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A trial of different nutritional supplements and subsequent support to secure and sustain the recovery of moderately undernourished young children recovering from an illness

Submission date
26/12/2022

Recruitment status
No longer recruiting

Registration date
03/04/2023

Overall study status
Completed

Last Edited
30/12/2025

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Moderate wasting is associated with a threefold higher risk of death in children under 5 years of age compared with their well-nourished peers. These deaths largely occur from infectious illnesses. The interactions between episodic infections and malnutrition are complex and bi-directional. There are very no clinical trials that have been done in this high-risk subgroup to investigate if it is possible to break the malnutrition-infection cycle and decrease the risk of deterioration/death by initiating interventions targeting the nutritional (anthropometric) deficit. The NUTRIMAM trial proposes to evaluate different nutritional supplements in young children who are moderately wasted and present with an acute infection.
The NUTRI-MAM trial will aim to evaluate the effectiveness of locally available foods (LAF) or microbiota-directed supplementary food (MDSF) compared to ready-to-use supplementary food (RUSF), when given to moderately wasted children presenting to health facilities with an acute illness, on initial anthropometric recovery (within 12 weeks of enrolment) and sustained recovery (at 24 weeks after enrolment).

Who can participate?
Moderately wasted children 6-24 months of age with an acute illness (diarrhoea, pneumonia, fever or malaria) in Bangladesh, India and Pakistan, Mali and Tanzania

What does the study involve?
Phase 1 of the study involves daily intake of the study supplement (RUSF, MDSF or LAF) for 12 weeks. Children who recover anthropometrically from moderate wasting will be randomised into a second phase to a follow-up intervention (including counseling and food vouchers) vs standard of care to assess the effect of continued follow-up on sustaining this recovery.

What are the possible benefits and risks of participating?
The child may benefit from the nutritional supplement received as part of the study, as these will provide additional nutrients that will help them to grow. The caregiver will be able to discuss

the child's growth and feeding habits with a trained counselor from the clinic.
It is possible that the child/family may not receive any direct benefit from taking part in the study. The study foods are commonly used and known to be safe for children. A few children may react to the foods. Reactions may include rash, itching, diarrhoea, nausea, vomiting and abdominal pain.

Where is the study run from?
World Health Organisation (Switzerland)

When is the study starting and how long is it expected to run for?
January 2021 to December 2025

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

Who is the main contact?
Dr Ayesha De Costa, deay@who.int

Contact information

Type(s)
Scientific

Contact name
Dr Ayesha De Costa

Contact details
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Additional identifiers

Protocol serial number
0.151

Study information

Scientific Title
A multi-country, multi-centre, three-arm, parallel-group, open-label, randomized trial of three supplements for the nutritional management of moderate wasting in children 6-24 months of age with acute illness

Acronym
NUTRIMAM

Study objectives
This trial has three hypotheses:
1. That supplementation with (i) locally available food (LAF) will be non-inferior to supplementation with ready-to-use supplementary food (RUSF) on the proportion of moderately wasted children showing initial anthropometric recovery by week 12 post-enrolment (ii) and superior to RUSF on the proportion showing sustained recovery by week 24 post-enrolment.
2. That supplementation with microbiome-directed supplementary food (MDSF) will be superior to supplementation with RUSF on the proportion of moderately wasted children showing initial anthropometric recovery by week 12 post-enrolment and sustained recovery by week 24 post-enrolment
3. That active follow-up of the recovered child including counselling and food vouchers will result in higher rates of sustained recovery at 24 weeks

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 21/01/2022, WHO research ethics committee (Av Appia 20, Geneve, 1211, Switzerland; -; ercsec@who.int), ref: ERC.0003631

Primary study design
Interventional

Study design
Multi-center open-label sequential multiple assignment randomized trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Moderate wasting in children 6-24 months of age

Interventions
Current interventions as of 26/08/2025:

Phase 1:
Children are randomised to one of three treatment arms: ready-to-use supplementary food (RUSF), locally available food (LAF) or microbiome-directed supplementary food (MDSF). This supplement will be provided daily for 12 weeks. Each day's provision would comprise 50% of the estimated daily caloric requirement.

Phase 2:
Children who recover anthropometrically in phase 1 will be randomised at the end of the 12 weeks of phase 1 into one of two groups for phase 2: follow-up intervention (comprising counselling on appropriate feeding practices and recognising need referral, monthly food vouchers) for a further 12 weeks OR standard of care i.e. follow up at the end of 12 weeks.

Randomisation for both phases: online electronic randomisation system.

NUTRIMAM mechanistic substudy (NMSS):
A nested observational sub-study of the main NUTRIMAM trial will be conducted in NUTRIMAM

sites located in Bangladesh, India, Mali, Pakistan and Tanzania. A representative sample of children aged 6-17 months (stratified 6-11 months and 12-17 months for some outcomes) who are enrolled in the main NUTRIMAM trial will be involved. NMSS was added to the trial registration database on 10th May 2024.

The sub-study includes three components:
1. Microbiome/multi-omics measures,
2. Measures of EED and systemic and local inflammation, and,
3. Body composition

Body composition assessments via deuterium dilution will be conducted at all five NUTRIMAM sites. Due to funding constraints, the EED and microbiome/multi-omics components will only be performed at three sites (Bangladesh, Mali and Tanzania). If additional funding becomes available, the full range of assessments will also be conducted in India and Pakistan.

Additionally, in sites conducting the microbiome/multi-omics measures, a healthy reference cohort (HRC) of infants 5-6 months of age will be established from the same catchment population from which the NUTRIMAM trial population is enrolled and followed until 24 months of age. The purpose of the HRC is to allow characterisation of the gut flora of healthy children in the absence of infection and inflammation and thereby enable comparison of baseline and follow-up gut flora examination of wasted children including responses to nutrition interventions.

The sample size is 1800 for body composition analysis (120 per intervention arm, categorised into two age groups 6-11 and 12-17 months n=60 per age group per intervention arm) across five sites, and 1080 for microbiome / multi-omics measures across three sites (Bangladesh, Mali and Tanzania).

The sample size is 180 for the Healthy Reference cohort (60 per site in Bangladesh, Mali and Tanzania).

Current status of NMSS: Follow-up and sample collection will continue until end August 2026.

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Randomisation for both phases: online electronic randomisation system.

A nested observational sub-study of the main NUTRIMAM trial will be conducted in NUTRIMAM sites located in Bangladesh, India, Mali, Pakistan and Tanzania. A representative sample of children aged 6-17 months (stratified 6-11 months and 12-17 months for some outcomes) who are enrolled in the main NUTRIMAM trial will be involved.

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Children who recover anthropometrically in phase 1 will be randomised at the end of the 12 weeks of phase 1 into one of two groups for phase 2: follow-up intervention (comprising counselling on appropriate feeding practices and recognising need referral, monthly food vouchers) for a further 12 weeks OR standard of care i.e. follow up at the end of 12 weeks.

Randomisation for both phases: online electronic randomisation system.

Intervention Type
Mixed

Primary outcome(s)
Phase 1: Anthropometric recovery at week 12 (defined as recovery from moderate wasting on weight-for-length z score [WLZ] or mid upper arm circumference [MUAC])
Phase 2: Anthropometric recovery at week 24 (defined as recovery from moderate wasting on weight-for-length z score or mid upper arm circumference)

Recovery is defined as WLZ >-2.0 or MUAC ≥125 mm (depending on whether the child was ascertained to have moderate wasting at enrolment based on a WLZ <-2 or a MUAC <125 mm or

both. The child must show improvement on the parameter (WLZ >-2.0 or MUAC ≥125 mm) that indicated moderate wasting at enrolment. If the child was moderately wasted on both parameters, improvement on any one as defined above is accepted as recovery.

Key secondary outcome(s)

Current secondary outcome measures as of 28/03/2024:

1. Time to recovery between the three groups within the first 12 weeks
2. Mean change in i) Mid-upper arm circumference (MUAC, in mm), ii) Weight-for-length z-score (WLZ), iii) Weight-for-age z-score (WAZ), iv) Length-for-age z-score (LAZ):
- between MDSF, LAF and RUSF from i) enrolment to 12 weeks and ii) enrolment to 24 weeks
- between food voucher and standard care post-recovery support groups from week 12 to week 24
3. Mean change in tricep skinfold thickness measurements:
- between MDSF, LAF and RUSF from i) enrolment to 12 weeks and ii) enrolment to 24 weeks
- between food voucher and standard care post-recovery support groups from week 12 to week 24
4. Deterioration to SAM or death:
- between MDSF, LAF and RUSF from i) enrolment to 12 weeks and ii) enrolment to 24 weeks
- between food voucher and standard care post-recovery support groups from week 12 to week 24
5. All-cause mortality:
- between MDSF, LAF and RUSF from i) enrolment to 12 weeks and ii) enrolment to 24 weeks
- between food voucher and standard care post-recovery support groups from week 12 to week 24
6. Any hospitalisation (>24h):
- between MDSF, LAF and RUSF from i) enrolment to 12 weeks and ii) enrolment to 24 weeks
- between food voucher and standard care post-recovery support groups from week 12 to week 24
7. Deterioration to SAM:
- between MDSF, LAF and RUSF from i) enrolment to 12 weeks and ii) enrolment to 24 weeks
- between food voucher and standard care post-recovery support groups from week 12 to week 24

Additional exploratory outcomes
We will also do an exploratory analyses of MDSF as compared to. LAF for all primary and secondary outcomes.

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Previous secondary outcome measures:

1. Time to anthropometric recovery within the first 12 weeks (time-to-event): this will be defined as the number of days to anthropometric recovery within the first 12 weeks. The day of anthropometric recovery will be the visit day of recovery
2. Anthropometric recovery from moderate wasting at any point up to 12 weeks after enrolment, compared between MDSF vs LAF groups
3. Mean change in MUAC measured using MUAC tapes from enrollment to 12 weeks: This will be the 12-week MUAC value minus the baseline MUAC value
4. Mean change in WLZ (weight measured with baby weighing scale, length measured with length board) from enrollment to 12 weeks: This will be the 12-week WLZ value minus the baseline WLZ value

5. Mean change in weight for age Z score (WAZ) measured with baby weighing scale from enrollment to 12 weeks: This will be the 12-week WAZ value minus the baseline WAZ value
6. Mean change in length for age Z score (LAZ) measured using with length board from enrollment to 12 weeks: This will be the 12-week LAZ value minus the baseline LAZ value
7. Mean change in skinfold thickness measured using Holtain caliper from enrollment to 12 weeks: this will be the 12-week skinfold thickness measurements minus the baseline measurement value
8. Severe acute malnutrition (SAM) or mortality up to 12 weeks: this is a composite outcome of SAM or death up to 12 weeks. SAM will be defined as a WLZ < -3 z-score or MUAC <115 mm or the presence of bilateral pitting oedema at any follow-up visit during the first 12 weeks of the study. Mortality up to 12 weeks will include all deaths that occur on or before day 84 of follow-up (12 weeks)
9. 24-week sustained recovery: 24-week sustained recovery will be considered a secondary outcome for LAF vs MDSF. The definition will be the same as listed under the primary outcome measure above
10. Mortality to 12 weeks: mortality up to 12 weeks will include all deaths that occur on or before day 84 of follow-up (24 weeks). This is during the active intervention period
11. Hospitalization to 12 weeks: hospitalization will be defined as a stay in a health facility >24 hours. Only hospitalizations on or before day 84 of follow-up (12 weeks) will be considered as meeting the outcome. This is during the active intervention period.

Completion date
27/10/2025

Eligibility

Key inclusion criteria
1. Age 6-24 months
2. Moderately wasted i.e. WLZ ≤-2 and > -3 or MUAC <125 mm and >115 mm
3. Presenting with any of the following acute illnesses at a facility out-patient clinic or discharged from hospital after <7 days for any of the following:
3.1. Diarrhea, defined as three or more loose or watery stools (with or without blood) in the previous 24 hours, and no dehydration on assessment. If the child has dehydration, the dehydration will be treated re-assessing for recruitment, or
3.2. Pneumonia, defined as the presence before of fast breathing or chest indrawing, or
3.3. Non-malarial fever, defined as reported or measured (≥38C) fever of >3 days but <7 days duration
[Acute illness in the context of this trial: Children with significant acute illness are at higher risk for severe outcomes like risk of developing SAM or hospitalization/death. Decreasing the risk in these children is important. Therefore, acute illness in this trial will be defined as diarrhea, signs of pneumonia, malaria or fever. If fever, then this should be present for >3 days duration. Milder illnesses, for example, skin or common cold/ cough will not be considered as significant acute illness as having these mild illnesses are less likely to cause children to enter a downward spiral of increased risk of morbidity/mortality]
3.4. malaria, defined as reported or measured (≥38C) fever and positive rapid diagnostic test, or
4. Consent for study participation from parent or legal guardian

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Child

Lower age limit
6 Months

Upper age limit
24 Months

Sex
All

Total final enrolment
6361

Key exclusion criteria
Current exclusion criteria as of 28/03/2024:

1. Severe acute malnutrition (WLZ <-3 or MUAC <115 mm or oedema of both feet)
2. General danger signs (lethargic/unconscious, convulsions, unable to drink, vomits everything)
3. Severe illness (severe pneumonia or very severe disease, severe dehydration, neck stiffness)
4. Persistent diarrhoea (≥14 days)
5. Chronic infections/illness or disability, e.g. TB, HIV, congenital defects, cerebral palsy
6. Require hospital admission
7. Well child attended clinic only for routine growth monitoring or immunization
8. Child receiving food supplements for moderate wasting
9. Treated for moderate wasting in the previous 3 months
10. Previously enrolled in the study
11. Child with any known history of food allergy or food intolerance
12. Another child in the same household already recruited into the study
13. Child lives outside the study area routinely or will be outside of the study area for more than two weeks in the upcoming 3 months.

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8. Child receiving food supplements for moderate wasting
9. Treated for moderate wasting in the previous 3 months
10. Previously enrolled in the study

11. Child with any known history of food allergy or food intolerance
12. Another child in the same household already recruited into the study
13. Child lives outside the study area

Date of first enrolment
24/04/2023

Date of final enrolment
30/06/2025

Locations

Countries of recruitment
Bangladesh

India

Mali

Nigeria

Pakistan

Tanzania

Study participating centre
International Centre for Diarrhoeal Disease Research
Mohakali
Dhaka
Bangladesh
1212

Study participating centre
Center for Vaccine Development
Ex—Institut Marchoux
Avenue Mohamed VI
Djikoroni Para
Bamako
Mali
251

Study participating centre
Center for Public Health Kinetics
214-A, Basement
Vinoba Puri

Lajpat Nagar II
New Delhi
India
-

Study participating centre
The Aga Khan University Hospital
Stadium Road
Karachi
Pakistan
-

Study participating centre
Muhimbili University of Health and Allied Sciences
United Nations Rd
Dar es Salaam
Tanzania
-

Sponsor information

Organisation
World Health Organisation

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 generated during and/or analysed during the current study are/will be available upon request from Dr Ayesha De Costa (deay@who.int).

The type of data that will be shared: this will depend on the request
Dates of availability: expected 2027
Whether consent from participants was required and obtained: only anonymised data will be shared

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		05/11/2024	06/11/2024	Yes	No
Statistical Analysis Plan	version 1.4		21/10/2025	No	No