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Reducing short and long-term consequences of early stunted growth

Submission date
25/07/2025

Recruitment status
Recruiting

Registration date
29/07/2025

Overall study status
Ongoing

Last Edited
17/10/2025

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol
Background and study aims
This is a follow-up study of the MAGNUS nutrition intervention trial (ISRCTN13093195) that was conducted in 2020. The MAGNUS trial was conducted to assess the role of milk protein and whey permeate in a large quantity lipid-based nutrient supplement (LNS) on the growth and development of 1–5-year-old children who were already stunted. Findings from this study showed that supplementation with LNS, irrespective of additional milk ingredients, supports linear catch-up growth and accretion of fat-free mass (FFM), but not fat mass (FM), in children with stunting. In contrast, among children who were not supplemented, stunting worsened and they gained fat at the expense of fat-free mass.
The MAGNUS 2 study aims to assess the long-term effects of LNS supplementation on the growth and development of children from the MAGNUS trial, who are now 6–10 years old. The study will also explore the association between stunting and early signs of cardiometabolic risk markers, and whether these are affected by supplementation with LNS. A new reference group of non-stunted children will be established for this purpose.

Who can participate?
Children with early stunted growth who participated in the former MAGNUS study can participate. In addition, we will recruit age- and sex-matched reference children without stunting from the same communities.

What does the study involve?
Children will be screened and referred to a clinic site for a full-day evaluation. After eligibility testing and informed consent/assent is obtained, the following data are collected: questionnaires on medical history, demographics and dietary information; clinical assessment including ultrasound scans (liver, spleen, kidneys, abdominal fat) and blood pressure assessment; anthropometrics of the mother (weight, height) and the child (weight, height, mid-upper arm and waist circumferences, subscapular and triceps skinfolds). Child bioelectrical impedance is measured to assess body composition, and child development is assessed by the Kaufman Assessment Battery for Children II test. School grades are collected, and grip strength and broad jump are measured. Finally, blood and stool samples are collected. After the examination at the study site, children are escorted home and WASH assessment and home-based questionnaires are conducted. Stool sample collection and home assessments may be done on another day.

What are the possible benefits and risks of participating?
Clinical benefits: Children will benefit from nutritional assessments, medical examinations, and blood haemoglobin and sugar tests. Families will also receive nutrition counselling and children will be referred if needed.
Community benefits: Training village health teams and clinical staff will build local capacity and raise awareness about child malnutrition, encouraging future screening at community clinics.
Procedural risks: Risks are minimal. Blood samples may cause brief discomfort but are taken by trained nurses. Ultrasound and bioelectrical impedance procedures are very safe and painless.

Where is the study run from?
The study is a community-based study. Participants will be recruited from villages around two health centres in Eastern Uganda: Walukuba Health Centre IV and Buwenge Health Centre IV.

When is the study starting and how long is it expected to run for?
September 2024 to April 2026

Who is funding the study?
The Novo Nordisk Foundation (Denmark)

Who are the main contacts?
1. Associate Professor Benedikte Grenov, University of Copenhagen, bgr@nexs.ku.dk
2. Associate Professor Dr. Ezekiel Mupere, Makerere University, ezekiel.mupere@mak.ac.ug, mupez@yahoo.com

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
S407

Study information

Scientific Title
Reducing short and long-term consequences of early stunted growth. MAGNUS 2 – Milk affecting growth, cognition and the gut in child stunting

Acronym
MAGNUS 2

Study objectives
Main objective:
To assess long-term effects of supplementation with large quantity LNS on child health

Primary objectives:
1. To assess the long term effects of 3-months supplementation with large-quantity LNS among 1-5-year old Ugandan stunted children on cardiometabolic risk markers at age 6-10 years.
2. To assess the association between stunting and cardiometabolic risk among 6-10-year-old Ugandan children.

Secondary objectives:
1. To assess the long-term effects of 3-months supplementation with large-quantity LNS among 1-5-year-old Ugandan stunted children on growth, body composition, child development, haemoglobin, micronutrient status and organ size (liver, kidney, spleen) at age 6-10 years.
2. To assess the long-term effects of 3-months supplementation with large-quantity LNS among 1-5-year-old Ugandan stunted children on gut microbiota and function at age 6-10 years.
3. To assess predictors of cardiometabolic risk markers among 6-10-year-old previously stunted Ugandan children.
4. To assess the associations between stunting and growth, body composition, child development, haemoglobin, micronutrient status and organ size (liver, kidney, spleen) among 6-

10-year-old previously stunted Ugandan children.
5. To assess the associations between stunting and gut microbiota and function among 6-10-year-old previously stunted Ugandan children.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 28/05/2025, Makerere University - School of Medicine Research Ethics Committee (PO Box 7072, Kampala, PO Box 7072, Uganda; +256 (0)414 533541; rresearch9@gmail.com), ref: Mak-SOMREC-2025-1248

2. approved 29/04/2025, De Videnskabsetiske Komitéer for Region Hovedstaden (Kongens Vænge, Hillerød, 3400, Denmark; +45 (0)38666395; vek@regionh.dk), ref: H-25020055

Study design
Observational multicenter follow-up study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Childhood stunting

Interventions
Children with early stunting who participated in the MAGNUS 1 trial will be invited for a 1-day follow-up at the same health facility as they attended in MAGNUS 1. We expect to be able to relocate up to 650 out of 750 children from MAGNUS 1. In addition, we will recruit 200 new reference children without stunting who will undergo the same questions, tests and examinations.

After inclusion, the following data are collected: questionnaires of medical history, demographics and dietary information, clinical assessment is conducted, including ultrasound scans (liver, spleen, kidneys, abdominal fat) and blood pressure assessment, anthropometrics of the mother (if available) and child are measured. Child bioelectrical impedance is measured to assess body composition and child development is assessed by the Kaufman Assessment Battery for Children II test, school achievement, grip strength and broad jump. Finally, blood and stool samples are collected. After the examination at the study site, children are escorted home and WASH assessment and home-based questionnaires are conducted. Stool sample collection and home assessments may also be done on another day.

Intervention Type
Other

Primary outcome(s)
Cardiometabolic risk markers:
1. Glucose , mmol/L (full blood, HemoCue 201) and HbA1c, mmol/mol (full blood, HemoCue501)
2. Insulin, pmol/L (serum, Cobas 400 immunoassay)

3. Lipids (total cholesterol, mmol/L, high density lipoprotein (HDL) cholesterol, mmol/L and low density lipoprotein (LDL) cholesterol, mmol/L and triglycerides, mmol/L) (serum, Pentra400, Horiba ABX)
4. Blood pressure, mmHg (Welch Allyn ProBP2000)
5. C-peptide, ng/mL (serum, Cobas 400 immunoassay)

All primary and secondary outcomes will be measured once. For children who participated in the MAGNUS trial, this corresponds to a 5-year follow-up. For new reference children, this is their first and only assessment.

Key secondary outcome(s))

1. Weight, kg (Seca scale)
2. Total height, cm (Shorr height board)
3. Knee-heel length, mm (Shorr knee-height caliper)
4. BMI-for-age z-scores (BAZ) (WHO Anthro)
5. Height-for-age z-scores (HAZ) (WHO Anthro)
6. Child development:
6.1. Cognition test (Kaufman assessment battery for children, KABC-II)
6.2. School achievement (school grades)
6.3. Motor function (grip strength, broad jump) (Takei, Japan and non-elastic measuring tape)
7. Haemoglobin, g/dL (full blood, HemoCue801)
8. Body composition measured by bioelectrical impedance: FM, kg, FFM, kg, FMI, kg/m2, FFMI, kg /m2 (BodyStat 500)
9. Organ size (liver, kidneys and spleen) (ultrasound, Sonoscape)
10. Skin folds: triceps, subscapularis, mm (Harpenden caliper)
11. Waist circumference, cm (non-elastic measuring tape)
12. Abdominal fat (ultrasound, Sonoscape)
13. Mid-upper arm circumference (MUAC), cm (non-elastic measuring tape)
14. Blood hormone markers:
14.1. Insulin-like Growth Factor-1 (IGF-1), ng/mL (serum, Cobas 400 immunoassay)
15. Blood markers of systemic inflammation
15.1. C-reactive protein (CRP), mg/L (serum, high throughput ELISA)
15.2. Alpha-1-acid glycoprotein (AGP), µg/mL (serum, high throughput ELISA)
16. Blood markers of micronutrient status:
16.1. Iron: serum ferritin, µg/L and soluble transferrin receptor, mg/L (serum, high throughput ELISA)
16.2. Vitamin B12: plasma cobalamin, pmol/L (Advia Centaur CP Immunoassay System) and plasma methyl malonic acid (MMA), µmol/L (plasma, mass spectrometry)
16.3. Folate, nmol/L (plasma, Advia Centaur CP Immunoassay System)
16.4. Vitamin A (retinol binding protein), µmol/L (serum, high throughput ELISA)
17. Gut microbiota (stool, 16S rRNA sequencing)
18. Gut function (e.g., plasma citrulline [mass spectrometry], faecal myeloperoxidase, faecal neopterin, faecal alpha-1-antritrypsin [stool, ELISA])
19. Morbidity (questionnaire)

All primary and secondary outcomes will be measured once. For children who participated in the MAGNUS trial, this corresponds to a 5-year follow-up. For new reference children, this is their first and only assessment.

Completion date

01/04/2026

Eligibility

Key inclusion criteria
Inclusion criteria for children who participated in the MAGNUS 1 trial:
1. Confirmed participation in MAGNUS 1*
2. Living within the catchment area
3. Written informed consent given by parent/caregiver
*Confirmed by birth certificate, identity card, or similar documents and/or other confirmation of previous participation in the MAGNUS 1 trial (e.g. informed consent form)

Inclusion criteria for the reference group:
1. Age 6-10 years
2. Height-age-z-scores >-1 according to the WHO growth standards
3. Living within the catchment area of MAGNUS 1 trial participants
4. Written informed consent given by parent/caregiver

Participant type(s)
Population

Healthy volunteers allowed
No

Age group
Child

Lower age limit
6 years

Upper age limit
10 years

Sex
All

Key exclusion criteria
Exclusion criteria for children who participated in MAGNUS 1 trial and the reference group:
1. SAM; measured as BMI-for-age z-score < -3 OR bilateral pitting oedema
2. Medical complications requiring hospitalization
3. Disability that makes height assessment problematic
4. Participation in another study or program which impacts on this study

Date of first enrolment
25/09/2025

Date of final enrolment
01/04/2026

Locations

Countries of recruitment

Uganda

Study participating centre
Walukuba Health Centre IV
-
Jinja
Uganda
-

Study participating centre
Buwenge Health Centre IV
-
Buwenge
Uganda
-

Sponsor information

Organisation
University of Copenhagen

ROR
https://ror.org/035b05819

Funder(s)

Funder type
Industry

Funder Name
Novo Nordisk Fonden

Alternative Name(s)
Novo Nordisk Foundation, Novo Nordic Foundation, NNF

Funding Body Type
Private sector organisation

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

Location
Denmark

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are not expected to be made available due to legal reasons

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 4	30/03/2025	29/07/2025	No	No