BMJ Open

Scaling-up high-impact micronutrient supplementation interventions to improve adolescents' nutrition and health in Burkina Faso and Tanzania: protocol for a cluster-randomised controlled trial

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To cite: Cliffer IR, Yussuf MH, Millogo O, *et al*. Scaling-up high-impact micronutrient supplementation interventions to improve adolescents' nutrition and health in Burkina Faso and Tanzania: protocol for a cluster-randomised controlled trial. *BMJ Open* 2023;**13**:e063686. doi:10.1136/bmjopen-2022-063686

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-063686).

Received 08 April 2022
Accepted 31 January 2023

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ABSTRACT

Introduction Adolescence is a critical time for growth and development, but this age group is often neglected in research and development of nutrition interventions. Despite recommendations from the WHO to provide nutrient supplements to adolescents, evidence remains scarce on the most effective supplementation strategy. This study aims to compare weekly iron and folic acid (IFA) supplementation with daily multiple micronutrient supplements (MMSs) in prevention of anaemia and improvement of school outcomes among adolescents in Burkina Faso and Tanzania.

Methods and analysis A three-arm cluster-randomised, school-based supplementation trial will be conducted among 84 schools (42 schools per site) and roughly 4500 students aged 10–17. Schools will be matched on three characteristics: number of students, school ranking profile, distance to main road (Tanzania) or distance to city council (Burkina Faso). Each school will be randomised to receive either weekly IFA, daily MMSs or serve as a control. Supplements will be delivered to students by teachers, who will provide monitoring data to the study team. Baseline and endline surveys will be conducted prior to and after each supplementation cycle (12 weeks in Burkina Faso; 1 year in Tanzania) to assess haemoglobin, anthropometry and sociodemographic variables. The primary outcome of haemoglobin will be analysed continuously using linear regression, and anaemia status will be analysed using logistic or multinomial regression, depending on categorisation level of the outcome. Secondary analyses of school performance indicators will also be conducted with either logistic or linear regression.

Ethics and dissemination This protocol has been approved by the Institutional Review Board of the Harvard TH Chan School of Public Health (IRB20-1108) and the Research Ethics Committees for the Ministries of Health in Tanzania (Zanzibar) and Burkina Faso. Results will be disseminated during meetings with the Ministries of Health and the participating communities as well as through peer-reviewed publications.

Trial registration number NCT04657640; NCT05104554

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This trial is one of the first to investigate micronutrient supplementation in an adolescent population of both males and females.
⇒ Being a multicountry trial increases generalisability of the results.
⇒ School-based design has the potential for national scale-up through existing distribution infrastructure.
⇒ School-based design may exclude the most vulnerable adolescents who are out of school.
⇒ Due to the nature of the supplementation intervention, blinding will not be possible, and randomisation will happen at the cluster level.

INTRODUCTION

Background and rationale

Adolescence, the period between ages 10 and 19, is a critical time for physical and cognitive growth, maturation and development. In Sub-Saharan Africa, high levels of micronutrient deficiencies and anaemia in school-aged adolescents, in part due to food insecurity and limited dietary diversity,[1] are especially important to address, as adolescents make up 23% of the overall population.[2] The serious physical and mental health consequences of micronutrient deficiencies, including those that cause anaemia during adolescence, can persist into adulthood and include lowered immunity to infections, impaired physical growth, fatigue, reduced work capacity and

physical fitness, impaired mental development and poor school performance.[3] Iron deficiency is one of the leading causes of death and disability among adolescents of both sexes globally and has long-term health and economic consequences, especially in low-income and middle-income countries (LMICs).[4] School drop-out rates are significant in LMICs, and an estimated 500 million school days are lost to illness per year.[5] In addition, early adolescent pregnancies occur at high rates in many Sub-Saharan African countries[6] and micronutrient deficiencies among adolescents during pregnancy have consequences not only for the adolescent, but also for the fetus and subsequently the next generation. With nearly 5000 adolescent deaths each day worldwide,[7] the majority preventable and in developing countries,[8] addressing adolescent health and nutrition can make a large impact on population health and economic development in addition to reducing inequities among countries.

Despite significant progress in reducing all forms of malnutrition among children between 2010 and 2015 in Tanzania, anaemia prevalence increased from 42% to 47% among adolescent girls aged 15–19 during the same period.[9] The vulnerability of adolescents to iron deficiency can have lasting effects on health and well-being, especially if the girls become pregnant. In Tanzania, 28% of adolescent girls become pregnant by age 18, and an estimated 45% of these girls experience anaemia during their pregnancies.[9 10] The situation is especially worrisome in Zanzibar, where anaemia rates in children are almost 15 percentage points higher than in mainland Tanzania.[11] Similarly, results from the most recent Demographic and Health Survey in Burkina Faso point to high prevalence of anaemia among both adolescent boys (43.7%) and girls (47.9%).[12] A report on child marriage in West and Central Africa found that over half (51.5%) of women in Burkina Faso were married, and likely to become pregnant before they turned 18.[13]

Addressing the basic health needs of adolescents is a key component of building resilient communities. Programmes to improve adolescent nutrition are critical to prepare girls to enter their reproductive years in a healthier state, which can improve pregnancy and birth outcomes, breaking the cycle of intergenerational malnutrition and poor health. By enhancing learning capacity, improving adolescent nutrition (including micronutrient status) also provides an investment into adolescent boys' and girls' futures, as school attendance and performance are significant predictors of job opportunities and lifelong economic prospects.[14] Micronutrient supplementation, including iron and folic acid (IFA), is one promising intervention to improve adolescent health in LMICs. Several recent systematic reviews indicate potential benefits of IFA; intermittent supplementation with IFA was shown to reduce anaemia by 35% in adolescent and adult women,[15] and weekly IFA supplementation was associated with 27% lower risk of anaemia among adolescent girls.[16] In many areas, multiple micronutrient deficiencies coexist, and additional benefits are likely with the provision of multiple micronutrient supplements (MMSs), which provide other vitamins and minerals, in addition to IFA. Evidence from recent meta-analyses of data from multiple LMICs indicate that MMSs may be more effective than IFA in addressing micronutrient deficiencies,[17 18] and various forms of MMSs (delivered as vitamin supplements, fortified beverages or food supplements) were associated with improvement in serum haemoglobin among both non-pregnant and pregnant adolescent girls in Southeast Asia[16]; however, evidence from Burkina Faso and Tanzania, and specifically pertaining to both adolescent boys and girls, remains limited.

Research problem and explanation of choice for comparators

Research and policies targeted specifically at adolescents are lacking, despite the importance of nutrition and health during this period. School-based intermittent supplementation with IFA is effective in reducing anaemia[19]; however, multiple micronutrient deficiencies coexist in many areas and additional benefit may be conferred from MMSs. The WHO guidelines on adolescent health recommend intermittent IFA supplementation in areas with high anaemia rates and call for policymakers in countries with high prevalence of multiple nutritional deficiencies to consider the benefits of using MMSs that include IFA.[20–22] However, such guidelines have not been implemented beyond pilot programmes, and there is an urgent need to advance the implementation of micronutrient interventions among adolescents, with rigorous evaluation of existing recommended regimens and deliberate plans for national scale-up.

Evidence gap

The governments of both Tanzania (Zanzibar) and Burkina Faso have national nutrition action plans that lay out their commitments to supplementation efforts among adolescents.[23 24] However, evidence supporting the choice of supplement in these populations is unavailable. Rigorous evaluation of the effectiveness and cost-effectiveness of preventing anaemia among adolescents in Tanzania and Burkina Faso using MMS versus IFA is needed before micronutrient interventions are to be scaled up at the national level.

Objective

The primary objective of the 'School-based assessment of micronutrient interventions in adolescents' (SAMIA) project is to clarify the optimal supplementation strategy to improve adolescent anaemia by implementing and evaluating school-based micronutrient supplementation and educational interventions. The ultimate goal is to provide an evidence-base for national scale-up of nutrition programmes that will contribute to building stronger, more resilient communities in Burkina Faso, Tanzania, and beyond, through reducing the consequences of anaemia such as impaired cognition, poor school performance, reduced work capacity and lower immunity to infections.

Research questions

There are two primary research questions for this study: (1) Is the use of MMS more effective in addressing anaemia among adolescents than IFA? and (2) Is the use of MMS more effective in improving school outcomes (performance, attendance, retention from year to year, drop out at any time) among adolescents than IFA?

Specific aims

The specific aims of the present protocol are as follows: (1) Evaluate a school-based micronutrient supplementation and education programme for adolescent boys and girls enrolled in secondary school, comparing the effects of weekly IFA versus daily MMS versus control on anaemia status, school performance/attendance and adolescent development outcomes. (2) Implement the more effective of the two programmes in all schools (for 1 year) and reassess outcomes to explore the feasibility and effectiveness of scale-up, including various supplementation delivery methods (ie, teacher administered, nurse administered, peer support, different levels of external supervision and monitoring).

METHODS AND ANALYSIS

Trial design

This is a cluster-randomised superiority study with parallel assignment to three arms: nutrition education and weekly IFA, nutrition education and daily MMS or control. We will aim to enrol an equal number of participants in each study arm, for an intended allocation ratio of 1:1:1. Each group will continue to receive the standard nutrition, water, sanitation and hygiene (WASH) education included in the school curricula.

Study setting

Burkina Faso

Burkina Faso is a landlocked country in West Africa with a total population of about 17 million. The study will be conducted in the Department of Koudougou, an urban and peri-urban area in the Boulkiemdé Province. Located in the Center-West region, only 75 km from the capital of Burkina Faso (Ouagadougou), Koudougou has a population of roughly 160 000 people. A list of study schools can be found in online supplemental appendix 1. The study was implemented in the post-primary level, which is the first cycle of secondary school teaching in Burkina Faso. Post-primary education has four main grades: sixth, fifth, fourth and third, in which sixth is the first level with the youngest post-primary students and third is the final level with the oldest students. Though expected age at the start of sixth grade is 13 years, fifth is 14 years, fourth is 15 years and third is 16 years, actual age ranges in each grade range from 10 to 17 due to highly varied ages at school entry. The province of Bulkiemdé had 251 secondary schools in 2020: 117 public and 134 private schools.

Tanzania

The Zanzibar Islands in Tanzania have a population of around 1.9 million people and are made up of Unguja and Pemba Islands. The study will be conducted in Unguja Island, where a total of 42 secondary schools in urban or peri-urban areas (Wilaya ya Magharibi A and Wilaya ya Kati districts) have been selected. A list of study schools can be found in online supplemental appendix 2. Secondary schooling begins from Form 1 (age 13–15 years) to Form 4 (ages 16–18 years) after which students undergo a national examination prior to proceeding to higher education (Form 5 and Form 6). The current study will enrol students from Form 1 to Form 3 depending on classroom size to ensure a minimum of 50 students aged 10–17 years are enrolled per school.

Eligibility criteria

Schools (clusters) are eligible for selection and randomisation if they are located in the intervention districts and classified as secondary schools with at least 50 enrolled students, according to the Ministries of Education. Classes will be either randomly selected and all students from the class eligible for enrolment, or entire grades will be enrolled if the classes are not large enough to meet the required sample size. Individual students are eligible for enrolment if they are between 10 and 17 years of age, enrolled in the selected class or grade at study initiation and fluent in Swahili (Tanzania) or French (Burkina Faso). In addition, parents must provide informed consent before a student is considered eligible, and the student must provide their assent to be enrolled. Students will be excluded if they self-report a pregnancy.

Experimental intervention

Adolescents randomised to the intervention arms will receive either weekly IFA or daily MMSs. The IFA preparation is based on the WHO recommendations for adolescents in settings with high anaemia prevalence and will be delivered by school teachers (Tanzania) or educational counsellors (Burkina Faso) weekly, according to WHO guidelines.[20] UNICEF will supply the IFA tablets, composed of 60 mg iron and 2800 µg folic acid. The MMSs will be administered by school teachers or educational counsellors daily since many of the micronutrients in the supplement are water-soluble and cannot be stored in the body. MMSs will be supplied by Kirk Humanitarian and include the 15 micronutrients in the United Nations International Multiple Micronutrient Preparation (UNIMMAP): vitamin A (800 µg), vitamin D (5 µg), vitamin E (10 mg), vitamin C (70 mg), vitamin B_1 (1.4 mg), vitamin B_2 (1.4 mg), niacin (18 mg), vitamin B_6 (1.9 mg), vitamin B_{12} (2.6 µg), folic acid (400 µg), iron (30 mg), zinc (15 mg), copper (2 mg), selenium (65 µg) and iodine (150 µg). While we are not currently aware of other interventions in the study areas, we will note any relevant external interventions if they arise.

We expect that the school-based design, administration by teachers or counsellors known to students and the fact that students will take the supplements on-site will result in high adherence to intervention protocols. Schools have been used effectively in many LMICs as a

platform for delivery of other health interventions such as deworming medications and vaccines.[25 26] Adherence will be monitored by the school teachers and counsellors who deliver the supplements to students. In addition to the supplements, teachers and counsellors will be trained to administer basic nutrition education to complement the standard WASH education in the secondary school curriculum. Teachers and counsellors will report any potential adverse events to the study team and refer students to the healthcare provider associated with the school. As both interventions have been previously implemented in other contexts and/or have been recommended by the WHO, we do not anticipate having to discontinue or modify either intervention.

In Burkina Faso, those in the IFA arm will be supplemented intermittently with IFA for 12 weeks on, 12 weeks off, as recommended by the WHO in settings where continuous supplementation is not possible. The first 12-week intervention period in Burkina Faso will include a loading dose of IFA for those in the MMS arm for the first 4 weeks, given the extremely high prevalence of anaemia in Burkina Faso. Supplementation in Tanzania will be continuous for the duration of the school year. After analyses of intervention year 1 outcomes, the more effective intervention will be scaled to all 42 schools in each country, and outcomes will be re-evaluated at the end of year 2.

Standard of care

The 14 control arm schools in each country will receive existing WASH education as part of the national secondary school curriculum.

Outcomes

The primary outcome is anaemia, defined based on WHO sex-specific and age-specific cutoffs for haemoglobin levels—children 12–14 years: <120 g/L; non-pregnant women ≥15 years: <120 g/L; men ≥15 years: <130 g/L.[27] Haemoglobin levels will be assessed at each baseline and endline survey.

Secondary outcomes include school attendance, retention (year-to-year, as well as any drop-out mid-year) and performance. Performance will be evaluated based on class rankings and test scores, where appropriate.

Participant timeline

Figure 1 shows the participant flow chart for academic year 1 of both the Burkina Faso and Tanzania studies. At the end of year 1, outcomes will be evaluated, and the more effective intervention (either IFA or MMS) will be scaled up to all 42 schools in each country to assess feasibility and effectiveness of scale-up using different supplement delivery methods. In academic year 2, the effectiveness of varied supplement delivery methods will be tested, including, for example, teacher provision of supplements with physical monthly visits from nurses or community health workers, or teacher provision of supplements with virtual support from nurses and community health workers plus student enrolment in peer-support clubs.

Sample size and power calculations

Using Stata's power command (College Station, Texas, USA), we calculated the minimum sample size needed to detect an expected relative risk of 0.65, set according to a recent systematic review on the effects of intermittent iron supplementation on reducing anaemia.[15]

To account for the lack of independence between students in each school cluster, with n=50 students per school, we calculated the design effect as:

$$\text{Design effect} = 1 + (n - 1)\,\rho = 1 + (49)\,(0.05) = 3.45$$

where n is the average cluster size (50) and ρ is the intracluster correlation coefficient (ICC) for the outcome of anaemia. We assume an ICC of 0.05 based on prior studies.[28] Pooled across both the Tanzania and Burkina Faso study sites, we assume an anaemia prevalence of 37.5% (24.3% in Tanzania,[9] 50.7% in Burkina Faso[12]). With alpha level=0.05, power=0.80, expected relative risk=0.65, design effect=3.45 and estimated 10% attrition, 736 participants are needed per study arm, for a total of 2208 participants (45 schools with a minimum of 50 students enrolled per school) across the two study sites. Using the same alpha level, power level, expected relative risk, design effect and expected attrition, assuming an anaemia prevalence of 24.3% for Tanzania and 50.7% for Burkina Faso, within-site power was calculated as 80 schools in Tanzania and 28 schools in Burkina Faso. Ultimately, due to feasibility and funding, we plan to enrol 42 schools per site (14 in each arm) to achieve pooled power, and will strive to enrol >50 students per site to reach the total desired sample size for within-site power.

Recruitment and allocation

Lists of all schools in the catchment areas of each study site were obtained from the Ministries of Education, along with key data on each school. Schools were then matched on three characteristics using coarsened exact matching (*cem* command) in Stata V.16 (StataCorp, College Station, Texas, USA)[29]: number of students, school ranking profile, distance to main road (Tanzania) or distance to city council (Burkina Faso). Following matching, each school was randomised to either IFA, MMSs or control arms by study personnel using a list randomiser available at: https://www.random.org/lists/.[30] Blinding is not possible in this study due to the different appearance of the supplements as well as the differing distribution timelines (weekly vs daily). Entire classes were then selected from each school. Within each school in Tanzania, one to three classes were selected depending on the number of students per class to enrol a minimum of 50 students per school.

Sensitisation meetings were called for each school where parents of the targeted schools were invited to learn about the study and provide informed consent for their adolescent children to participate in the study.

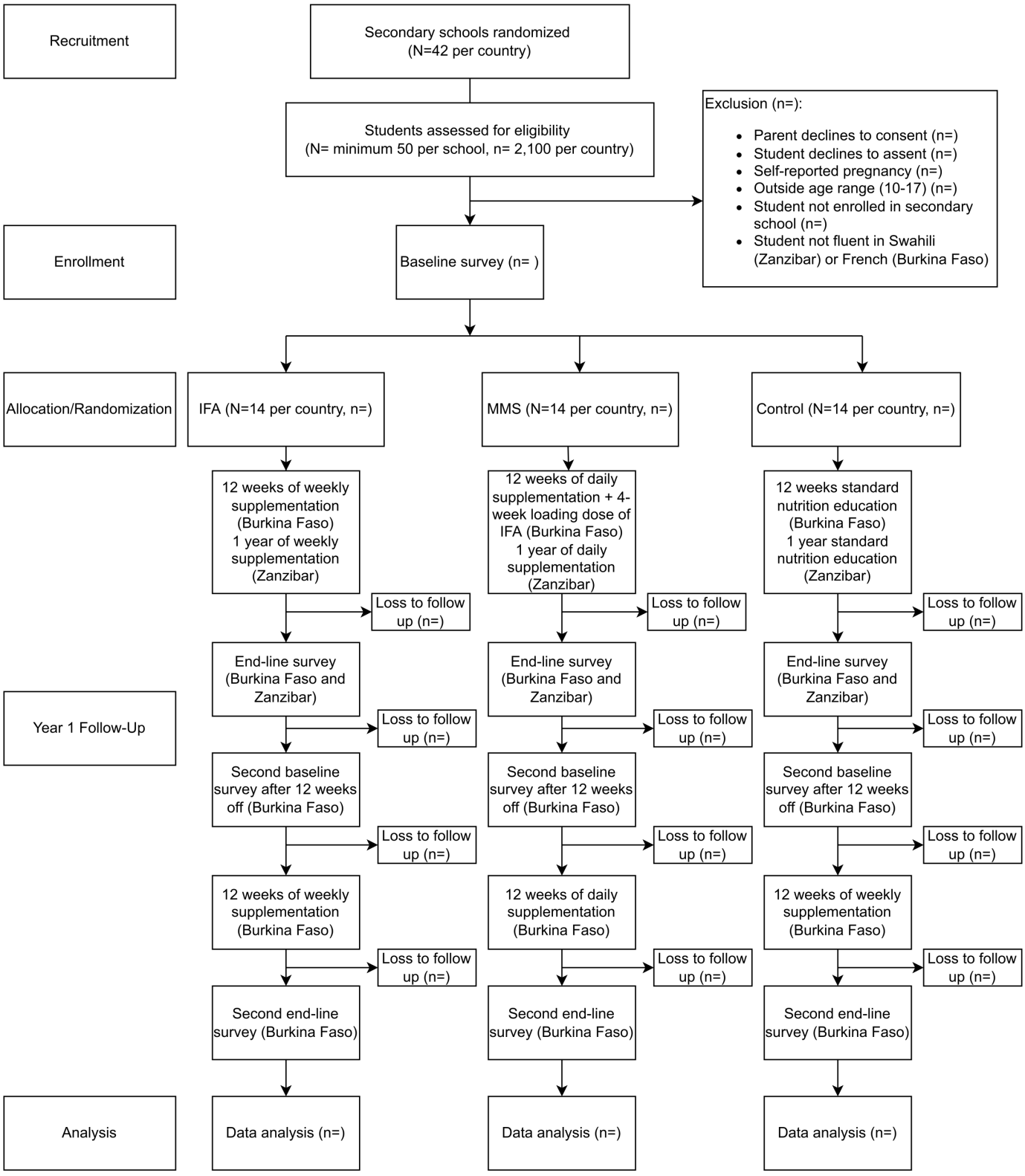

Figure 1 Consolidated Standards of Reporting Trials (CONSORT) diagram for planned flow of participants in 'School-based Assessment of Micronutrient Interventions in Adolescents' (SAMIA) project, academic year 1. IFA, iron and folic acid.

In Burkina Faso, meetings were held with parents and authorities of all 42 schools, and in Tanzania, meetings were held only for intervention arm schools. For control schools in Tanzania, consent forms were distributed to the adolescents who were asked to take them to their parents and obtain signatures to mark informed consent. The students then returned the signed consent forms back to school for collection by study staff.

Contact details of the study team were provided in the consent forms, should parents have questions or

clarifications about the study prior to providing their consent. Furthermore, adolescents were asked to provide assent to participate in the study on the day of baseline survey. Only adolescents who provided assent and whose parents provided consent were enrolled to participate in the study.

Data collection

Baseline and endline survey

At the beginning and end of each academic year (Tanzania) or each supplementation cycle (Burkina Faso), a survey will be conducted by trained enumerators to gather data from adolescents on their haemoglobin status, demographics, socioeconomic status, physical activity, WASH, female menstruation, home gardening practices, food preferences, food frequency, food security, socioemotional development, health supplementation, mental health, malaria status and anthropometry. Haemoglobin will be assessed using HemoCue, model Hb 201+ (Angelholm, Sweden). Anthropometric measurements include the assessment of body height (cm) to the nearest 0.1 cm and weight (kg) to the nearest 10 g. Seca 874 dr scales will be used (Seca, Germany) for weight and Infant/Child ShorrBoard measuring boards (ShorrBoard, USA) used for height. Weights and heights will be double-measured, and the average reported. Malaria status will be assessed using finger-prick blood samples and rapid diagnostic tests (SD Bioline Malaria Ag P.f/Pan, Abbott, USA). Validated scales will be used to assess food security (Household Hunger Scale, FAO), adolescent development (Strengths and Difficulties Questionnaire, Child Outcomes Research Consortium) and diet diversity (Household Diet Diversity Score, FAO). School outcomes will be assessed using school and individual-level data obtained from each school director. These surveys will happen before and after each supplementation cycle (up to four times per study site).

The baseline survey tool will be piloted by study enumerators on a small sample of adolescents prior to data collection and adjusted as necessary. Data will be collected using electronic tablets and uploaded to a central database daily. Field supervisors will verify the collected data before submitting to the database, and consistency checks will be conducted by the data manager before final approval of the data.

Supplementation

Supplementation will be provided weekly for IFA schools and daily for MMS schools. For IFA schools, focal teachers or educational counsellors at each school will identify a specific day during the week on which to provide IFA to the students. Students will be assigned unique IDs and identified by their teachers by a list of names and unique IDs. Study team members will visit each intervention school on a weekly basis to collect monitoring data from the teachers as well as provide them with fresh distributions of supplements. Monitoring data will include information on whether the student was present at school, whether they took the supplement and reasons for non-compliance if relevant.

Promotion of participant retention

We aim to promote retention of study participants by using schools as platforms to engage adolescents in the supplementation programme. Teachers known to the students will deliver the supplements after holding sensitisation meetings with parents and students, increasing student comfort with supplementation. Study team members will address any challenges to supplementation distribution and uptake during their weekly visits.

Data management

Enumerators will enter data into SurveyCTO (Burkina Faso) or Survey Solutions (Tanzania) using tablets, and the data will then be uploaded to a central database. Weekly monitoring reports will be generated and discussed with the study team via virtual team meetings, and any challenges identified will be addressed.

Data quality control, including range and plausibility checks, will be implemented weekly to ensure implausible data are identified while data collection is ongoing to allow for rectifications. Additional data cleaning will be done at the end of data collection to format and merge datasets, label variables and recode any variables into covariates of interest.

Electronic data will be collected through password-protected tablets and data in the central database will be accessible only through password entry to the research team.

Data monitoring

No external data monitoring board is engaged with this study, as the interventions are not experimental in nature, and have been recommended by the WHO. However, interim analyses will be conducted after each baseline and endline survey, before final analyses are conducted using data from all surveys.

Statistical analysis

Prior to modelling, bivariate analyses and balance tests using t-tests and χ^2 tests will be conducted to explore factors related to anaemia status and identify potential confounding factors. Primary outcomes will be analysed using logistic regression (anaemia as a binary outcome), multinomial regression (anaemia as a multicategorical outcome for none, mild, moderate and severe) or linear regression (haemoglobin as a continuous outcome). Log-binomial regression may also be used for common outcomes with an incidence over 10%. Secondary outcomes will be analysed using logistic regression (eg, school retention, stunting and underweight as binary variables) or linear regression (eg, class ranking and anthropometric z-scores as continuous variables). Mixed-effects models may also be estimated using repeated measures of outcomes at each baseline or endline survey. Main analyses will be intention-to-treat, and average treatment effects will be explored as sensitivity analyses.

Harms

There is some evidence that iron supplementation in malaria endemic zones may increase risk of severe illness from malaria. However, supplementation has been shown to be safe in settings with high coverage of malaria control interventions.[31] The WHO continues to recommend provision of iron-containing supplements in malaria endemic zones as long as adequate measures are taken to prevent, diagnose and treat malaria.[22] Given these guidelines, we will test students for malaria each time a baseline or endline survey is conducted and refer any cases for immediate care.

The benefits of supplementation with either IFA or MMS outweigh the risks,[32] however, adverse events will be monitored by the teachers who distribute supplements. Teachers will be trained to report any adverse events that could be plausibly related to supplementation (any physical health related symptoms that do not have other identified causes) to the study team by filling out and submitting an adverse event form, and to refer students to healthcare providers. Whether the adverse event may be related to the study and needs to be reported to the Institutional Review Board will then be determined by the study clinician.

Patient and public involvement statement

The design and logistics of the supplementation programme in this study were informed by input from adolescents, parents and teachers from the participating communities during community information meetings introducing the study. Various implementation schemes were discussed with communities, and advice was received regarding the most acceptable intervention design. School personnel, community leaders, government ministries, parents and students will continue to be involved in informing future study design and implementation (for any subsequent studies) as the study is rolled out through occasional meetings and feedback sessions.

ETHICS AND DISSEMINATION

Ethics

This study protocol has been approved by the Institutional Review Board of the Harvard TH Chan School of Public Health (IRB20-1108, data safety approval: DAT20-0241) as well as the ethics committees for the Ministries of Health in both Tanzania (Zanzibar) and Burkina Faso. Amendments to the protocol will go through all necessary ethics committee reviews, and the Harvard IRB will conduct yearly continuing reviews. The trial is registered on ClinicalTrials.gov under identifiers: NCT04657640 (Burkina Faso) and NCT05104554 (Zanzibar).

Parent written consent and adolescent assent will be required prior to study enrolment. An example consent form can be found in the supplementary material (online supplemental appendix 3). Data will be deidentified prior to generation of any reports. All study reports will use aggregated data without the use of any identifiable information about study participants.

Dissemination

Access to the datasets will be restricted to researchers from all partner institutions who are listed on the study protocol. Final results, whether positive, negative or neutral, will be sent for publication in peer-reviewed journals as well as presented in dissemination meetings to the Ministries of Health in Burkina Faso and Tanzania. In addition, dissemination meetings will be planned at the community level to inform study participants of the results and gather their input for next steps. All researchers who participated in data collection will be eligible to author final papers and participate in dissemination meetings.

DISCUSSION

This multicountry cluster-randomised controlled trial testing the effectiveness of supplementation with IFA or MMS compared with no supplementation in the prevention of anaemia among secondary school children will provide an evidence base informing government strategy to reduce anaemia in adolescents. Results of each trial (Burkina Faso and Tanzania) will be analysed and published separately and as a combined report comparing results in both countries. We expect to report the year one Burkina Faso results by mid-2022, and the Tanzania results by mid-2023.

Through the school-based design, we will assess the potential for national scale-up of supplementation programmes through existing distribution infrastructure. If effective, this strategy may prove to be an important mechanism through which governments can feasibly and cost-effectively improve nutrition and health among adolescents. However, its drawback is that the school-based delivery platform may exclude the most vulnerable adolescents who do not attend school. Nevertheless, as there are currently few government initiatives targeting adolescents, this trial is an important first step in shaping policies that will help build healthier and more resilient populations.

Trial status

We report protocol version 3, dated 2 December 2021. Enrolment for the Burkina Faso trial began in January 2021 and data collection is ongoing. Data collection for phase I of the study is expected to continue until April 2022. For the Tanzania trial, enrolment began in February 2022 and is ongoing. Data collection is expected to begin in May 2022.

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Contributors IRC, MHY and OM wrote the manuscript. MHY, MM-S, OM, ASA, YB, AT, GC, IK, ISY and DM are implementing the study. DW and ECH performed sample size calculations, matching and randomisation. WF designed the study and received grant funding. All authors read and approved the final manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/disclosure-of-interest/ and declare that all authors had financial support from an anonymous donor for the submitted work and received donation of multiple micronutrient supplements from Kirk Humanitarian; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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