ISRCTN10026749 https://doi.org/10.1186/ISRCTN10026749

A trial to test whether micronutrient status in a rural Ethiopian population can be improved through the consumption of teff flour biofortified using selenium and zinc fertilizers

Submission date
22/12/2020

Recruitment status
No longer recruiting

Registration date
04/01/2021

Overall study status
Stopped

Last Edited
31/03/2022

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Deficiencies of micronutrients including selenium and zinc are widespread in Ethiopia. This study aims to test a novel method for alleviating population selenium and zinc deficiencies, through consumption of teff (a staple cereal widely consumed in Ethiopia) that has been biofortified using selenium and zinc fertilizers. The fertilizers are applied during crop production leading to greater concentrations of selenium and zinc in the grain – a process known as agronomic biofortification. Agronomic biofortification may be particularly valuable as an approach for low-income or subsistence households in rural areas of Ethiopia (and other countries) where access to diverse diets or foods fortified at processing stage is very limited by low purchasing power or lack of market availability. There is currently insufficient evidence to know whether agronomic biofortification is an effective approach to alleviate selenium and zinc deficiencies in the context of rural Ethiopia. The AHHA Ethiopia trial aims to test the efficacy of improving human selenium and zinc status through consumption of teff flour agronomically biofortified with selenium and zinc.

Who can participate?
Non-pregnant adult women aged 20-45 years and children aged 5-10 years will be recruited from the study area, which comprises four villages in Burie woreda, Amhara Region, Ethiopia.

What does the study involve?
Households with at least one non-pregnant adult woman and at least one school-aged child will be considered eligible, with participants recruited from a random selection of 140 households. Participant households will be randomly assigned to receive a 60 day supply of either teff flour biofortified with selenium and zinc or teff flour not biofortified. Households will receive enough flour for all constituent members for 60 days at a rate of 250 g per person per day. Flour will be distributed at four timepoints through the intervention period. About 5 days before the intervention is complete, participants will be invited to provide a blood sample (6 ml) at a local clinic. Blood plasma will be extracted and analysed in a laboratory to determine selenium and

zinc status of participants. The results will be communicated to participants and to local, national, and international scientific and policy communities.

What are the possible benefits and risks of participating?
Participant households will receive free flour during the intervention, which they can use in place of their normal flour. This will allow households to reserve their normal flour for later in the year, or save money rather than purchasing flour. There are minimal risks to participating.

Where is the study run from?
Addis Ababa University (Ethiopia), the London School of Hygiene & Tropical Medicine (LSHTM; UK), and the University of Nottingham (UK)

When is the study starting and how long is it expected to run for?
September 2018 to September 2021

Who is funding the study?
The Bill & Melinda Gates Foundation (USA)

Who is the main contact?
Dr Edward Joy
Edward.joy@lshtm.ac.uk

Contact information

Type(s)
Public

Contact name
Dr Edward Joy

ORCID ID
https://orcid.org/0000-0002-0106-866X

Contact details
Faculty of Epidemiology and Public Health
LSHTM
Keppel Street
London
United Kingdom
WC1E 7HT
+44 2079272214
edward.joy@lshtm.ac.uk

Type(s)
Scientific

Contact name
Dr Edward Joy

ORCID ID
https://orcid.org/0000-0002-0106-866X

Contact details
Faculty of Epidemiology and Public Health
LSHTM
Keppel Street
London
United Kingdom
WC1E 7HT
+44 2079272214
edward.joy@lshtm.ac.uk

Additional identifiers

Protocol serial number
Protocol version 4.1

Study information

Scientific Title
Alleviating Hidden Hunger with Agronomy: a randomised, controlled trial in rural Ethiopia to test the efficacy of improving selenium and zinc status through consumption of teff flour biofortified using selenium and zinc fertilizers

Acronym
AHHA Ethiopia

Study objectives
The selenium and zinc status of women of reproductive age and school-aged children in rural Ethiopia can be improved through the consumption of teff flour that is biofortified with selenium and zinc through the application of micronutrient-enriched fertilizers.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 21/12/2020, London School of Hygiene & Tropical Medicine Interventions Research Ethics Committee (Keppel Street, London, WC1E 7HT, UK; +44 (0) 20 7636 8636; ethics@lshtm.ac.uk), ref: 17977 - 2
2. Approved 27/01/2020, Addis Ababa University College of Natural & Computational Sciences (PO BOX 1176 Addis Ababa, Ethiopia; +251 (0)11 123 94 72; dean_cns@aau.edu.et), ref: IRB/42/2019
3. Approved 28/7/2020, Ministry of Science and Higher Education, Ethiopia; +251 (0) 118 7217 47; info@ethernet.edu.et), ref: P5M/14.1/507/20

Study design
Single centre two-arm double-blind randomised controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Selenium and zinc deficiency

Interventions
Using a computer-based randomisation programme, participant households will be randomly allocated in a 1:1 ratio to either the intervention or control arm. The intervention arm will receive teff flour biofortified with selenium and zinc, while the control arm will receive teff flour not biofortified for 60 days.

Biofortification of teff, to increase the concentration of selenium and zinc in the teff grain, was achieved through the application of selenium and zinc fertilizers during crop production. The concentrations of selenium in the intervention and control flour are, respectively, 0.290 mg/kg and 0.026 mg/kg. The concentrations of zinc in the intervention and control flour are, respectively, 31.8 mg/kg and 26.4 mg/kg. Households will receive enough flour to satisfy their household requirements (250 g/capita/day), with distributions occurring at 4 time points.

Intervention Type
Supplement

Primary outcome(s)
1. Blood plasma selenium concentration (in µg/l) measured using Inductively Coupled Plasma Mass Spectrometry (ICPMS) with plasma samples collected at endline

Key secondary outcome(s)
Current secondary outcome measures:

1. The Relative Risk of selenium deficiency, defined as <70µg/l at endline
2. Plasma zinc concentration (mg/l) measured by ICPMS at endline
3. Plasma copper to zinc molar ratio measured using plasma samples at endline

———

Previous secondary outcome measures:

1. The Relative Risk of selenium deficiency, defined using established thresholds for the optimal activity of Glutathione peroxidase 3 (GPx-3) (<84.9µg l-1) and iodothyronine deiodinase (IDI) (<64. 8µg l-1) at endline
2. Plasma zinc concentration (mg l-1) before and after correction for inflammation status measured using ICPMS at endline
3. Plasma copper to zinc molar ratio measured using plasma samples at endline
4. Plasma Linoleic Acid to Dihomo-γ-Linolenic Acid ratio (LA:DGLA) measured using plasma samples at endline
5. Plasma Arachidonic acid to Dihomo-γ-Linolenic Acid ratio (AA:DGLA) measured using plasma samples at endline
6. Concentration of haemoglobin in whole venous blood (g dl-1) measured in the field using a portable HemoCue Hb301+ (HemoCue AB, Ängelholm, Sweden) at endline

Completion date

30/09/2021

Reason abandoned (if study stopped)
Unfortunately this trial was terminated early, with no data generated on the primary or secondary outcomes. Early termination was advised by the Trial Steering Committee due to very high drop out rates.

Eligibility

Key inclusion criteria
Household level:
1. Household members include at least one non-pregnant woman of reproductive age (20-45 years) and at least one school-aged child (5-10 years)
2. Household typically prepares and consumes meals at home
3. Household head agrees that the household will receive and all members consume teff flour for the 60 day flour distribution period
4. No confirmed, suspected, or probable cases of COVID-19 in the household in the past 14 days

Individual level:
1. Individual is not pregnant (self-reported) and is apparently healthy
2. Planning to be in residence in the household during the intervention period
3. Participant woman of reproductive age is willing and able to provide consent, and the caretaker of the participant school-aged child is willing and able to provide assent

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Key exclusion criteria
Does not meet inclusion criteria

Date of first enrolment
15/03/2021

Date of final enrolment
23/03/2021

Locations

Countries of recruitment
Ethiopia

Study participating centre
Addis Ababa University
P. O. Box 1176
Center for Food Science and Nutrition
Arat Killo Campus
Addis Ababa
Ethiopia
-

Sponsor information

Organisation
London School of Hygiene & Tropical Medicine

ROR
https://ror.org/00a0jsq62

Funder(s)

Funder type
Charity

Funder Name
Bill and Melinda Gates Foundation

Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, Gates Learning Foundation, William H. Gates Foundation, BMGF, B&MGF, GF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

The datasets of plasma selenium and zinc concentrations and participant characteristics generated during and/or analysed during the current study will be stored in a publically available repository, LSHTM Data Compass (https://datacompass.lshtm.ac.uk/). Consent obtained from participants will cover the sharing of this data and appropriate protections will be put in place to ensure participant anonymity. De-identified data will become publically available at the time of publication of the results manuscript and will be available for a minimum of 10 years for download without restriction. Analysis of the data will be restricted to the analysis of population micronutrient status, consistent with the obtained consent.

IPD sharing plan summary