iron Supplementation and Nutritional Counseling Interventions to Improve Availability and Safety of Blood in Ghana

SHORT TITLE: Bloodsafe Ghana- Iron and Nutritional Counseling Strategy Pilot Study (BLIS)

Amended Protocol

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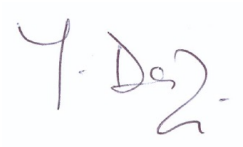
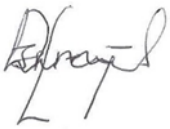
DECLARATION

We the undersigned declare that the contents of this proposal is original.



Sign: …… **Date: 28th May, 2021**

Dr. Yvonne Dei-Adomakoh (PI)



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STATEMENT TO COMPLY WITH ETHICAL PRINCIPLES

I, Dr. Yvonne Dei-Adomakoh, the Principal Investigator (PI) of this study titled "Iron Supplementation and Nutritional Counseling Interventions to Improve Availability and Safety of Blood in Ghana" and on behalf of my research team state that we will comply strictly to all ethical principles, which includes the principles of beneficence and non-maleficence i.e. promoting the interest and wellbeing of others, not doing harm and respect for the right of others. The above ethical principles will be adhered to throughout the study, by ensuring that the research is based on full informed consent and that the participants' right to confidentiality is maintained. Data collected will be used solely for the purpose of this research.

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LIST OF ACRONYMS

ABC	Area Blood Centre
DCC	Data Coordinating Centre
DSMB	Data and Safety Monitoring Board
eCRF	Electronic Case Report Forms
FBC	Full Blood Count
FRD	Family replacement donor
GCP	Good Clinical Practice
Hb	Haemoglobin
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HSP	Human Subjects Protection
ICF	Informed consent form
ICH	International Conference for Harmonization
ID	Iron Deficiency
IDA	Iron Deficiency Anaemia
IRB	Institutional Review Board
MCV	Mean Corpuscular Volume
NBSG	National Blood Service Ghana
NHLBI	National Heart, Lung, and Blood Institute
OSMB	Observational Study Monitoring Board
QSR	Qualitative Software and Research
SSA	Sub-Saharan Africa
SZBC	Southern Zonal Blood Centre
TTI	Transfusion Transmissible Infections
UMN	University of Minnesota
WHO	World Health Organisation

ABSTRACT

Background

The major challenge for blood transfusion services in Sub-Saharan Africa (SSA) is the juxtaposition of an increasing clinical demand for blood and a historically insufficient supply of safe blood in the region. The system of blood donation in Ghana, has been identified as the major barrier to providing adequate and regular blood to meet the transfusion needs of the country. This study is therefore planned as a feasibility and acceptability pilot trial of iron supplementation to increase blood donation among blood donors deferred for low levels of haemoglobin within the catchment areas of the Southern Zonal Blood Centre (SZBC).

Methods

This pilot study has 2 components: 1) a cross-sectional assessment designed to estimate the prevalence of anaemia leading to donor deferral, the prevalence of iron deficiency (ID) and iron deficiency anaemia (IDA) among first-time donors, and 2) a longitudinal 2-arm parallel groups trial among first-time voluntary donors that compares haemoglobin levels at 4 months among those with ID or IDA who receive iron supplementation to those without ID or IDA who do not receive iron supplementation. A structured questionnaire will be used to extract demographic characteristics. Participants will be followed for a total of 6 months with study visits at 2, 4 and 6 months after the baseline assessments. Blood draws for full blood count (FBC), peripheral film comment, malaria rapid diagnostic tests (RDT) and ferritin assessment will occur at baseline and all follow-up visits. In addition, we will use a qualitative approach to identify barriers and facilitators of blood donation and the use of dietary and iron supplementation strategies to address iron deficiency and/or anaemia. This will involve conducting focus group discussions during the last month of the intervention and key informant interviews.

Expected Outcomes

The expected outcomes of the study have been grouped into two, primary and secondary. Primary Outcome will be haemoglobin level after 4 months. Secondary Outcomes are **A**. Change in haemoglobin levels **B**. Diagnosis of ID or IDA at 4 months **C**. Serum ferritin concentration after 4 months of intervention

D. Acceptability of iron supplementation among participants and stakeholders **E**. Incidence of gastrointestinal adverse events F. Incidence of suspected malaria or bacterial infections **G**. Incidence of ID and IDA H. Successful return (non-deferred) to the blood donor pool after intervention within 6 months of enrolment **I.** Key barriers and facilitators of intervention implementation.

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INTRODUCTION

The major challenge for blood transfusion services in sub-Saharan Africa is the juxtaposition of an increasing clinical demand for blood and a historically insufficient supply of safe blood in the region [1,2]. We have identified the system of blood donation in Ghana as the major barrier to providing adequate and regular blood to meet the transfusion needs of the country. Currently, over 66% of blood collection in Ghana is obtained through a Family Replacement Donor (FRD) system, which is associated with insufficient, unsustainable and relatively unsafe supply of blood particularly for emergencies[3,4].

Iron balance in donors is also an important safety issue. Iron deficiency is initially without anaemia, manifesting as reduced iron stores (iron depletion) and iron deficient erythropoiesis, and without intervention is complicated by overt anaemia[5]. Major causes of iron deficiency are inadequate dietary iron, malabsorption and loss of iron[6]. One complete whole blood donation (400-500 ml) leads to the loss of almost 250mg of iron[7]. In adolescents and adult females, the iron stores are about 300mg [5]. The female blood donor therefore loses a significant amount of her total body iron, and risks becoming iron depleted after one donation of whole blood.

Problem Statement

With continuous loss of iron from repeat whole blood donations and inadequate replacement, blood donors inevitably develop ID and, later, IDA. From 2015 to 2018, between 33 and 53% of deferred voluntary blood donors attending National Blood Service blood drives in southern Ghana were deferred for low haemoglobin. Although these individuals are motivated to donate blood for reasons other than replacement for family and friends, iron deficiency anaemia emerges as a significant challenge to increasing the limited voluntary blood donor population in Ghana. Only 39% of voluntary donors registered at the SZBC donate blood at least twice in a year. An unpublished prospective study looking at characterization of anaemia in 150 blood donors showed a prevalence of anaemia in potentially healthy blood donors to be 48% with IDA accounting for 63.9% and ID 86.1%.

Another unpublished prospective study on iron status of blood donors at the SZBC estimated the overall prevalence of ID to be 68.8%.

The WHO advocates the use of repeat voluntary blood donations since these are associated with both blood safety and availability. However, in the absence of adequate interventions to prevent anaemia, repeat attempts by previously iron deficient blood donors leads to IDA and deferment at subsequent donations. The prevalence of anaemia among men globally is 12.7% whilst that of women in reproductive age is 30.2%[6]. The prevalence of anaemia in Ghana is higher than the global average, estimated at 42.4% in women of reproductive age[7] and 18.8% among peri-urban men[8].

This high prevalence of anaemia in the general population may contribute to an increased rate of deferrals due to anaemia in potential blood donors in Ghana**.** This results in a loss of valuable members of the donor pool who could have been retained if they had been identified, counseled, and treated appropriately for iron deficiency and iron deficiency anaemia.

Aim

To determine the potential for iron supplementation and nutritional counseling strategy to increase blood donations in Ghana.

HYPOTHESIS: Haemoglobin levels among deferred blood donors with anaemia will improve to near normal after iron supplementation compared to those who were not deferred with normal haemoglobin.

Objectives

Primary Objectives

The primary objective of this study is to determine the potential for an iron supplementation strategy to increase blood donations in Ghana. To determine this potential, the study will investigate the feasibility and acceptability of this intervention along with key return blood donation measures among first-time blood donors deferred for low haemoglobin or found to have IDA or be ID within the

catchment areas of the SZBC. These aspects of the potential for this intervention will be operationalized as follows:

- **Feasibility** of recruitment, enrolment, retention, and adherence will be evaluated with a target retention rate > 90% of all participants recruited completing the trial. If we are unable to achieve this target, alternative strategies will be considered for the UH3 phase.

- **Acceptability** will involve establishing the safety profile of 3 times weekly low dose ferrous sulphate (65mg elemental iron) supplements among deferred prospective blood donors with ID and IDA. This safety profile will be established by comparison to a similar group of participants who do not receive iron supplementation. Participant and key informant views and perspectives of barriers and recommendations for using iron supplementation and nutritional counseling to increase the blood donor pool will also be investigated with participant questionnaires. In addition, focus group discussions and key informant interviews will provide critical insights into the acceptability of this intervention.

- **Key blood donation measures** include haemoglobin levels at 4 months, the change in haemoglobin concentration, ferritin levels at 4 months, the proportion of participants with corrected ID, the proportion of participants who return to the blood centre to donate blood and the proportion of returners who are able to successfully donate (not deferred). In addition, the incidence of ID and IDA among blood donors will be determined using a group of participants who were not deferred, were not ID and did not have IDA at baseline.

To achieve this objective, a pilot study will be conducted for one year. This allows for enrolment over a maximum of 6 months and 6 months of follow-up for the last individual enrolled. The follow-up period incorporates 4 months of the iron supplementation intervention.

Secondary Objectives

- To determine changes in haemoglobin in blood donors over a 6-month period.
- To determine the impact of iron supplementation on the change in haemoglobin.
- To estimate the prevalence of iron deficiency and iron deficiency anaemia in prospective first-time blood donors.
- To determine the factors associated with iron deficiency and iron deficiency anaemia among prospective blood donors.
- To determine the prevalence of malaria or adverse events among the prospective first-time blood donors.
- To identify the barriers and facilitators of repeat donation and the use of dietary and iron supplementation interventions to address iron deficiency and/or anaemia among blood doors.
- To determine feasibility of the intervention, through documenting implementation fidelity, intervention adaptation, and intervention strengths and weaknesses.
- To understand participant and key informant acceptance of the intervention.
- Develop and implement key strategies aimed at increasing the blood donor pool.
- To compare Hb levels as determined by copper sulphate versus automated haematology analyzer.

Justification

The system of blood donation in Ghana has been identified as the major barrier to providing adequate and regular blood to meet the transfusion needs of the country. Currently, over 66% of blood collection in Ghana is obtained through a Family Replacement Donor (FRD) system. In countries with a 100% voluntary blood donor base, the average blood donation rate is 31 units per 1000 population. In contrast, the blood donation rate in Ghana saw little increase from 5.8 to 6.0 units per 1000

population between 2016 and 2018, with the proportion of voluntary unpaid donors stagnant at less than 35% over that period[3]. As a direct result, the blood supply is characterized by chronic inadequacy with frequent critical shortages and represents a major developmental challenge. In addition, deferrals among potential blood donors in Ghana is high[9,10]. Anaemia accounted for 33-53% of voluntary donor deferrals at the Southern Zonal Blood Centre between 2015 and 2018 and is, therefore, a major focus of the current study.

LITERATURE REVIEW

The reduction in iron stores in regular blood donors has become a recognized safety issue, because multiple donations are associated with increasing frequency of ID. In Enugu, Southern Nigeria, 11% of donors who had donated blood once within four years were observed to be iron deficient[11]. However, the prevalence of ID in voluntary blood donors can be as high as 40% and 50% in persons donating 6 and 7 times in two years, respectively[12]. In the REDS-II Donor Iron Status Evaluation study in the USA, 15% of donors had absent iron stores (serum ferritin <12ng/ml) and 41.7% iron deficient erythropoiesis (log TfR/ferritin 2.07)[13]. Increasing the inter-donation interval[14], iron supplementation [15] or regular iron status monitoring [16] are some measures used to reduce the risk of iron deficiency from repeated blood donations.

At the SZBC of the NBSG, blood donors are routinely advised to eat iron-rich diet. However, unlike a typical Western diet which provides about 10 to 15 mg of iron daily in the form of heme proteins found in meat, with good intestinal absorption[5], the Ghanaian diet is mainly cereal and plant-based with low iron and a high phytate content that further reduces iron bioavailability[17]. Iron absorption from non-heme sources of iron such as cereals and legumes has been noted to be between 1% to 22% [18] and even less bioavailable in a cereal porridge-based diet with absorption of 2-3%[19]. Dietary measures for restoring a blood donor's low haemoglobin levels from depleted iron stores requires about 24 weeks of adequate dietary modification in the absence of iron supplementation [15].

Currently, over 66% of blood collection in Ghana is obtained through a Family Replacement Donor (FRD) system, which is associated with insufficient, unsustainable and relatively unsafe supply of blood particularly for emergencies[3],[4]. In countries with a 100% voluntary blood donor base, the average blood donation rate is 31 units per 1000 population. In contrast, the blood donation rate in Ghana saw little increase from 5.8 to 6.0 units per 1000 population between 2016 and 2018, with the proportion of voluntary unpaid donors stagnant at less than 35% over that period[3]. As a direct result, the blood supply is characterized by chronic

inadequacy with frequent critical shortages and represents a major developmental challenge. In addition, deferrals among potential blood donors in Ghana is high [9,10].This project is directed towards transforming the blood donor pool in Ghana from FRDs to sustainable voluntary collections, in support of Ghana's national blood policy that aims at a 100% voluntary blood donation pool to secure and sustain an adequate and safe blood supply.

The effect of replacement blood collections in health service delivery: (1) The FRD system places undue burden on patients because the transfusion of patients or their discharge from wards is delayed until friends and/or family can be mobilized to 'donate' equivalent numbers of units transfused. As a result, eligible donors refrain from voluntary donations in case they are called on to replace blood for relatives. (2) Because of the lag time in organizing FRDs, reliance on replacement donations accounts for inadequate blood for emergencies such as obstetric haemorrhage and severe malaria in children. Haemorrhage remains the leading cause of maternal mortality in Ghana as a direct consequence. (3) FRD collections are generally less safe compared to voluntary donations, with higher prevalence of seropositivity to markers for Hepatitis B and C and HIV. Paid donors, and less often FRDs, have a vested interest in providing false information during the pre-donation assessment designed to exclude those potential donors at high risk for transfusion transmissible infections. Paid donors have higher rates of transfusion-transmitted infections (TTI) [20]. Although the Ghana national blood policy proscribes paid blood donations, the FRD system provides cover for these donors, who pose as relatives of patients.

Importance of pre-emptive correction of inevitable iron loss to sustain regular voluntary donations: The project will address ID and IDA as a preventable cause of donor deferrals and to promote blood donor safety. While the national blood policy encourages repeat donations among the small voluntary unpaid blood donor pool in Ghana, iron depletion from regular scheduled venesections has not been addressed. Deferral of donors on account of anaemia contributes to the slow growth of the voluntary donor pool, in spite of recruitment

campaigns. The prevention of ID through nutritional education and iron supplementation programs is an important intervention where repeat voluntary donations are well established[15]. This ID and IDA prevention arm of the project will inform workable strategies to protect and maintain the improved pool of blood donors to sustain improved collection rates.

METHODOLOGY

Design

This pilot study has 2 components: 1) a cross-sectional assessment designed to estimate the prevalence of anaemia leading to donor deferral, the prevalence of ID and the prevalence of IDA among first-time donors, and 2) a longitudinal 2-arm parallel groups trial among first-time voluntary donors that compares haemoglobin levels at 4 months among those with ID or IDA who receive iron supplementation to those without ID or IDA who do not receive iron supplementation. The primary outcome will be haemoglobin levels at 4 months. Participants will be followed for a total of 6 months with study visits at 2, 4 and 6 months after the baseline assessment. Blood draws for FBC, peripheral film comment, Malaria rapid test and ferritin assessment and the administration of a structured questionnaire will occur at all follow-up visits.

The parallel group's component is designed as a non-inferiority trial for haemoglobin levels at 4 months. At baseline, the 2 groups will be determined based on the need for iron supplementation: all individuals with ID or IDA, who satisfy our eligibility criteria regardless of deferral status, will receive iron supplements while all others will not. While a high prevalence of ID and IDA is expected, enrolment will be staggered so that an equal number of participants from each group are enrolled from each site with at least 1 participant who is found to be ID or have IDA. If there are more potential participants in one group at some site, randomization will be used to select the individuals to enroll in the trial to maintain balance over time. The extent of adherence is a central question for this study, and it is also unclear if the haemoglobin deficiency can be improved above what is seen in the control group, hence it is not hypothesized that those receiving

iron supplementation will have higher levels of haemoglobin at 4 months. The hypothesis about iron supplementation intervention is that it will improve haemoglobin levels to near that seen among those who were not deferred. If haemoglobin levels are higher in those receiving iron supplementation the intervention would also be deemed a success. Hence a non-inferiority trial is most appropriate for this hypothesis.

Selection of the margin is a critical component of a non-inferiority trial. Here, we specify a margin of 1 g/dL for haemoglobin levels at 4 months. Under a collection of reasonable assumptions, this margin will ensure that the majority of those with low haemoglobin at baseline will have haemoglobin levels at 4 months above the threshold for anaemia and should therefore qualify as donors. To see this, assume that half of donors are anaemic at baseline (using the thresholds for anaemia of 13 g/dL for men and 11.5 g/dL for women). A simple calculation finds that if we assume haemoglobin levels are normally distributed (which is a reasonable assumption based on observed distributions for haemoglobin in healthy individuals) and the standard deviation of baseline haemoglobin levels is 1.89 g/dL (this estimate will be described below) then the mean haemoglobin level among men who are deferred is 11.5 g/dL and the mean haemoglobin level among men who are not deferred is 14.5 g/dL (these values for women are 10.0 g/dL and 13.0 g/dL). If we assume that the haemoglobin level among those who are not deferred is the same 4 months later then a margin of 1 g/dL implies a mean haemoglobin level among those with anaemia at baseline of at least 13.5 g/dL for men and 12.0 g/dL for women. Thus, the mean haemoglobin level after 4 months of iron supplementation among those who should have been deferred will exceed the threshold for anaemia and consequently, if the distribution of haemoglobin levels is symmetric, the majority of those who were anaemic at baseline would qualify as donors (in fact at least 60.4% would pass the threshold for both sexes if this distribution is normal). Note that the threshold for the copper sulphate test used for women is 12 g/dL, not 11.5 g/dL, so under these assumptions 50% of women would pass the copper sulphate test. Nonetheless, since well over 50% of donors are men the majority of deferred donors would pass the copper sulphate test. It is

likely that fewer than half of all donors will be anaemic at baseline. In this case the difference in the means between those with anaemia and those without anaemia will be larger, the gain in haemoglobin levels in the anaemic group will be larger and the proportion of donors who would be deferred at baseline but would not be deferred after 4 months of iron supplementation will be even larger. It is possible that the difference between the 2 groups is smaller than the margin at baseline. This seems unlikely since the 2 groups are defined by a threshold for haemoglobin levels, but if the standard deviation of haemoglobin levels is 0.62 then the difference between the groups among men would be less than the margin under the assumptions of the previous paragraph (this standard deviation is less than one third of the standard deviation used for design). To address this, when enrolment reaches 50% of the total planned sample size, the statisticians supporting the trial at the data coordinating center (DCC) will compute the standard deviation of haemoglobin levels at baseline and revisit the margin calculation and the sample size. If the standard deviation is low enough so that the difference between the groups is less than the margin, then the study will be overpowered for the current margin and a smaller margin will be selected so that the trial is still testing for differences at 4 months that exceed the baseline difference. Any changes to the study design based on these analyses will be discussed with the DSMB.

In addition, we will use a qualitative approach to identify barriers and facilitators of blood donation and the use of dietary and iron supplementation strategies to address iron deficiency and/or anaemia. This will involve conducting focus group discussions during the last month of the intervention. The interviews will focus on issues including culture concerning food selection and consumption, cost of micronutrient-rich foods as well as other potential issues that might contribute to the success or otherwise of the dietary and iron supplementation interventions.

Duration

The duration of this UG3 phase (Pilot trial) is 1 year

Sample Size

Qualitative study: In all, ten focus groups of 8-10 participants purposively selected with one group from each blood donation group category (i) religious organisations, (ii) educational institutions, (iii) corporate institutions, (iv) organised community groups, and (v) walk-in blood donors. The aim of the focus groups is to identify barriers and recommendations for using iron supplementation and nutritional counselling to increase the blood donor pool. These will be gender-sensitive such that there will be two groups of each blood donation category by gender (e.g., 8-10 females, 8-10 males). The female and male focus groups will meet in separate spaces so only one gender will be interviewed at a time. Thus, there is one male and one female group for each donation category.

Quantitative method: Cross-sectional study to determine the prevalence of anaemia among prospective blood donors: There are 2 distinct components of the cross-sectional study: estimation of the proportion of potential donors deferred due to low haemoglobin and the proportion of first-time potential donors who are ID and IDA. The determination of deferral due to low haemoglobin is routinely collected by the NBSG and does not require consent of potential donors in this study. The proportion deferred will be determined using the same donation sites as the other components of the study with an estimated sample size of 600 and resulting margin of error less than 0.04. Consequently, the 95% confidence intervals for deferment prevalence will have a total width of less than 0.08 giving a more precise estimate than the year-to-year variation in the total percentage deferred. Participant consent is needed to draw blood for determination of ID and IDA. We anticipate that 292 participants will consent and be enrolled with resulting margin of error less than 0.057 and total confidence interval width of less than 0.11 for likely values of the prevalence of ID and IDA among first-time potential donors. Thus the ID and IDA prevalence estimates will have comparable precision to the estimated proportion of deferred using all potential donors at recruitment sites.

Parallel groups' trial to assess the acceptability of iron supplementation: Using a non-inferiority design with a non-inferiority margin of 1 g/dL for haemoglobin levels

at 4 months, a 1-sided alpha level of 0.025, at least 85% power and under the assumption that the true difference in the means is 0.3 requires 262 participants (131 per arm). This number has been increased to allow up to 10% loss to follow-up or iron supplementation for those initially not requiring supplements (such individuals will be excluded from the primary analysis: see Section 12 for further details), thus the sample size is 292. For efficiency, participants will be enrolled into both parts of the quantitative study.

For efficiency, participants will be enrolled into both parts of the quantitative study.

Sample size justification

Cross-sectional study: Since all potential donors will contribute to the estimate of the proportion of potential donors who are deferred due to low haemoglobin, the estimate of this proportion will be sufficiently accurate to allow for comparisons against yearly rates. As stated above, the annual proportion of deferrals from 2015-2018 ranged from 33-53%. If we assume that 5 blood donors attempt to donate each business day, then there should be about 600 donation attempts over the 6-month enrolment period. Table 1 shows values for the prevalence of low haemoglobin, the corresponding margin of error and the corresponding 95% confidence interval. For example, if the prevalence of low haemoglobin leading to deferral is 50% then a 95% confidence interval would be (46%, 53%) which allows for determination of the prevalence in a range that is smaller than the range of yearly estimates. Note: these estimates were obtained using the usual normal approximation to the sampling distribution of a proportion without a continuity correction.

Table 1: Precision of prevalence estimates for low haemoglobin leading to deferral.

Prevalence	Margin of error	95% confidence interval
0.2	0.032	0.17, 0.23

0.3	0.037	0.26, 0.34
0.4	0.039	0.36, 0.44
0.5	0.040	0.46, 0.54
0.6	0.039	0.56, 0.64

Since not all participants will consent to participate in the study and only a subset of donors are first-time donors, the precision of estimates of the prevalence of ID and IDA will be lower. Based on the unpublished estimates of the prevalence of ID and IDA provided above (i.e., 63.9% of those with anaemia had IDA and 86.1% of those with anaemia had ID, so 30.7% of the total had IDA and 41.3% had ID), estimates of the prevalence of these conditions cover almost the same range as our estimates of the prevalence of low haemoglobin. Since enrolment for this component of the study entails enrolment in the longitudinal study, the sample size was determined by the requirements for the longitudinal study which is 292 participants. Since some participants in the cross-sectional study of ID and IDA may be found to have Hb<10g/dl and will therefore be excluded from the longitudinal study, the sample size for the cross-sectional study may exceed 292. This will require that, on average, almost 2.5 participants per day consent to the study to get to about 300 over the 6-month enrolment period. Table 2 shows values for the prevalence of ID/IDA, the corresponding margin of error and the corresponding 95% confidence interval. For example, if the prevalence of IDA is 30% then a 95% confidence interval would be (25%, 35%) which has a total width comparable to the confidence intervals obtained using all potential donors.

Table 2: Precision of prevalence estimates for ID and IDA.

Prevalence	**Margin of error**	**95% confidence interval**

0.2	0.046	0.15, 0.25
0.3	0.053	0.25, 0.35
0.4	0.056	0.34, 0.46
0.5	0.057	0.44, 0.56

Parallel groups study: The primary outcome for this portion of the study is haemoglobin levels at 4 months. Formally the null hypothesis for this outcome is inferiority of treatment of low haemoglobin with iron supplementation among those with low haemoglobin at baseline to no treatment among those without low haemoglobin at baseline. The non-inferiority margin is fixed at a value of 1.0 g/dL. Based on recent work in west Africa, the DCC has access to haemoglobin measurements from 1548 individuals between the ages of 17 and 60 who weigh at least 50 kg. Among these individuals the standard deviation of haemoglobin was 1.89 g/dL (the mean was 13.4 g/dL). These individuals did not pass the strict screening criteria used by the NBSG, so this estimate might be slightly inflated and so our power calculations may be somewhat conservative. We specify an alpha level of 0.025 and require power of at least 85%. With these values we can determine the number of participants per arm if we assume a value for the true difference between the groups (the absolute value of this difference must be less than our margin and will generally be negative when the margin is positive to be consistent with the lack of superiority of iron supplementation). Table 3 presents the number of participants per arm under these assumptions for a selection of values for the true difference. We assume that the true difference is -0.3 g/dL and obtain a sample size of 131 participants per arm. If the true difference is larger than -0.3 g/dL (e.g., if there is no difference) then the power will exceed 85%. To allow for loss to follow-up and some participants requiring iron supplementation due to incident ID or IDA the sample size has been increased to 292.

Table 3: Number of participants per arm for 1-sided alpha of 0.025 and power of at least 85%.

Mean Hb treated-mean Hb control (i.e., true treatment difference)	Sample size (per group)
0	65
-0.1	80
-0.2	101
-0.3	131
-0.4	179

Study site and Population

The National Blood Service, Ghana (NBSG) SZBC located in the capital Accra annually collects voluntary blood donations from 200-300 blood donor groups that are categorised as (i) religious organisations, (ii) educational institutions, (iii) corporate institutions, (iv) organised community groups, (v) walk-in blood donors and (vi) mass/media events. Data for the prevalence of deferral assessment will be collected from all prospective voluntary blood donors within the catchment areas of the SZBC. The prevalence study of ID and IDA as well as the parallel groups' trial will be restricted to first-time donors. Generally, prospective voluntary blood donors are healthy, unlikely to be severely anaemic and are more likely to be male.

The study population will be all adults between the ages of 17 and 60 years who visit blood donation sites at the time of recruitment. The lower limit takes into account the lawful requirements of a country for giving consent, the intensified threat of vasovagal reactions in younger donors, and the augmented iron needs of adolescents and young females [21,22]. The upper age limit is so set because of an increase in various medical conditions with age especially cardiovascular diseases making donations more hazardous[23]. A stringent screening and selection process is performed to evaluate the suitability of prospective donors. This is essential to

guarantee the safety and adequacy of the blood supply; protecting the wellbeing of the recipients of transfusion as well as the fitness of the donors while ensuring that qualified donors are not deferred needlessly.

Stratification and Sampling

The SZBC contributes to the blood service needs of the Western, Central, Greater Accra, Eastern and the Volta Regions of Ghana. In 2018 and 2019, the SZBC attended to an average of 550 prospective voluntary blood donors a week, including 80 walk-in donors. Out of this number, the study will recruit all participants (who fall within the inclusion criteria) reporting per day for up to 6 months until the sample size is attained. Eligible participants will form the sampling frame for the study.

Out of the sampling frame, participants will be purposively sampled for Focus Group Discussions (FGDs). In all there will be ten FGDs i.e. two groups (male-only and female-only) randomly selected to represent each of the five NBSG voluntary blood donation categories (excluding mass/media event donors), and with each group composed of both first-time and repeat donors. In-depth interviews will also be conducted with blood donation staff and medical officers responsible for blood donation.

Regimen

The prevalence study will be conducted over the first 6 months of the study period. For the cross-sectional deferral assessment, all donation attempts and deferrals from sites where recruitment for the parallel groups study will take place will be recorded. The number of deferrals among first-time donors will also be determined. Potential first-time donors will be asked if they are interested in participating in a study of the prevalence of ID and IDA and the impact of iron supplementation on haemoglobin levels and repeat donation. Those who express interest and consent to the study will be asked to return in approximately 2 weeks. During this 2-week period a full blood count (FBC) and plasma ferritin measurement will be determined, and participants will be classified as ID, IDA or otherwise (which we refer to as controls in this protocol). Those found to be ID or IDA will receive oral

iron supplementation and nutritional counseling. Controls will not be given iron supplementation but will receive the standard practice of nutritional counseling for blood donors. Additional baseline data will be collected at the 2-week return visit. The duration of the intervention period is 4 months with two interim visits (approximately 2 months apart) and a final visit at 6 months. A blood draw will be conducted for a FBC, peripheral film comment, malaria rapid test and ferritin measurement at both interim visits and the final visit. Participants will receive bi-weekly follow-up phone calls for adherence and monitoring for adverse events. Qualitative assessment of acceptability of oral iron supplementation among donors previously deferred will be performed during the final month of the pilot study.

Inclusion Criteria

There are 3 components of the quantitative study (observational study of deferral, observational study of the prevalence of ID and IDA, and the clinical trial of supplementation) with slightly different inclusion and exclusion criteria, hence we indicate which criteria apply to which component of the study below.

Items 1-3 are required for the observational study of deferral, items 1-4 are required for the observational study of the prevalence of ID and IDA and items 1-5 are required for the clinical trial. Only participants who meet ALL the following inclusion criteria will be eligible for the clinical trial:

1. Males or females aged between 17 and 60 years who weigh at least 50kg.
2. Pass pre-donation screening using the NBSG standardised donor screening questionnaire for medical conditions and lifestyle risks for transfusion transmissible infections (Appendix 5).
3. Vital signs must meet the NBSG requirement for blood donation: systolic and diastolic blood pressures between 90-140 mmHg and 60-90 mmHg, respectively; pulse rate between 50-100 bpm; non-contact forehead temperature not exceeding 37.5°C; meeting acceptable requirements for skin lesions, needle marks and physical appearance.
4. Must be willing and able to give study consent or assent.

5. Intend to remain in the study location/site during the entire length of the study.

Exclusion Criteria

There are no additional exclusion criteria for the observational study of deferral, items 1-2 are required for the observational study of the prevalence of ID and IDA, and items 1-5 pertain to the clinical trial. All persons who meet ANY of the following exclusion criteria will be excluded from participating in the clinical trial.

1. Persons who have used iron supplementation within the past one month.
2. Participant reports having previously donated blood.
3. Evidence for a TTI at baseline among those who successfully donated.
4. Evidence of Malaria and helminthic infections at baseline
5. Participants who have Hb <10g/dl at screening

Potential donors who are found to have Hb < 10g/dl at screening will be referred for further evaluation and care by a haematologist. Any clinical trial participant found to have Hb < 10g/dl at any follow-up visit will be referred for evaluation by a haematologist.

Approach to Inter-current Therapies and Clinical Trial Co-enrolment:

Nutritional counselling for all study subjects will be provided by the study nutritionist and trained counsellors at each visit. The counselling will cover nutritional advice and drug interactions. Participants will be advised to eat a meal before taking the assigned capsule or tablet each time to minimize the possibility of gastrointestinal effects. Participants will also be counselled on minimizing potential adverse iron-food interactions and on the danger of consumption of large quantities of iron supplements. The supplements will be administered in child-safe containers. A consumer-friendly brochure on benefits of adhering to iron, and safe use of medicines including food interactions and medicine interactions involving iron will be provided to participants. (Appendix 3)

Costs to Participants

Travel costs for study visits will be reimbursed to the participants. Study participants are not compensated for other costs to avoid participation based on remuneration. During the course of this study all laboratory tests, visits and interventions will be free of charge for study participants. Participants who during the course of the study are found to have malaria or helminthic infection will be treated free of charge by study physicians.

Study Products, Procedures and Assessments

Description of Product

Oral iron supplements specifically ferrous sulphate 200mg (65mg Elemental iron).

Handling of Study Product

The iron supplements are already available at the Korle-Bu Teaching Hospital Pharmacy. The study principal investigators and study pharmacist will ensure the medicine is stored properly and dispensed only when needed for study participants. The following will be monitored and completed on a continuous basis to ensure the medicine is within study guidelines, pharmaceutical compliance, and manufacturer guidelines:

- Drug Accountability Record
- Iron supplement Safety and Handling Sheet

Study Procedures and Assessments

Evaluation of Factors leading to ID and IDA

- *Systematic Literature Review*

We will systematically review the literature on factors contributing to iron deficiency in prospective blood donors.

- *Community Engagement*

We will carry out community engagement meetings with stakeholders in our blood donor communities to introduce the project to them.

Screening /Baseline Assessments

- *Donor Eligibility Screening by NBSG*

Individuals in blood donor groups will proceed with routine assessment by blood donation staff for eligibility for whole blood donation as defined by the NBSG. As part of this assessment, these potential blood donors will undergo routine semi-quantitative haemoglobin assessment using the copper sulphate ($CuSO_4$) gravimetric method with a cut- off Hb concentration value of <13.0 g/dL for males and <12.0 g/dL for females. Prospective blood donors who consent and meet the eligibility criteria will be eligible for the study. The site will log potential blood donors who are approached to participate in the study and document whether the participant elects or declines involvement with the study.

- *Consenting Procedure*

Prospective blood donors who pass all pre-donation assessments, and those who are deferred specifically on account of failed $CuSO_4$ will be approached and informed about the study by trained research assistants. All eligible participants will provide written informed consent and, in the case of minors, additional assent. Eligible enrolled minors who turn 18 during the course of the study will need to be re-consented as adults.

- *Rescreening*

Rescreening will be allowed for previously excluded participants after four months. In this case a new study identification number will be assigned to the participant and the participant will be identified with this new number for the rest of his/her participation in the study. If participant has been enrolled, re-screening is not allowed. In case rescreening occurs, all evaluations re-assessed should meet the eligibility criteria. A new informed consent form (ICF) must be signed only if there is an interruption in the participant's eligibility evaluation and the investigator chooses to re-screen the participant following screen failure. If a new ICF is signed,

AEs and medical history will be assessed relative to the new informed consent date.

- *Blood Sampling:*

Participants who consent/assent to participate will have 5ml of whole blood sampled into an EDTA tube for full blood count, peripheral film comment, malaria rapid test and plasma ferritin analysis. This blood draw will take place prior to donation for those participants who can donate to prevent a classification of ID due to sampling immediately after a donation.

- *Estimation of Iron Deficiency and Iron Deficiency Anaemia*

Anaemia is a state in which the amount of red blood cells (RBCs) is insufficient to meet the body's physiologic needs [24]. Mild anaemia is defined as Hb ranging from 11-12.9 g/dL in adult males and 11-11.9 g/dL in adult females. Moderate anaemia is defined as Hb level of 8-10.9 g/dL and severe anaemia is defined as Hb level of less than 8 g/dl for all the age groups [25,26].

Following FBC and plasma ferritin estimation, screened participants will be classified by the WHO criteria as shown in Table 4:

Table 4: Definition of Iron Status Criteria

Haemoglobin concentration, g/dL	**Plasma ferritin concentration µg/L**	**Interpretation**
[Male] >13.0 [Female] >11.5	< 15	Iron deficiency without anaemia
[Male] ≥8.0-13.0 [Female] ≥8.0-11.5	< 15	Iron deficiency with mild to moderate anaemia

[All] <8.0	< 15	Iron deficiency with severe anaemia

Schedule of Assessments (Table 5)

Assessment	**Screening (Day -14 to 0)**	**Enrolment (Day 0)**	**Biweekly (Throughou**	**Interim Visit 1 (Week 8-10)**	**Interim Visit 2 (Week 16-**	**Final Visit (Week 24)**
NBSG Pre-Donation Assessment	X					X
Informed Consent	X					
Inclusion and Exclusion Criteria	X					
Demographics	X					
Full Blood Count and peripheral blood comment	X			X	X	X
Plasma Ferritin	X			X	X	X
Malaria Parasites Testing (RDT)	X	X		X	X	X
Nutritional Counselling		X		X	X	
Qualitative Assessment						X
Follow-Up Calls			X			
Return Blood Donation Status				X	X	X
Assessment for Adverse Events		X	X	X	X	X
Adherence Assessment (for those receiving supplemental iron)			X	X	X	X
RDT – Rapid Diagnostic Test						

Enrolment

Participants will be re-assessed with their laboratory results at the Day 0 visit.

- *Eligibility Check*

The investigator will be responsible to ensure only participants who meet all inclusion and none of the exclusion criteria are included in this study. Following registration for screening, participant eligibility will be checked once all screening procedures are completed.

- **Screening failures**

Participants who sign an ICF and are subsequently found to be ineligible prior to enrolment will be considered a screen failure. The reason for screen failure should be recorded on the appropriate eCRF. The demographic information, informed consent, and Inclusion/Exclusion pages must also be completed for screen failure participants. No other data will be entered into the clinical database for participants who are screen failures, unless the participant experienced a SAE during the screening phase (see SAE section for reporting details). Prospective donors who are found after baseline screening to have haemoglobin values less than 10g/dl will be referred to the haematology outpatient clinic or community clinic for further investigations and management. This includes participants who are found to have haemoglobin values less than 10g/dl at a follow-up visit. These participants will continue to be followed for the duration of follow-up. If use of iron supplementation is consistent with recommended medical care, the study will provide iron supplements to these participants and this will be captured in the study database.

Follow Up Assessments

The assessment schedule lists all of the assessments and indicates with an “X” (table 5), the visits when they are performed. All data obtained from these assessments will be entered into a database.

Study participants will be seen for all visits/assessments as outlined in the assessment schedule or as close to the designated day/time as possible. Participants who have not previously been provided with iron supplementation and

are found to have ferritin <15g/dl or low haemoglobin by the sex-based thresholds during study visits will be offered iron supplementation. This will be recorded in the study database and these participants will be followed for the duration of follow-up. Participants will be instructed to report missed doses to the study team and this will be documented. They will be instructed to wait till the next dosing day and not to double their dose. Missed or rescheduled visits will not lead to automatic discontinuation.

Participants will be followed up every 2 months and will be interviewed by members of the research team and appropriate CRFs completed by study staff. Adherence to iron supplementation and nutritional counseling will be assessed biweekly by phone and at each visit.

Participants with suspected adverse events of iron supplementation will be appropriately managed. Participants with suspected bacterial infections will be assessed with blood cultures (if indicated) and tested for malaria parasites during study visits. Malaria preventive measures will be discussed with all study participants on enrolment, and they will be encouraged to use these preventive measures throughout the study. A history of medical events and selected potential adverse events will be obtained at each scheduled visit and during biweekly follow up phone calls. Participants will also be given identification cards to carry with them at all times providing instructions directed to any health care provider who sees them for an unscheduled medical care visit.

- ***Treatment***

The planned duration of treatment is 4 months. Participants with a low plasma ferritin <15µg/L, with or without anaemia, will be given oral iron supplementation and nutritional counseling. Treatment will continue for 16 weeks or until the end of follow-up, during which participants will be followed up for adherence counseling at each visit. Clear written instructions for use 3 times a week will be discussed with them. Research staff will contact participants every 2 weeks by phone for adherence and feedback, and to remind participants to keep their scheduled study visits.

Testing of plasma ferritin and FBC after 4 months of supplementation will allow us to assess for response to study treatment with regards to iron stores. After correction of iron depletion or IDA, FBC and plasma ferritin will be monitored at 4 months from baseline. Participants after the end of the intervention phase still found to be iron deficient or anaemic will continue management and further evaluation at the haematology clinic.

- **Discontinuation**

If discontinuation of study treatment occurs, the investigator should make a reasonable effort to understand the primary reason for the participant's premature discontinuation of study treatment and record this information.

Participants who discontinue study treatment or who decide they do not wish to participate in study assessments are not considered withdrawn from the study UNLESS the participant withdraws their consent. When possible, participants are encouraged to return for the follow up visits. If they fail to return for the follow up visit for unknown reasons, every effort (e.g., telephone calls) should be made to contact the subject/pre-designated contact. This contact should preferably be done according to the study visit schedule.

The investigator may discontinue study treatment for a given subject if he/she believes that continuation would be detrimental to the subject's well-being.

Adherence Strategies

The study team will perform adherence improvement techniques by phone biweekly and at each study visit. All study participants will have nutritional counseling, dietary advice, and for those receiving iron, the need for iron therapy to be used consistently 3 days a week. The study team will call each participant biweekly and ask about the number of days during the past 2 weeks he/she consumed or did not consume the iron supplement and dietary recall. At each scheduled visit, they will be encouraged to bring back the bottle he/she received so any remaining amount can be counted. If participants demonstrate verbal non-

adherence, they will be provided pillboxes and called up by phone weekly for adherence counseling.

- *Adherence Assessment*

To evaluate the various methods for adherence, several strategies to be employed will include pill counting and administering adherence questionnaires. Adherence will also be calculated as the percent of follow-up days/expected pill consumption days, participant did consume the pill. We will also use a validated simplified self-report medication adherence measure with six items [27].

Retention Strategies

The use of simple, clear, detailed written and verbal instructions regarding therapy, possible side effects of iron supplementation and tests required for the study increases comprehension of the purpose and importance of the study and yields better adherence to the trial. Study research assistants are to regularly communicate with donors in the study and provide feedback to them using a structured guideline. Reminders will be sent to donors for their study visits by the research assistants. A consumer-friendly brochure on safe use of medicines including food interactions and medicine interactions involving iron is to be provided to participants.

The key to the success of retention and follow-up will be attention to detail, consistency of the research team and trust among the potential blood donors and staff. The staff will contact potential blood donors immediately and reschedule appointments when missed. Close monitoring of participants' visits and need for return appointments with follow-up telephone calls are key elements for monitoring attendance and prevention of study participants' being lost to follow-up.

Every attempt will be made by the study team to contact participants prior to their scheduled visit based on the allotted schedule for participants on both arms of the study. Identification of a stable contact person (such as a neighbor or a friend) who does not live with the study participant's family, but always knows his or her

whereabouts will assist in tracking study participants and will decrease the number lost to follow up.

Safety Assessment

Definitions

- *Adverse Event (AE)*

An AE is any untoward or unfavourable medical occurrence in a study participant, including any abnormal sign (e.g., abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with their participation in research. Only AEs potentially related to iron supplementation will be recorded as AEs.

At each follow-up visit all participants will be asked if they have experienced each item from a list of common side effects of iron supplementation. Furthermore, the occurrence of additional AEs will be sought by non-directive questioning of the study participant at each visit during the study. AEs also may be detected when they are volunteered by the study participants during or between visits or through physical examination findings, laboratory test findings, or other assessments.

Adverse events will be recorded in the Adverse Events eCRF under the signs, symptoms, or diagnosis associated with them, accompanied by the following information (as far as possible):

- AEs will be assessed.
- Its relationship to the study treatment.
- Its duration (start and end dates) or if the event is ongoing, an outcome of not recovered/not resolved must be reported.
- The grade of the AE.
- Whether it constitutes a SAE.
- Action taken regarding with study treatment.

All AEs will be treated appropriately. Treatment may include one or more of the following:

- Dose not changed
- Dose Reduced/increased
- Drug interrupted/withdrawn.
- Its outcome (i.e., recovery status or whether it was fatal).

If the event worsens the event will be reported a second time in the eCRF noting the start date when the event worsens. For Grade 3 and 4 AEs only, if improvement to a lower grade is determined a new entry for this event will be reported in the eCRF noting the start date when the event improved from having been Grade 3 or Grade 4.

Adverse events (including lab abnormalities that constitute AEs) will be described using a diagnosis whenever possible, rather than individual underlying signs and symptoms.

Once an AE is detected, it will be followed until its resolution or the end of follow-up and an assessment will be made at each visit (or more frequently, if necessary) of any changes in severity, the suspected relationship to the interventions required to treat it, and the outcome. If an AE has not resolved by the end of follow-up for a participant, the outcome of the AE will be recorded as unknown.

Common adverse events associated with iron supplementation are minor and include:

- Unpleasant taste,
- Constipation
- Dark stools
- Nausea
- Vomiting
- Abdominal pain
- Diarrhoea.

Abnormal laboratory values or test results constitute AEs only if they fulfil at least one of the following criteria:

- they induce clinical signs or symptoms
- they are considered clinically significant
- they require therapy.

Clinically significant abnormal laboratory values or test results will be identified through a review of values outside of normal ranges/clinically notable ranges, clinically significant changes from baseline or the previous visit.

Follow-Up for AEs

Study Subjects who experience any AEs will be followed up at least once a week (or more frequently if required by institutional practices, or if clinically indicated) for 4 weeks, or until resolution or stabilization of the event, whichever comes first. Appropriate clinical experts will be consulted as deemed necessary.

Serious Adverse Event (SAE)

Serious adverse events (SAEs) are defined as the following:

- Death
- Life-threatening (i.e., an immediate threat to life)
- Hospitalization or prolongation of hospitalization
- Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- Congenital abnormalities/birth defects

Other important medical events that may jeopardize the participant and/or may require intervention to prevent one of the outcomes listed above.

Information about all SAEs will be collected and recorded on the electronic Serious Adverse Event Report Form; all applicable sections of the form will be completed

in order to provide a clinically thorough report. The investigator will assess and record the relationship of each SAE to the study intervention, complete the SAE Report Form in English, and submit the completed form within 24 hours to the College of Health Sciences IRB.

All follow-up information for the SAE including information on complications, progression of the initial SAE and recurrent episodes will be reported as follow-up to the original episode within 24 hours of the investigator receiving the follow-up information. An SAE occurring at a different time interval or otherwise considered completely unrelated to a previously reported one will be reported separately as a new event.

Follow-up information will be submitted in the same way as the original SAE Report and will describe whether the event has resolved or continues, if and how it was treated, and whether the study participant continued or withdrew from study participation.

We do not anticipate any SAEs directly related to iron supplementation in this study. However, accidental ingestion of a large amount of oral iron preparation may result in acute iron poisoning which can manifest as severe diarrhoea, acidosis, shock, and death. Study participants will be educated and strict instructions on iron supplementation given and the need to store them away from children. Study pills will be distributed in child-safe containers. The pills will be taken three times weekly, specifically Mondays, Wednesdays and Fridays.

- *Unanticipated Problems*

An Unanticipated Problem (UP) is any incident, experience or outcome that is:

- Unexpected in terms of nature, severity, or frequency in relation to:
- the research risks that are described in the IRB-approved research protocol and informed consent document; Investigator's Brochure (IB) or other study documents; and
- the characteristics of the population being studied; and

- Possibly, probably, or definitely related to participation in the research; and
- Places study participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized per the IB.

Furthermore, an UP could be an expected event that occurs at a greater frequency than would be expected based on current knowledge of the disease and treatment under study. The DSMB providing oversight to the study may make such an assessment based on an aggregate analysis of events.

- *Severity*

The investigator will evaluate all AEs related to iron supplementation with respect to both seriousness (results in outcomes as above) and **severity** (intensity or grade).

The following generic scale will be used:

Grade 1	Symptoms causing no or minimal interference with usual social and functional activities
Grade 2	Symptoms causing greater than minimal interference with usual social and functional activities
Grade 3	Symptoms causing inability to perform usual social and functional activities
Grade 4	Symptoms causing inability to perform basic self-care functions, or medical or operative intervention indicated to prevent permanent impairment, persistent disability, or death
Grade 5	Events resulting in death

- *Causality*

Causality refers to the likelihood that the event is related to the study intervention. It will be assessed for SAEs and UPs.

The causality assessment is based on available information at the time of the assessment of the event. The investigator may revise these assessments as additional information becomes available.

Expectedness

Expectedness will be assessed for SAEs using the Reference Safety Information section of the IBs for the investigational agent and any study-provided background therapy.

The expectedness assessment is based on available information at the time of the assessment of the event. The investigator may revise these assessments as additional information becomes available.

Schedule for Data Collection and Reporting of Specific Events

Safety assessments will consist of monitoring and recording all AEs related to iron supplementation. It will also include regular monitoring of laboratory assessments including FBC and plasma ferritin.

Steps to limit adverse events due to iron supplementation:

All study participants will be evaluated at each visit as well as during an acute event. Malaria preventive measures will be discussed with all study participants on enrolment, and they will be encouraged to use these preventive measures throughout the study. A history of medical events and potential adverse events will be obtained at each visit. Participants will also be given a card to carry with them at all times providing instructions directed (including contact number of PIs) to any health care provider who sees them for an unscheduled medical care visit. Treatment will be given to those with signs and symptoms suggestive of an adverse event. They will be monitored with a FBC, cultures will be done if bacterial infection suspected and tests for malaria parasites will be done.

Iron supplementation with nutritional counseling for potential blood donors will be given for 4 months (16 weeks). Nutritional counseling for all study subjects receiving iron supplementation will be done at each visit including the need for participants to eat before taking study treatment to help minimize gastrointestinal effects. Participants will also be counseled on potential iron-food interactions and how to minimize that from occurring. A consumer-friendly brochure on safe use of medicines including food interactions and medicine interactions involving iron will be provided to participants.

However, it is anticipated that AEs will occur infrequently in this population. There is no predefined type or frequency of AEs or SAEs for a stopping rule in this study. Review of SAEs and deaths on study will be performed routinely by the DSMB. If a safety concern arises that warrants review for possible study termination, the DSMB (or party identifying such concern) will notify the NHLBI immediately. Enrolment in the study may be temporarily halted for further review of safety data. This further assessment of safety data will include review by the DSMB, which may include a recommendation to terminate the study early. Termination of the clinical study may also occur due to a regulatory authority decision or if the sponsor or regulatory authority decides that subject safety may be compromised by continuing in the study. If the study is halted temporarily or prematurely terminated, a written statement fully documenting the reasons for study halt or termination will be provided to the Institutional Review Board (IRB)/ Independent Ethics Committee (IEC) and NHLBI.

Covid-19 Mitigation Strategies

Staff contact with participants for follow-up biweekly by phone for adherence and feedback. During study visits staff and participants will practice social distancing when possible and wear face masks that cover the mouth and nose. The study will provide facilities for frequent hand washing and alcohol-based sanitizers.

Halting Enrolment for Safety Reasons

The study may be discontinued at any time by the IRB, OSMD/DSMB or NHLBI as part of their duties to ensure that research participants are protected.

Data Analysis

- ***Qualitative Data Analysis***

Qualitative data collection and analysis will proceed simultaneously. In all, ten focus groups of 8-10 participants purposively selected with one group from each blood donation group categories (i) religious organizations, (ii) educational institutions, (iii) corporate institutions, (iv) organized community groups, and (v) walk-in blood donors. The aim of the focus groups is to identify barriers and recommendations for using iron supplementation and nutritional counseling to increase the blood donor pool. These will be gender-sensitive such that each focus group is equality split by gender (e.g., 4-5 females, 4-5 males). The female and male focus groups will meet in separate spaces so only one gender will be present. Thus, there is one male and one female group for each donation category.

Focus Group Discussions will be audio recorded with consent from the participants. Information obtained will be transcribed verbatim and translated when appropriate. The qualitative analysis protocol will include: (1) preliminary exploration of the data by reading through the transcripts and writing memos; (2) coding the data by segmenting and labelling the text; (3) using codes to develop themes by aggregating similar codes together; (4) connecting and interrelating themes; (5) constructing a narrative. Data will be coded and analysed for themes using the Qualitative Software and Research (QSR) Nvivo 1.0 (March 18, 2020).

The qualitative study that will precede the trial will be used to guide implementation and evaluation of the larger study at the UH3 Phase, including identifying barriers and recommendations for using iron supplementation and nutritional counseling to increase the blood donor pool. Moreover, qualitative findings resulting from focus groups to be conducted at the end of the trial at the UG3 phase and key informant interviews will be used to guide the planning, implementation, and evaluation of the UH3 phase.

- ***Quantitative Data Analysis***

Prior to database lock a detailed statistical analysis plan will be written and shared with the DSMB. Here, a summary of the proposed approach is provided.

As data collection proceeds, descriptive statistics will be provided on reports posted to the study website to summarize donor characteristics such as age in years, sex, and first-time donation status. These summaries will be presented in the form of counts and percentages for binary and categorical variables, and medians (with first and third quartiles) for continuous variables. Percentages, means, medians and quartiles will be rounded to one significant digit. The frequency and percent of missing or unknown data will also be presented for each characteristic.

Analytical approaches to the analysis of data from the prevalence study will focus on univariate summaries but will also investigate risk factors for deferral, ID, and IDA. Exact confidence intervals for the probability of deferral, the probability of ID and the probability of IDA will be computed using the method first described by Clopper and Pearson. Logistic regression will be used to assess risk factors for these outcomes. For deferral, these risk factors will include age and sex but likely little else as the data we can obtain for these individuals is limited. For ID and IDA, the role of demographics will be investigated as well as other factors including socio-economic status, medical history, and diet. Final models for the impact of risk factors on deferral, ID, and IDA will include demographics and a selection of covariates found to have a statistically significant univariate association with each of these outcomes.

The analysis for the primary outcome of haemoglobin levels at 4 months will be conducted using a linear model with haemoglobin levels at 4 months as the response variable. It is unlikely that there is a need to transform the response variable as haemoglobin levels are usually symmetrically distributed with tails that decay at rates consistent with the normal distribution. However, if informal univariate assessments of normality (e.g., qq-plots) indicate strong departures from these expectations, the Box-Cox transformation will be used to select a transformation. The set of explanatory variables will be group membership (i.e.,

received iron supplementation or not), baseline haemoglobin, sex, and age. A 1-sided t-test for the regression coefficient associated with group membership will be conducted with a significance level of 0.025 to test the inferiority hypothesis. This analysis will exclude individuals who did not receive iron supplementation at baseline but received it during follow-up due to changes in ferritin or haemoglobin values. The frequency of this will be closely tracked and if more than 10% of participants in the group initially not receiving iron supplementation receive iron supplementation during follow-up, alternative analysis approaches will be considered and presented to the DSMB. At a minimum, sensitivity analyses which include those requiring iron supplementation during follow-up will be pursued. These analyses will include those requiring supplementation during follow-up in each of the 2 groups.

Several secondary outcomes relate to the efficacy of iron supplementation. The treatment of those not requiring iron supplementation at baseline but requiring iron supplementation during follow-up will be the same as for the primary outcome. These secondary outcomes include:

- change in haemoglobin over 4 months,
- ferritin levels at 4 months,
- diagnosis of ID or IDA at 4 months,
- attempt to return for donation within 6 months,
- successful donation within 6 months.

The first 2 of these outcomes will be treated as continuous variables and will serve as response variables in multiple regression models. It is anticipated that there will not be a need to transform the change in haemoglobin (however the Box-Cox transformation will be pursued if there is evidence for skewness), but it is anticipated that ferritin will need to be transformed. Usually logarithmic transformations are required to reduce the skewness of variables of this sort (i.e., measured by an ELISA), and this will be pursued, but other transformations may be more appropriate. The multiple regression models will include group

membership, baseline haemoglobin, baseline ferritin, sex, and age. The remaining 3 outcomes will be examined using logistic regression models with group membership, baseline haemoglobin, baseline ferritin, sex, and age as covariates. A significance level of 5% will be used to determine statistical significance of effects and 95% confidence intervals will be used to summarize effect sizes.

Several secondary outcomes relate to the safety of iron supplementation. To maximize the power to detect an association between group membership and safety outcomes a composite of SAEs, gastro-intestinal problems, malaria, and bacterial infections will be constructed and compared between the groups. The frequency of this composite will be compared between groups using Fisher's exact test. Furthermore, logistic regression models will be fit with group membership, sex, and age as covariates and the odds ratio associated with group membership will be estimated along with a 95% confidence interval. Components of the composite will also be investigated using a similar approach. The incidence of grade 3 or 4 AEs will be treated in a similar fashion. The frequency of responses to specific questions about known side effects to iron supplementation will be compared between the groups using logistic regression, controlling for sex and age. Each question will be investigated in addition to a response to any of the questions.

Since the treatment is not assigned at random there is a strong potential that confounders will introduce bias into the estimates of the treatment effects. As an attempt to remedy this, sensitivity analyses using inverse probability weighting will be conducted. If we use to represent group membership for participant i and Z_i is a vector of predictors for this participant, the first step of the analysis is to estimate the stabilized inverse probability of "treatment" weights W_i for subject i, $W_i = P(X_i = x_i)/P(X_i = x_i|Z_i)$. An estimate of $P(X_i = x_i|Z_{ij})$ can be obtained by logistic regression and $P(X_i = x_i)$ can be estimated by the sample proportion. One then uses these weights in a regression model to adjust for participant characteristics that differ between the groups.

The incidence of ID or IDA will be examined among participants in the control group (who are not ID and do not have IDA at baseline by definition). These estimates will be in the form of events per unit time. If someone is found to be ID or IDA and then resolves that person re-enters the risk pool for an event. To account for multiple events in the same individual, the generalized estimating equation version of Poisson regression will be used with the robust standard error if necessary. The same approach will be used to examine the incidence of ID and IDA separately.

Questionnaires developed to investigate responses to questions around feasibility and acceptability will serve as response variables in logistic (for binary responses) or proportional odds (for Likert scale type responses) regression models with group membership, sex, and age as covariates. There will likely be many such items and no attempt to control for multiple hypothesis testing will be conducted. As such, the results will be interpreted with caution. Additional analyses will include longitudinal models for ID, IDA, haemoglobin levels and ferritin levels. These models will use generalized estimating equations to account for the repeat measurements from subjects. Conventional significance levels will be utilized for model interpretation. Comparison of the results from the cupper sulphate test and haemoglobin levels from the FBC will be examined with logistic regression models. These models will model the probability of the cupper sulphate test being positive as a function of haemoglobin levels. Models will be fit separately for men and women. Exploratory analyses will investigate if age or factors relating to diet impact the nature of this relationship.

Subgroup analyses for the primary endpoint and major secondary outcomes, will be performed to determine whether the intervention differs qualitatively across various baseline-defined subgroups. Subgroup analyses will be performed by age and gender. These analyses will be performed by modelling an interaction between the subgroup factor and group membership and testing the null hypothesis that the regression coefficient associated with the interaction is zero.

If necessary, missing data will be handled by multiple imputation via chained equations (MICE), as implemented in SAS PROC MI procedure[28].

All statistical analyses will be completed using SAS or R by the University of Minnesota (UMN) DCC

Data Monitoring Guidelines for an Independent DSMB

A DSMB will provide independent monitoring of this pilot study in accordance with the BLOODSAFE DSMB charter. The DSMB will have an opportunity to review the protocol and informed consent and provide feedback prior to study initiation. An open report will be prepared by a DCC statistician without access to the data and a closed report will be generated by statisticians from the DCC with access to the full data set. Interim data summaries will be prepared by the DCC statisticians and reviewed at regular intervals by the DSMB (at least twice a year). The DSMB will review adverse event data, other safety data, quality and completeness of study data, and enrolment data at each meeting to ensure proper trial conduct. Study personnel should provide any new literature particularly pertinent to the trial, along with their recommendation as to whether it affects the trial conduct or design. The DSMB will review the consent periodically and/or as needed and consider whether the consent form requires revision in light of any new findings or amendments. In addition to regular meetings, it may be necessary to convene the DSMB urgently on an *ad hoc* basis to discuss new data or other information that raises questions about equipoise, safety, or other issues identified by DSMB members.

DISSEMINATION OF RESULTS

The study results will be disseminated to the National Institute of Health, Ghana Health Service, Hospitals, Community leaders and members, Church leaderships within communities and all other policy makers who are relevant where issues of blood are concerned.

Results of the study will also be disseminated at workshops, conferences and seminars and posted on www.clinicaltrials.gov and published in a peer-reviewed journal.

The final clinical study reports will be submitted to regulatory authorities.

ETHICAL ISSUES

Local Review of Protocol and Informed Consent

The study protocol and consent procedures will be reviewed by the College of Health Sciences (University of Ghana) Institutional Review Board (IRB) and the Ghana Health Service IRB, and written approvals obtained will be from these institutions prior to commencement of the study.

- Ethical Conduct of the Study

The study will be conducted according to the Declaration of Helsinki in its current version; the requirements of Good Clinical Practice (GCP) as defined in Guidelines, EU Clinical Trials Directive (2001/20/EC), and EU GCP Directive (2005/28/EC); International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guidelines; Human Subject Protection and Data Protection Acts; the US Office for Human Research Protections (OHRP); or with the local law and regulation, whichever affords greater protection of human subjects.

- Informed Consent of Study Participants

Eligible participants will be informed about the project in English or their preferred local language by one of the senior project staff trained in obtaining informed consent. Consent and assent forms will be Institutional Review Board (IRB)-approved and the participant will be asked to read and review the document.

The information provided for participants will include a description of the project, potential benefits and risks to themselves, and the expected outcomes and impact of the project. They will be assured of anonymity of their data and that if they choose not to participate it will not affect their normal donor care. They will be allowed time to ask questions and consider whether or not they want to participate before being asked to sign (or thumbprint if they cannot write, witnessed where required by law or regulation) the consent form. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures.

The participants will be given a copy of the signed form and the original will be stored in a locked cabinet which is only accessible to the project team.

The investigators will explain the research study to the participant and answer any questions that may arise. Participants will have the opportunity to carefully review the written consent/assent form and ask questions prior to signing. The participants will be given a copy of the informed consent/assent form so that they may discuss the study with their family or think about it prior to agreeing to participate.

For participants who are under 18 years, where their legal guardian(s) gives consent, the participant will be informed about the study to the extent possible given his/her understanding. If the participant is capable of doing so, he/she will be required to indicate agreement by personally signing and dating the written informed consent document. Participants who turn 18 years during the study period will be required to re-consent.

The ICF used will comply with the International Conference for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) guidelines and regulatory requirements.

Information about common side effects already known about iron supplements, can be found in the protocol. This information will be included in the participant informed consent and will be discussed with the participant during the study as needed. Any new information about this drug that is relevant to this study will lead to an update to the informed consent which will then be discussed with the study participants.

- Confidentiality of Study Participants

At study entry each potential blood donor will be assigned a unique study identification number (Study ID). To maintain confidentiality, study specific ID numbers will be used on all samples and related documentation ensure anonymity (samples will be coded with a distinct identifier to ensure the laboratory is blinded). Participants' privacy will also be maintained using standard operating procedures that are already in place at the National Blood Service for engaging with blood

donors. Briefly these involve interviewing and counseling participants in a private area or by phone after confirming their identity, using a pre-defined procedure.

Standardized questionnaires administered by trained interviewers will be used to collect demographic and clinical information from all study subjects into an electronic form directly linked to a password protected database. This database can only be accessed by investigators or study staff designated by the Principal investigators. Paper consent/assent forms which as a matter of necessity have participant names or initials and signatures on them, will be stored securely in a locked cabinet at the study site and accessible only to the principal investigators. These will be stored for 3 years after study procedures, primary analyses, study publications are completed. They will be destroyed by agencies that provide such services. The data collection on all study subjects will conform to requirements of international legislation on data protection. Databases will be password protected. The electronic databases will be kept for a minimum of 5 to 10 years after completion of study reports and publications. No study participant will be identified in data collection, publication, meeting abstract or report derived from the study results or the information collected. Regular data backups will mitigate against risks of fire/flooding. All personnel who handle any personal data will be required to undertake and maintain Good Clinical Practice (GCP) and Human Subjects Protection (HSP) training.

- Regulatory Oversight

Before initiating this trial, we will obtain approval/favourable opinion from the Steering Committee, DCC, PRC/ NHLBI and IRB/IEC for the trial protocol, written ICF, consent form updates, participant recruitment procedures and any other written information to be provided to study participants. Prior to study start, all of the instructions and procedures found in this protocol will be read and accepted by study team. An inspection of the clinical site (site initiation visit) will be done by NHLBI (or a designated representative) before start of study. This visit may be virtual due to the ongoing COVID-19 pandemic.

Monitoring will occur in coordination with the DCC, the PI and an independent DSMB. Regulatory requirements and site level interim monitoring will be tracked by the DCC. The PI will ensure the required documentation is available to the DCC and site monitoring personnel. The US National Heart, Lung, and Blood Institute (NHLBI) will be responsible for providing program oversight through an independent DSMB.

Study initiation and site initiation

This pilot study will be registered on clinicaltrials.gov by the DCC prior to enrolment into the trial.

The principal investigator will ensure the required documentation has been submitted to the DCC for each site participating in this pilot study. This includes:

- A federal-wide Assurance (FWA) number and expiration date
- The required IRB numbers linked to the FWA.
- The required IRB approval letters (original letter and an English translation if not in English and a Translation Verification Statement in the latter case)
- Approved site consent (if different from overall consent, and if not in English, an English translation, and a Translation Verification Statement)
- Information on the investigator of record (name, contact information, completion date of HSP training, completion date of Good Clinical Practice (GCP) training, a signed investigator of record form, and a signed curriculum vitae).
- Medical license of investigator of record
- Information on sub-investigators (name, contact information, completion date of Human Subjects Protection (HSP) training, completion date of GCP training, and a signed curriculum vitae)
- Information on study coordinator (name, contact information, completion date of HSP training, completion date of GCP training, and a signed curriculum vitae)

Laboratory reference ranges (and if available online, URL).

Data collection towards the objectives of this pilot study will not be initiated until the required documentation has been reviewed by the DCC and a site activation letter has been issued to the site investigator of record and the protocol PI.

Interim site level monitoring

In addition, all individuals participating in this pilot study will need to sign an ICF. All study sites will maintain a copy of the ICF for all participants at that study site. Any individuals who are less than 18 years old will have an ICF signed by a parent or other representative with required assent as needed. Upon a site monitoring visit, study data and case report forms will be made available to site monitoring personnel.

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APPENDICES

APPENDIX 1 –Data Collection Instruments

FOCUS GROUP DISCUSSION GUIDE

Aim: *To identify barriers and recommendations for using iron supplementation and nutritional counseling to increase the blood donor pool.*

DATE: _____ LOCATION: _____
NUMBER OF FGD PARTICIPANTS: _____
FGD FACILITATOR: _____
FGD NOTE-TAKER: _____
FGD START TIME (HH:MM): _____
FGD END TIME (HH:MM): _____

Welcome the focus group participants:

Good morning/afternoon. My name is _____ and I will be your moderator for this focus group discussion. I am part of the BLOODSAFE Project Team, which is a group of researchers from within and outside of Ghana carrying out a study to understand and improve blood donation in Ghana.

I am a trained focus group moderator and I would like to hear your honest opinions about the topics we will discuss today. There is no right or wrong answer to the questions I'm going to ask. Please just relax and enjoy the discussion.

Please keep in mind that your participation is completely voluntary. If for any reason you wish to leave the discussion, you may do so.

I am accompanied by_____ who will be responsible for note taking. Other project staff from the Project Team will also be in the room observing the focus group discussion. Kindly state whether it is okay to continue with the discussion.

Rules or Guidelines

- You have been invited here to offer your views and opinions. We will like to have a successful discussion where everyone feels comfortable expressing their perspectives and opinions
- Again, there are no right or wrong answers and it is okay to be critical. I want to hear your views and opinions about whether you like or dislike something you see or hear.
- There will be observers.
- You may excuse yourself from the conversation at any time for any reason.

- This session will be audio taped so that we can capture everything being discussed today, for the purpose of listening to it again to get the message well. All the discussions will remain confidential. Please feel free to say exactly what is on your mind as nothing will be attributed to any particular person in our report.
- Everyone's participation is important.
- Please speak one at a time and avoid side conversations.
- Please use any of your names that you are comfortable with only during the discussion.
- Respect each other's opinions.
- Lastly, please turn off the ringers on your cell phones.

Views from Individual Members in the FGD

Demography and social characteristics of participants

- Name: _____
- Name of Community (Group): _____
- Age: _____
- Sex: _____
- Highest Educational level attained: _____
- Religion: _____
- Ethnic background: _____
- Occupation: _____

You participated in this project, which involved blood donors.

- How did the project influence your knowledge about iron supplementation for deferred blood donors?

  Probe:
  - *Are you aware of any cultural reasons why people do not use iron supplements?*
  - *Are you aware of any religious reasons why people do not use iron supplements?*
  - *Did it increase your awareness of iron supplements?*
  - *Did it improve your knowledge on the usefulness of iron supplements?*
  - *Do you believe people will like to use iron supplements after the project?*

- How did the project influence your attitudes to iron supplementation for deferred blood donors?

  Probe:
  - *Are you aware of any cultural reasons why people do not use iron supplements?*
  - *Are you aware of any religious reasons why people do not use iron supplements?*
  - *Did it increase your attitude to use of iron supplements?*
  - *Do you believe people will like to use iron supplements after the project?*

- How did the project influence your beliefs about iron supplementation for deferred blood donors?

  Probe:
  - *Are you aware of any cultural beliefs why people do not use iron supplements?*
  - *Are you aware of any religious beliefs why people do not use iron supplements?*
  - *Did it influence your beliefs (either positively or negatively) of iron supplements?*
  - *Do you believe people will like to use iron supplements after the project?*

- What influenced your participation in this project?

  Probe:
  - *Was the colour of the iron supplement culturally acceptable?*
  - *Was the dosage of the iron supplement culturally acceptable?*
  - *Did taking these supplement affect your participation, negatively or positively?*
  - *Was there in any religious and cultural aspects of your life that affected how you participated in the project generally?*

- Please describe the counselling you received about iron supplementation?

  Probe:
  - *Were you given adequate information and guidance on eating iron or micronutrient-rich foods?*
  - *Were any cultural or religious concerns or inhibitions to eating these foods addressed?*

- *Were there issues you did not understand during the counselling sessions?*
- *Were there issues you disagreed with during the counselling sessions?*
- *What other information would have preferred to receive?*

- How will you describe the quality of the nutritional counselling you received as part of the project?

  Probe:
  - *Were you given adequate information and guidance on nutrition?*
  - *Were any cultural or religious concerns or inhibitions on adequate nutrition addressed?*
  - *Were there issues you did not understand during the counselling sessions?*
  - *Were there issues you disagreed with during the counselling sessions?*
  - *What other information would have preferred to receive?*

- From your experience, what do you consider as barriers to people like you participating in an iron supplementation and nutritional counselling project?

  Probe:
  - *Do you have any concerns or fears in being able to adhere to the use of the iron supplements/ medications?*
  - *Do you have any concerns or fears on the side effects of the medications?*
  - *Do you have any concerns in making time for the counselling sessions and visits?*
  - *Do you have any concerns or fears of repeat donation if your iron stores improve?*
  - *Do you have any concerns or fears that iron supplements may cause you to eat more?*
  - *Do you have any concerns or fears that iron supplements may cause you to eat more and come with additional cost to you?*

- How do you think we could carry out this intervention differently to ensure people participate fully?

  Probe:
  What do you propose to be solutions to these?

- *Concerns or fears in being able to adhere to the use of the iron supplements/ medications?*
- *Concerns or fears on the side effects of the medications?*
- *Concerns in making time for the counselling sessions and visits?*
- *Concerns or fears of repeat donation if your iron stores improve?*
- *Concerns or fears that iron supplements may cause you to eat more?*
- *Concerns or fears that iron supplements may cause you to eat more and come with additional cost to you?*

- What recommendations do you have for using iron supplementation and nutritional counselling for improving the blood donor pool?

  Probe:
  - *Do you have any ideas from the discussions so far on the use of iron supplementation and nutritional counselling for improving the blood donor pool in Ghana?*

Composite Views from Members in the FGD

- How many participants have ever donated blood? _____
- For those who have never donated, what are the main reasons?
  _____
  _____
  _____
  _____
  _____
- How many times have participants been donating blood? average:_____ minimum:_____ maximum: _____
- How long ago was the last donation? average:_____ minimum: _____ maximum: _____
- How many participants have ever used iron supplementation after blood donation?
  _____
- How many participants have ever had nutritional counselling after blood donation?
  _____

- What are the views of participants on the usefulness of iron supplementation and nutritional counselling after blood donation?

  _____

- What have been the major barriers to blood donation in the community/ cluster?

  _____
  _____
  _____
  _____

- What are the key suggestions / recommendation to improve blood donation in the community/group?

  _____
  _____
  _____
  _____
  _____

- What will make participants be willing to re-donate blood?

  _____
  _____
  _____
  _____
  _____

- Any other comments you have on the project?

  _____
  _____
  _____
  _____
  _____
  _____

KEY INFORMANT INTERVIEW GUIDE

Basic characteristics

- Name: _____
- Age: _____
- Sex: _____

- Designation/position _____
- Organization: _____

- How do you envisage iron supplementation to influence knowledge of deferred blood donors?

  Probe:
  - *Are you aware of any cultural reasons why people do not use iron supplements?*
  - *Are you aware of any religious reasons why people do not use iron supplements?*
  - *Do you believe people will like to use iron supplements after the project?*

- How do you envisage iron supplementation to influence attitudes of deferred blood donors?

  Probe:
  - *Are you aware of any cultural attitudes why people do not use iron supplements?*
  - *Are you aware of any religious attitudes why people do not use iron supplements?*
  - *Do you believe people will like to use iron supplements after the project?*

- How do you envisage iron supplementation to influence belief systems of deferred blood donors?

  Probe:
  - *Are you aware of any cultural beliefs why people do not use iron supplements?*
  - *Are you aware of any religious beliefs why people do not use iron supplements?*
  - *Do you believe people will like to use iron supplements after the project?*

- What aspects of your culture affected your participation in the project?

  Probe:
  - *Will the colour of the iron supplement affect culturally acceptability?*
  - *Will the dosage (number of tablets or frequency of dosing in a day) of the iron supplement affect culturally acceptability?*

- *Are there in any religious and cultural aspects that may influence the use of iron supplementation by deferred donors?*

- What should go into the quality and quantity of the counseling on taking iron as recommended for deferred blood donors?

  Probe:
  - *What key issues should be discussed?*
  - *What other information would you preferred to include?*

- From your experience, what do you consider as barriers to deferred donors participating in an iron supplementation and nutritional counseling project?

  Probe:
  - *What are the fears and concerns?*

- What do you consider as solutions to the barriers?

  Probe:

  What do you propose to be solutions to these?
  - *Concerns or fears in being able to adhere to the use of the iron supplements/ medications*
  - *Concerns or fears on the side effects of the medications*
  - *Concerns in making time for the counseling sessions and visits?*
  - *Do you have any concerns or fears of repeat donation if iron stores improve?*

- What recommendations do you have for using iron supplementation and nutritional counseling for improving the blood donor pool?

  Probe:
  - *Do you have any ideas from the discussions so far on the use of iron supplementation and nutritional counseling for improving the blood donor pool in Ghana?*

- Any policy guide or direction on use of iron supplementation for deferred blood donors?

APPENDIX 2: Informed Consent Forms

PARTICIPANT INFORMATION AND CONSENT TO BE PART OF A RESEARCH STUDY
ON BLOOD SAFETY AND AVAILABILITY

Protocol Title: ***Iron supplementation and nutritional counselling interventions to improve availability and safety of blood in Ghana*****.**

Participant number: _____

Name of Investigator: _____

Hello, my name is _____. I am a Study Doctor/Research Assistant. I would like to invite you to consider participating in a research study entitled '*Iron supplementation and nutritional counselling interventions to improve availability and safety of blood in Ghana*.

Principal Investigators:

Dr Yvonne Dei-Adomakoh

Consultant Haematologist,

Department of Haematology,

University of Ghana Medical School

Phone: +233-24-355-0980,

Email: yadei-adomakoh@ug.edu.gh

Dr Lucy Asamoah- Akuoko

Head, Research and Development,

National Blood Service, Korle-Bu, Accra

Phone: +233206301006

Email: lucyasamoah@yahoo.com

1. Why have I been given this document to read?

We would like to invite you to join this research study to find out if giving iron pills will improve the nutritional status and blood level of blood donors with anaemia so that they will be able to donate blood.

Participants signing this consent form will be aged 18 years and older. Please read the information carefully and discuss it with the study doctors and family. The study doctors will be happy to answer all questions.

Decision to participate in this study is voluntary. This means:

- You are free to decide to participate in this study or not
- You are free to stop study treatment and study-related activities at any time and without the need of giving any reason

- If you do not want to participate in this study, then this decision will not affect your care as a blood donor

This trial protocol has been submitted to the College of Health Sciences Ethical Review Board and has been granted written approval.

2. What is the purpose of this study?

This trial is funded by National Heart, Lung, and Blood Institute (NHLBI), USA.

The amount of iron that a blood donor has is an important safety issue. Iron deficiency is initially without anaemia and affects red blood cell production only. Without intervention anaemia occurs. Major causes of iron deficiency are inadequate dietary iron, reduced absorption and loss of iron. Knowledge of donors' iron status provides evidence for blood centres to provide appropriate and timely donor care. With deferrals from donation-induced anaemia minimized, more willing blood donors are fit enough to repeat blood donations on schedule, thus contributing to blood adequacy for patients requiring blood transfusion therapy.

This project is directed towards transforming the blood donor pool in Ghana from family replacement donations to sustainable voluntary collections.

What do I need to know if I join this study?

The study is designed as an open label trial with nutrition counselling and iron supplementation. Iron supplementation will be an oral medication and will be given for 4 months duration. 291 other participants may be recruited to join the study.

If you accept to participate baseline assessment will be conducted. Those who are found to have adequate iron will receive counselling on good nutrition only. Those found to have very low iron stores will be invited to share baseline assessment results and then referred to a doctor specializing in care for those with very low iron stores. Those who are found to be moderately low in iron stores will receive both nutritional counselling and oral iron supplementation. For these participants, iron supplementation will be prescribed by a haematologist in accordance with standard treatment guidelines for Ghana and this will include education on side effects of iron supplementation. Those study participants who are moderately low in iron will be given a two-month supply of the iron tablets by the study pharmacist, which they will take home. They will be instructed to take the iron tablets with water 3 times in a week. All participants will receive standard nutritional counselling provided by the study nutritionist and trained counsellors. The duration of the intervention period is 4 months with two interim visits (approximately 2 months apart) and a final visit at 6 months.

Following baseline assessments, all study participants will have blood sampling done every 8 weeks for Full Blood Count (FBC), peripheral film comment, malaria RDT and ferritin concentration, with follow-up phone calls to see how you are doing and if you are taking your pills if you are receiving any. Any participant who started with adequate iron stores and is later found to have moderately low iron stores will be given iron supplementation. Any participant who is found to have very low iron stores over the course of the study will be referred to a doctor specializing in care for those with very low iron stores.

In case you experience concerning signs or symptoms, kindly call a study doctor.

In addition, you might be asked, through another questionnaire, to provide feedback and take part in our focus group discussion, on your personal experience in this trial. This is optional and will not affect the care you receive. It might help to improve the trial experience for others in the future. Side effects reported as part of a feedback questionnaire, may need to be shared with the study doctors or study team, who will follow up to collect more information. All other feedback will remain anonymous and confidential.

After the study is completed and all data examined, a summary of the study results will be shared with the National Blood Service Ghana (NBSG). The NBSG may share these results with you if you wish.

3. Can I decide to stop my participation in the study?

You are free to stop your participation in this study at any time by notifying the study doctors/research assistants.

The information already collected during the study including samples (defined as Personal Data in this consent) will still be used together with the data collected from other participants in the study according to this informed consent.

We still care about how everything is going therefore, the study research assistant may ask if they can call you to check on you.

4. Can I withdraw my consent to collect and use my Personal Data?

You may decide to withdraw your consent from this study by informing your study doctor at any time in writing. This means that full participation in the study will be stopped and any further collection of your Personal Data.

The study team will continue to keep and use your collected study information (including any data resulting from the analysis of your samples until your time of withdrawal) according to applicable law. This is done to guarantee the validity of the study, to determine the effects of the study treatment, and to ensure complete study documentation.

5. Are there any reasons that my study treatment or participation may be stopped early?

The study doctor may remove you from this study for any justified reason and will discuss your options.

Examples why you may have to stop some or all study-related activities, including study treatment are:

i. You need treatment that is not allowed in this study
ii. Instructions for the study are not being followed
iii. You become pregnant (for female participants)
iv. Side effects from the study treatment are unacceptable
v. The study doctor thinks keeping you in the study might be harmful and/or is not in your best interest

6. Who owns the data and results created during the study?

NHLBI and study team will own all data and results created during this study.

7. What are the possible benefits if I join this study?

This study might not be of direct benefit for you however, with your participation in this research, the results of this research will likely help us better understand acceptability of iron supplementation among blood donors deferred for iron deficiency anaemia and other reasons why people do not donate blood. Additionally, this research will help us find a strategy to manage and prevent prospective blood donors with iron deficiency and iron deficiency anaemia thereby improving the voluntary blood donor pool in Ghana.

8. What are the possible risks if I join this study?

Some risks or discomforts may be experienced. Collecting blood from a vein in someone's arm is a standard medical procedure, although you may feel some pain where we use the needle to take blood from your vein. You may get a bruise from the needle. Some people feel faint when they give a blood sample. In addition, side effects usually minor, may be experienced when taking iron tablets and include: unpleasant taste, constipation, dark stools, nausea, vomiting, abdominal pain and diarrhoea.

Kindly tell us about any unusual effects even when these effects are mild.

9. What are my responsibilities and are there any costs for me if I agree to join this study?

Follow the instructions given by the study doctor and staff. Attend all of the study appointments. If you have to miss an appointment, reschedule with the study doctor or research assistant. Inform the study doctor about any medicines you are currently taking or may take during the course of the study (e.g. prescription, vitamins, over the counter herbal supplements etc.) You will be reimbursed for out of pocket expenses to and from the study site. A minimum amount of 10 USD (in cedi equivalent) per visit will be reimbursed for such expenses. If study related costs exceed the specified amount and you have proof of such expenses, please discuss it with the study team.

10. Your rights as a Participant

This research has been reviewed and approved by the Ethical and Protocol Review Committee of the College of Health Sciences (CHS-EPRC). If you have any questions about your rights as a research participant you can contact the College of Health Sciences EPRC office (UGMS Research Office, GEMP Building, Korle-Bu) between the hours of 8am-5pm through the landline +233 03-02-665103/4 or email addresses: eprc@chs.edu.gh.

11. Where can I receive more information?

If you are injured because of the study or if you have questions about the study, please contact:

Study Doctor: .....

Telephone number: .....

After office hours number: .....

VOLUNTEER AGREEMENT

The above document describing the benefits, risks and procedures for the research title '*Iron supplementation and nutritional counselling interventions to improve availability and safety of blood in Ghana'* has been read and explained to me. I have been given an opportunity to have any questions about the research answered to my satisfaction. I agree to participate as a volunteer.

_____ _____

Date Name and signature or mark of volunteer

If volunteers cannot read the form themselves, a witness must sign here:

I was present while the benefits, risks and procedures were read to the volunteer. All questions were answered and the volunteer has agreed to take part in the research.

_____	_____
Date	Name and signature of witness

I certify that the nature and purpose, the potential benefits, and possible risks associated with participating in this research have been explained to the above individual.

_____	_____
Date	Name Signature of Person Who Obtained Consent

ASSENT FORM FOR 17-YEAR-OLD PARTICIPANTS

Protocol Title: ***Iron supplementation and nutritional counselling interventions to improve availability and safety of blood in Ghana*.**

Participant number:_____

Name of Investigator: _____

Hello, my name is _____. I am a Study doctor/Research Assistant. I would like to invite you to consider participating in a research study entitled '***Iron supplementation and nutritional counselling interventions to improve availability and safety of blood in Ghana*.**

Principal Investigators:

Dr Yvonne Dei-Adomakoh

Consultant Haematologist,

Department of Haematology,

University of Ghana Medical School

Phone: +233-24-355-0980,

Email: yadei-adomakoh@ug.edu.gh

Dr Lucy Asamoah- Akuoko

Head, Research and Development,

National Blood Service, Korle-Bu, Accra

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1. Why have I been given this document to read?

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Participants signing this consent form will be aged 18 years and older. Please read the information carefully and discuss it with the study doctors and family. The study doctors will be happy to answer all questions.

Decision to participate in this study is voluntary. This means:

- You are free to decide to participate in this study or not
- You are free to stop study treatment and study-related activities at any time and without the need of giving any reason

- If you do not want to participate in this study, then this decision will not affect your care as a blood donor

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2. What is the purpose of this study?

This trial is funded by National Heart, Lung, and Blood Institute (NHLBI), USA.

The amount of iron that a blood donor has is an important safety issue. Iron deficiency is initially without anaemia and affects red blood cell production only. Without intervention anaemia occurs. Major causes of iron deficiency are inadequate dietary iron, reduced absorption and loss of iron. Knowledge of donors' iron status provides evidence for blood centres to provide appropriate and timely donor care. With deferrals from donation-induced anaemia minimized, more willing blood donors are fit enough to repeat blood donations on schedule, thus contributing to blood adequacy for patients requiring blood transfusion therapy.

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If you accept to participate baseline assessment will be conducted. Those who are found to have adequate iron will receive counselling on good nutrition only. Those found to have very low iron stores will be invited to share baseline assessment results and then referred to a doctor specializing in care for those with very low iron stores. Those who are found to be moderately low in iron stores will receive both nutritional counselling and oral iron supplementation. For these participants, iron supplementation will be prescribed by a haematologist in accordance with standard treatment guidelines for Ghana and this will include education on side effects of iron supplementation. Those study participants who are moderately low in iron will be given a two-month supply of the iron tablets by the study pharmacist, which they will take home. They will be instructed to take the iron tablets with water 3 times in a week. All participants will receive standard nutritional counselling provided by the study nutritionist and trained counsellors. The duration of the intervention period is 4 months with two interim visits (approximately 2 months apart) and a final visit at 6 months.

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In case you experience concerning signs or symptoms, kindly call a study doctor.

In addition, you might be asked, through another questionnaire, to provide feedback and take part in our focus group discussion, on your personal experience in this trial. This is optional and will not affect the care you receive. It might help to improve the trial experience for others in the future. Side effects reported as part of a feedback questionnaire, may need to be shared with the study doctors or study team, who will follow up to collect more information. All other feedback will remain anonymous and confidential.

After the study is completed and all data examined, a summary of the study results will be shared with the National Blood Service Ghana (NBSG). The NBSG may share these results with you if you wish.

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6. Are there any reasons that my study treatment or participation may be stopped early?

The study doctor may remove you from this study for any justified reason and will discuss your options.

Examples why you may have to stop some or all study-related activities, including study treatment are:

vi. You need treatment that is not allowed in this study
vii. Instructions for the study are not being followed
viii. You become pregnant (for female participants)
ix. Side effects from the study treatment are unacceptable
x. The study doctor thinks keeping you in the study might be harmful and/or is not in your best interest

7. Who owns the data and results created during the study?

NHLBI and study team will own all data and results created during this study.

8. What are the possible benefits if I join this study?

This study might not be of direct benefit however, with your participation in this research, the results of this research will likely help us better understand acceptability of iron supplementation among blood donors deferred for iron deficiency anaemia and other reasons why people do not donate blood. Additionally, this research will help us find a strategy to manage and prevent prospective blood donors with iron deficiency and iron deficiency anaemia thereby improving the voluntary blood donor pool in Ghana.

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Some risks or discomforts may be experienced. Collecting blood from a vein in someone's arm is a standard medical procedure, although you may feel some pain where we use the needle to take blood from your vein. You may get a bruise from the needle. Some people feel faint when they give a blood sample. In addition, side effects usually minor, may be experienced when taking iron tablets and include: unpleasant taste, constipation, dark stools, nausea, vomiting, abdominal pain and diarrhoea.

Kindly tell us about any unusual effects even when these effects are mild.

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Follow the instructions given by the study doctor and staff. Attend all of the study appointments. If you have to miss an appointment, reschedule with the study

doctor or research assistant. Inform the study doctor about any medicines you are currently taking or may take during the course of the study (e.g. prescription, vitamins, over the counter herbal supplements etc.) You will be reimbursed for out of pocket expenses to and from the study site. A minimum amount of 10 USD (in cedi equivalent) per visit will be reimbursed for such expenses. If study related costs exceed the specified amount and you have proof of such expenses, please discuss it with the study team.

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Where can I find more information?

If you are injured because of the study or if you have questions about the study, please contact:

Study Doctor: .....

Telephone number: .....

After office hours number: .....

VOLUNTEER AGREEMENT

The above document describing the benefits, risks and procedures for the research title '***Iron supplementation and nutritional counselling interventions to improve availability and safety of blood in Ghana*** has been read and explained to me. I have been given an opportunity to have any questions about the research answered to my satisfaction. I agree to participate as a volunteer.

_____ _____

Date Name and signature or mark of volunteer

A parent or Guardian must sign here:

I was present while the benefits, risks and procedures were read to the volunteer. All questions were answered and the volunteer has agreed to take part in the research.

_____ _____

Date Name and signature of parent/guardian

I certify that the nature and purpose, the potential benefits, and possible risks associated with participating in this research have been explained to the above individual.

_____ _____

Date Name Signature of Person Who Obtained Consent

PARTICIPANT INFORMATION SHEET FOR FOCUS GROUP DISCUSSION

Title of Study: - ***Iron supplementation and nutritional counseling interventions to improve availability and safety of blood in Ghana***

Introduction

Thank you for taking the time to listen to what I have to say. My name is _____, and I am here because I am working on behalf of BLOODSAFE GHANA concerning the documentation of iron deficiency anaemia in blood donors. This work is being led by Dr. Yvonne Dei-Adomakoh from the Department of Haematology, University of Ghana Medical School/ Korle Bu Teaching Hospital. Her telephone number is 0243550980, and her email is deiadom@yahoo.com.

Background and Purpose of research

The amount of iron that a blood donor has is an important safety issue. Iron deficiency is initially without anaemia, manifesting as reduced iron stores (iron depletion) affecting red blood cell production, and without intervention is complicated by overt anaemia. Major causes of iron deficiency are inadequate dietary iron, reduced absorption and loss of iron. With continuous loss of iron from repeat whole blood donations and inadequate replacement, blood donors inevitably develop iron deficiency and, later, iron deficiency anaemia. Knowledge of donors' iron status provides evidence for blood centres to provide appropriate and timely donor care. With deferrals from donation-induced anaemia minimized, more willing blood donors are fit enough to repeat blood donations on schedule, thus contributing to blood adequacy for patients requiring blood transfusion therapy.

This project is directed towards transforming the blood donor pool in Ghana from family replacement donations to sustainable voluntary collections, in support of Ghana's national blood policy that aims at a 100% voluntary blood donation pool to secure and sustain an adequate and safe blood supply. Treatment of iron deficiency and iron deficiency anaemia require iron supplementation as well as nutritional counseling as standard of care in Ghana.

Nature of research

We are aiming to have a discussion with you concerning your knowledge about blood transfusion practices and iron deficiency anaemia in Ghana. All interviews and other data collected as part of this documentation will be summarized into a report for the Data Collecting Centre (DCC) based in the University of Minnesota, USA, and the National Heart Lung Blood Institute (NHLBI), USA, which may be shared with others.

Participant's involvement

We would like to ask you to take part in this discussion. If you agree to do so, we will ask you questions concerning iron deficiency anaemia, iron supplementation, nutrition interventions for blood donors, factors that contribute to iron deficiency anaemia, cultural practices that may affect iron supplementation. The discussion will last up to one hour of your time. The discussions will be audio recorded.

Potential Risks

Some of the issues we will discuss with you may make you uncomfortable, because you may have to talk about the performance of a project/intervention you were involved in. You may feel tired whilst going through the interview. Having an interview with the researcher may expose you to COVID-19. Apart from these, we do not think there are any other major risks associated with your participation.

To prevent the spread of COVID-19, we will do the following to protect you:

- All field workers will wear a face mask throughout all project activities.
- We will provide a face mask for study participants attending a data collection session if they arrived at the session without a mask.
- Before data collection, one field worker will check the temperature of each participant using a thermometer gun. He/she will also ask whether the participant has a cough/cold, difficulty in breathing or sore throat. Anyone with a temperature above 37.4°C (i.e. considered to have fever) and/or showing flu-like symptoms will be asked to return home and subsequently seek medical attention.
- We will spend at least 5 minutes each morning before the start of work to educate participants who have come for office visit on Covid-19. In addition, videos on Covid-19 measures will be shown to the participants. We will display approved health promotion materials on COVID-19 at vantage points to remind study workers and participants to keep to social distancing protocols, wearing of the masks, regular handwashing, coughing and sneezing etiquettes.
- We will maintain at least 2m distance between participants at all time during project work.
- Interviews will be conducted in a place with adequate ventilation (i.e. open windows to allow for the maximum circulation of fresh air, if possible, avoid confined air-conditioned rooms) as much as possible.
- We will provide handwashing and drying facilities including liquid soap, running water and paper napkins and/or FDA-approved alcohol-based hand sanitizer at interview venues so participants can wash/sanitize their hands.

Benefits
You will not benefit directly by participating in this discussion, but the report we will produce will help to further efforts to address iron deficiency anaemia among blood donors and hopefully will improve donor care and increase voluntary blood donations in Ghana.

Costs
If you take part in this interview, it will not cost you any money.

Compensation
We will give participants a hand sanitizer as a small gift for your participation.

Confidentiality
The information you provide will be protected to the best of our ability. The things you tell us will be kept securely by the DCC, NHLBI and the Research Team. The data generated in this documentation will be stored for 5 years after completing this documentation and after the 5 years, we will work with the DCC, to ensure that the data are destroyed correctly, without being able to be recreated. Your name will not be mentioned in any in any public communications, documents or reports and all the things we will hear from participants will be put together as one so that people won't know anything about you.

Voluntary participation/withdrawal
You are free to decide if you want to take in the interview. Participation is entirely voluntary. In the course of the interview, you may choose not to answer a question at any time without penalty and without having to give any reasons.

Outcome and Feedback
After we have finished the documentation, the DCC and NHLBI will know the findings.

Funding information

This study is being sponsored (funded) by National Heart, Lung, and Blood Institute (NHLBI), USA.

Sharing of participants Information/Data
The DCC and NHLBI, will solely own the data that will be generated from the study.

Provision of Information and Consent for participants
A copy of the Information sheet and Consent form will be given to you after it has been signed or thumb-printed to keep.

Whom to Contact for Further Clarification/Questions:

Key study contacts:	
Dr. Yvonne Dei- Adomakoh (Principal Investigator) Department of Haematology, Korle-Bu Teaching Hospital Tel: +233 243 550980 Email: deiadom@yahoo.com yadei-adomakoh@ug.edu.gh	**Dr Lucy Asamoah- Akuoko (Principal Investigator)** Head, Research and Development National Blood Service, Ghana Tel: +233 302 663701 Ext 339 lucyasamoah@yahoo.com

For further clarification on ethical issues and rights of participants, contact:
Administrator
College of Health Sciences ethical committee
Tel: +233 03-02-665103/4
Email: eprc@chs.edu.gh

PARTICIPANT INFORMATION SHEET FOR KEY INFORMANTS

Title of Study: - ***Iron supplementation and nutritional counseling interventions to improve availability and safety of blood in Ghana***

Introduction

Thank you for taking the time to listen to what I have to say. My name is _____, and I am here because I am working on behalf of BLOODSAFE GHANA concerning the documentation of iron deficiency anaemia in blood donors. This work is being led by Dr. Yvonne Dei-Adomakoh from the Department of Haematology, University of Ghana Medical School/ Korle Bu Teaching Hospital. Her telephone number is 0243550980, and her email is deiadom@yahoo.com.

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This project is directed towards transforming the blood donor pool in Ghana from family replacement donations to sustainable voluntary collections, in support of Ghana's national blood policy that aims at a 100% voluntary blood donation pool to secure and sustain an adequate and safe blood supply. Treatment of iron deficiency and iron deficiency anaemia require iron supplementation as well as nutritional counseling as standard of care in Ghana.

Nature of research

We are aiming to have interviews with key informants (*Director and Deputy-Southern Zone Blood Service, Director- Family Health Division-GHS, Deputy Director- Reproductive and Child Health –GHS*, Staff of the national blood service Ghana, study team) who have experience working with blood donors and have taken part in blood donation drives for over 2 years or being instrumental in the design and implementation of national blood policies and programs. All interviews and other data collected as part of this documentation will be summarized into a report for the funding agency, the National Heart, Lung, Blood Institute (NHLBI), USA, and the Data Collecting Centre (DCC) based in the University of Minnesota, USA.

Participants' involvement

We would like to ask you to take part in this interview. If you agree to do so, we will ask you questions concerning iron deficiency anaemia, iron supplementation, nutrition interventions for blood donors, factors that contribute to iron deficiency anaemia, cultural practices that may affect iron supplementation. The interview will last up to 30 minutes of your time. The interviews will be audio recorded.

Potential Risks

Some of the issues we will discuss with you may make you uncomfortable, because you may have to talk about the performance of a project/intervention you were involved in. You may feel tired whilst going through the interview. Having an interview with the researcher may expose you to COVID-19. Apart from these, we do not think there are any other major risks associated with your participation.

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After we have finished the documentation, the DCC and NHLBI will know the findings.

Funding information

This study is being sponsored (funded) by National Heart, Lung, and Blood Institute (NHLBI), USA.

Sharing of participants Information/Data
The DCC and NHLBI, will solely own the data that will be generated from the study.

Provision of Information and Consent for participants
A copy of the Information sheet and Consent form will be given to you after it has been signed or thumb-printed to keep.

Whom to Contact for Further Clarification/Questions:

Key study contacts:	
Dr. Yvonne Dei-Adomakoh (Principal Investigator) Department of Haematology, Korle-Bu Teaching Hospital Tel: +233 243 550980 Email: deiadom@yahoo.com yadei-adomakoh@ug.edu.gh	**Dr Lucy Asamoah-Akuoko (Principal Investigator)** Head, Research and Development National Blood Service, Ghana Tel: +233 302 663701 Ext 339 lucyasamoah@yahoo.com

For further clarification on ethical issues and rights of participants, contact:
Administrator
College of Health Sciences ethical committee
Tel: +233 03-02-665103/4
Email: eprc@chs.edu.gh

CONSENT FORM - KEY INFORMANTS

STUDY TITLE: ***Iron supplementation and nutritional counseling interventions to improve availability and safety of blood in Ghana***

Participant's Statement

I acknowledge that I have read or have had the purpose and contents of the Participants' Information Sheet read and all questions satisfactorily explained to me in a language I understand (English, Ga, Twi). I fully understand the contents and any potential implications as well as my right to change my mind (i.e. withdraw from the research) even after I have signed this form.

I voluntarily agree to be part of this research.
Name of Participant_____

Participant's Signature _____or Thumb Print_____

Date: _____

Our interview with you may be recorded. However, before we can record the interview, we need your consent. All recordings will be kept securely by the Department of Haematology, University of Ghana and the DCC. Your personal information will not be used to label audio recordings and transcriptions. Identification codes will be assigned to you. If you agree or not agree that we should record the interview, kindly indicate below:

	Should we record this interview? ***(Kindly tick if you want to be record or not)***
Yes	
No	

Interpreter's Statement

I interpreted the purpose and contents of the Participants' Information Sheet to the afore named participant to the best of my ability in the (English, Ga, Twi) language to his proper understanding.
All questions, appropriate clarifications sort by the participant and answers were also duly interpreted to his/her satisfaction.
Name of Interpreter_____

Interpreter's Signature _____or Thumb Print_____
Date: _____

Contact Details_____
_____

Statement of Witness

I was present when the purpose and contents of the Participant Information Sheet was read and explained satisfactorily to the participant in the language he/she understood (English, Ga, Twi).

I confirm that he/she was given the opportunity to ask questions/seek clarifications and same were duly answered to his/her satisfaction before voluntarily agreeing to be part of the research.

Name of Witness_____

Witness' Signature _____or Thumb Print_____

Date: _____

Investigator Statement and Signature

I certify that the participant has been given ample time to read and learn about the study. All questions and clarifications raised by the participant have been addressed.
Name _____
Signature _____

Date: _____

Nutritional Counselling

Preventing Iron deficiency and Iron Deficiency anaemia (Iron rich and balanced meals)

What you eat is important in the treatment of iron deficiency anaemia. Good nutrition can help to reduce the risk of iron deficiency anaemia and help with effective management.

Common foods rich in iron

Vegetables

Dark green leafy vegetables are rich in iron and should be consumed frequently. Examples of such vegetables include kontomire, *borkorborkor*, **gboma**, **ademe**, **aleefi,** spinach, abeduru, and okro.

Meat and Fish

Try to include protein-rich foods in your diet. Protein is needed for the growth and repair of the body's tissues and cells and can be used as an energy source if energy intake is low. Examples of foods rich in protein are lean beef, lean pork, goat meat, kidney, liver (pregnant women should avoid liver), poultry, fish, shrimps, sardines, tuna, salmon, nuts, beans, and milk. Eggs are also a good source of protein.

Legumes, Nuts and seeds

Pumpkin seeds (Egusi), wrewre, cashews, Groundnuts/peanuts, soybeans, black-eyed Beans, peas, fortified breakfast cereals

Foods that can interfere with iron absorption:

- foods that contain tannins, such as grapes, corn, and sorghum

- foods that contain phytates or phytic acid, such as whole-grain wheat products
- tea and coffee

Iron supplements can interact with some medications such as decreasing the absorption of tetracycline antibiotics. Other antibiotics include calcium lowering drugs (Bisphosphonates) Ciprofloxacin, norfloxacin, antihypertensives such as levodopa and many more. Discuss with the study doctor when you are prescribed other drugs by your regular physician during the study period.

Some important tips:

Avoid drinking tea and coffee when eating green leafy vegetables and other iron-rich foods, a substance in them (tannic acid) lowers iron absorption.

Ensure adequate fluid intake – 12 cups or glasses (approximately 2-3 litres daily).

Eat iron-rich foods alongside vitamin C such as citrus fruits e.g., oranges, tangerines, pineapples, alassa, and yooyi. It is also a good idea to enrich foods whenever possible; for example, you may add groundnuts to porridge, soy beans to cereals.

National Blood Service Ghana
Donor Clinical Record

NBSG/DS/DC/F-001
Ver6
July 2020

Date _____ Venue _____

1. PERSONAL INFORMATION

1.1 **Title** ☐ Mr ☐ Mrs ☐ Ms ☐ Dr ☐ Prof ☐ Other 1.2 **First Name** _____

1.3 **Last Name** _____ 1.4 **Calling Name** _____

1.5 **Date of Birth** [DD/MM/YY] _____ 1.6 **Sex** ☐ Male ☐ Female

1.7 **Area of Residence** _____ 1.8 **Address (Workplace)** _____

1.9 **Occupation** _____ 1.10 **ID Number** _____

1.11 **ID Type** ☐ National ID ☐ Passport ☐ Driver's License ☐ Voter ID ☐ NHIS Card ☐ Student ID ☐ Employment ID

1.12 **Phone Number** ☐☐☐☐☐☐☐☐☐☐ 1.13 **E-mail** _____

1.14 **Preferred Contact Method** ☐ Phone ☐ SMS ☐ E-mail ☐ Do not contact for blood donation

2. DONATION HISTORY

2.1 **Have you donated blood before?** ☐ Yes ☐ No 2.2 **If Yes, last donation date?** [DD/MM/YY] _____

2.3 **How many times as Voluntary** _____ **Replacement** _____ 2.4 **Donor Card #** _____

3. REPLACEMENT/FAMILY DONORS ONLY

3.1 **Name of Patient** _____ 3.2 **Hospital** _____

3.3 **Ward** _____ 3.4 **Relationship to Patient** _____

Name of Clerking Officer _____ Signature of Clerking Officer _____

Please turn over to proceed to Section 4 →

OFFICE USE ONLY

5. DONOR SELECTION

5.1 **Appearance** ☐ Passed ☐ Failed 5.2 **Medical History** ☐ Passed ☐ Failed 5.3 **Weight** _____kg

5.4 **Blood Pressure** _____mmHg 5.5 **Pulse** _____bpm 5.6 **Hb by $CuSO_4$** ☐ Passed ☐ Failed

5.7 **Hb checked** _____ g/dL 5.8 **HBsAg checked**? ☐ Yes ☐ No HBsAg Result _____

5.9 **Outcome of Screening:**

Qualifies to Donate	**Permanently Deferred**	**Temporarily Deferred**	
☐ Yes ☐ No	☐ High Risk Behaviour ☐ Medical Condition ☐ Test Outcome	☐ Low Hb ☐ Low Weight ☐ Medical Condition ☐ Iron Stores Risk ☐ TTI Risk ☐ Other _____	*Duration of Temporary Deferral* ☐ 1 week ☐ 1 month ☐ 6 months ☐ ≥1 year ☐ Other _____
Comments:		**Name of Nurse**	**Signature**

6. BLOOD DONATION

6.1 **Donation Number**: ☐☐☐☐☐☐ 6.2 **Pack Type** ☐ Single ☐ Double ☐ Triple ☐ Quad

6.3 **Bleed Time**: Start _____ End _____ ☐ Dry Pack ☐ Apheresis ☐ Test Only ☐ Did not bleed

6.4 **Outcome of Phlebotomy** ☐ Successful
☐ Unsuccessful please specify: ☐ Venous Access ☐ Underbled _____mL ☐ Donor Reaction

6.5 **Donor Adverse Event:** ☐ Vasovagal Reaction (mild) ☐ Vasovagal Reaction (complicated or with injury)
☐ Haematoma/Abnormal Bleed ☐ Painful Arm ☐ Multiple Pricks ☐ Other _____

Name of Nurse _____ **Signature** _____

4. HEALTH QUESTIONNAIRE

Blood donation should be safe for both the donor and the eventual recipient of the blood donated. The following questions will help us determine whether it is safe for YOU to donate blood today, and whether the blood is likely to be safe enough to give to a sick person. We cannot rely entirely on laboratory tests, as they may not always be able to detect infectious agents and other problems, so please answer the questions TRUTHFULLY. Thank you!

Please check "✓" in the boxes and qualify responses by underlining the specific item that applies.

1.	Are you feeling well today, i.e. no fever, cough, headache or cold?	Yes ☐ No ☐
2.	Have you ever been deferred as a blood donor or told not to donate blood? If Yes, for what reason? _____	Yes ☐ No ☐
3.	Are you taking medication? If Yes, for what condition? _____ and what medication? _____	Yes ☐ No ☐
4.	Have you had, or do you have epilepsy, stomach ulcer, heart disease or cancer?	Yes ☐ No ☐
5.	Have you had tuberculosis?	Yes ☐ No ☐
6.	Have you been vaccinated in the last 4 weeks? If Yes, what vaccine?_____	Yes ☐ No ☐
7.	Have you had jaundice, liver disease or a positive blood test for hepatitis?	Yes ☐ No ☐
8.	Do you have sickle cell disease (not sickle trait, 'AS'), or joint pains that usually occur during cold seasons?	Yes ☐ No ☐
9.	Have you ever injected yourself with drugs or medication?	Yes ☐ No ☐
10.	Have you in the last 6 months had a needle-stick injury or an injection in a place that is not a hospital or clinic; or skin scarring/tattoo; or cutting by a traditional healer (including circumcision)?	Yes ☐ No ☐
11.	Have you ever had a headache?	Yes ☐ No ☐
12.	Have you had dental treatment in the last 1 week, or taking antibiotics now?	Yes ☐ No ☐
13.	Have you in the past 6 months had any surgery with general anaesthesia?	Yes ☐ No ☐
14.	Have you in the last 6 months received blood or blood component transfusion?	Yes ☐ No ☐
15.	Have you in the last 6 months lost more than 5kg in weight unintentionally?	Yes ☐ No ☐
16.	Have you in the last 6 months had unprotected sex with more than one partner or have paid/been paid to have sex?	Yes ☐ No ☐
17.	Have you ever had gonorrhoea, genital or urinary pain or discharge?	Yes ☐ No ☐
18.	[For Men Only] Have you in the last 6 months had sex with a man?	Yes ☐ No ☐
19.	Have you or your partner ever tested positive for HIV (AIDS)?	Yes ☐ No ☐
20.	After blood donation, are you going to take part in any vigorous activity, such as climbing, driving a heavy vehicle, operating heavy machinery, or working at hazardous areas or heights?	Yes ☐ No ☐
21.	Are you coming to donate blood because you have been told you have too much blood?	Yes ☐ No ☐
22.	Have you been pregnant in the last 12 months or currently breastfeeding?	Yes ☐ No ☐
	Additional question(s) _____ _____	

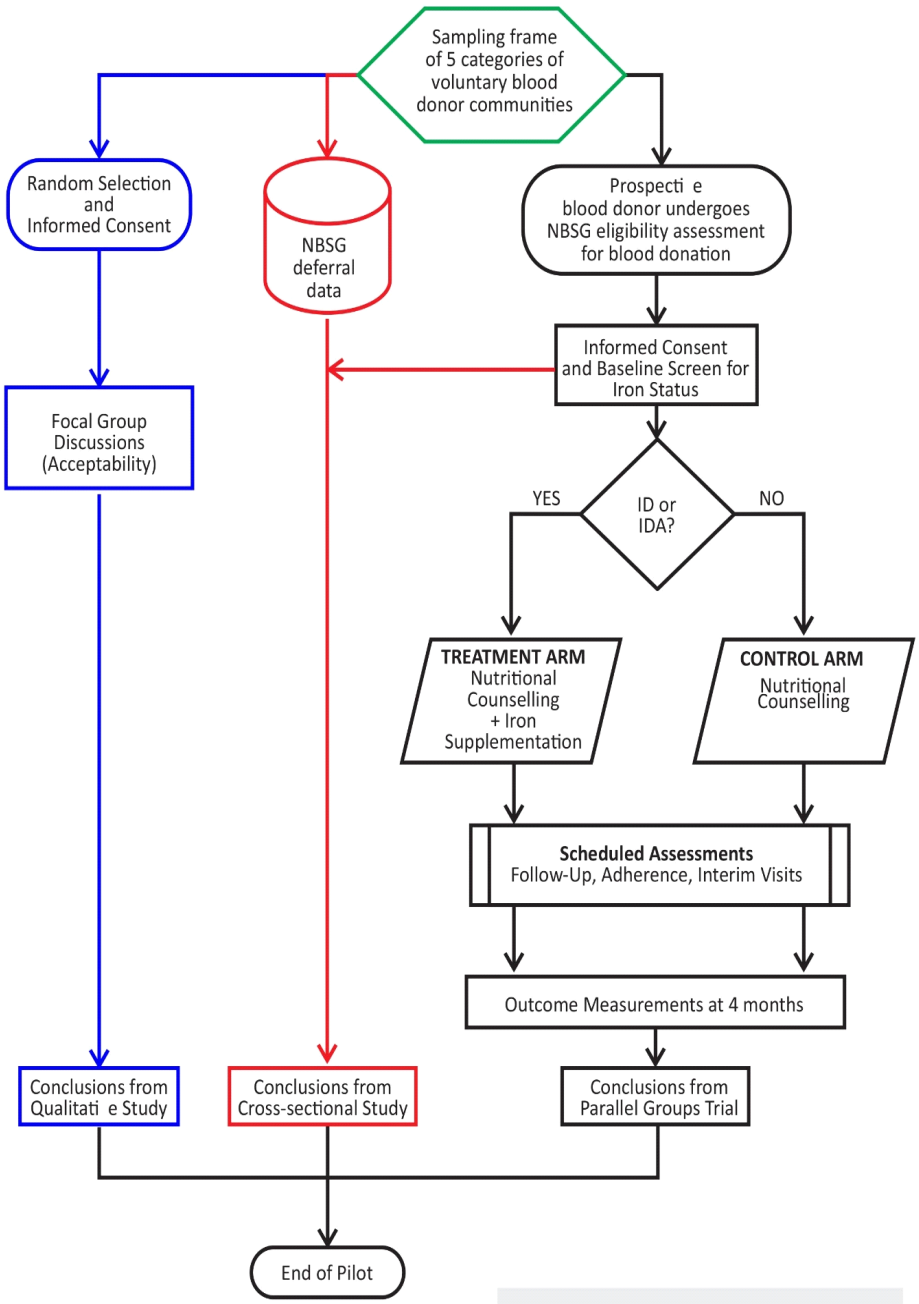
Refer to the *"Medical History Selection Guide for Donor Attendants"* in the Donor Selection & Care Manual to guide your evaluation of the donor.

Donor Declaration

I have read and understood the NBSG donor information leaflet "**Giving Blood - Frequently Asked Questions**". I confirm that the information I have provided regarding my current state of health, previous illnesses, medication history and sexual health are TRUE and CORRECT to the best of my knowledge. I understand my blood will be tested for HIV, Hepatitis B, Hepatitis C and Syphilis and I have no reason to believe I am a carrier of any. I understand that if my donation gives a positive result for any of these tests, I will be contacted and informed, and may be asked for further confirmatory tests and advice. I understand that any incorrect answer to the questions above may harm my health or that of a person who will receive the blood I donate. I understand my donation may be used by the Blood Service or mandated organizations for the purpose of research, teaching, quality assurance or the making of essential diagnostic reagents, and samples of my blood may be stored for possible future testing and research. I agree to the National Blood Service holding information about me, my health, my intended and actual blood donations, and using it for the purposes of information, patient and donor safety, audit, research as stated in the donor information leaflet. Therefore, I consent to all the above, and I give my blood to the National Blood Service to be used for the benefits of patients. I promise to notify the Blood Service/Blood Bank of any change to the information I have provided as soon as I am aware of it.

Donor's Signature _____ Counsellor's Name & Signature _____ Date _____

APPENDIX 4: Study Design Flowchart



APPENDIX 5: Study Timelines

BLOOSAFE Ghana Site Project - UG3 Timelines																										
UG 3	ACTIVITY	YEAR 1												YEAR 2												
		2020						2021												2022						
		JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	
1	**Systematic Literature Review**																									
	Protocol Development																									
	Literature Search																									
	Data Extraction																									
	Data Analysis & Synthesis																									
	Write up																									
	Revisions and submission																									
2	**Study Protocol Development and Approvals**																									
	Protocol Version 0.1																									
	Steering C'tee Review 1																									
	Protocol Version 0.2																									
	Steering C'tee Review 2																									
	Protocol Version 0.3																									

	DSMB Review																									
	Protocol version 0.4																									
	DSMB Review																									
	UH3 Protocols																									
(Nutritional Counseling + Iron Supplemention)																										
	Baseline																									
	25% Enrollment																									
	50% Enrollment																									
	75% Enrollment																									
	100% Enrollment																									
	Pilot 2- (Iron Supplement and nutritional counselling and Follow-Up																									
	Data Collection, Analysis (adherence, Return)																									
	Reports, Manuscripts																									
	UH3 Protocols																									