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The role of milk protein and other dried milk products in the growth and development of stunted children

Submission date	Recruitment status	[X] Prospectively registered
06/01/2020	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
13/01/2020	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
09/08/2024	Nutritional, Metabolic, Endocrine	

Plain English summary of protocol

Background and study aims
Stunting affects one of every four children globally, and is associated with delayed physical and cognitive development, and reduced working capacity and educational achievement. Childhood stunting therefore impairs human capital, and it may also increase the risk of chronic diseases later in life. Milk has been shown to play a role in growth, but it is not clear if such effects are due to the protein or to lactose and minerals (in whey permeate) in milk.
This study aims to assess the effects of milk protein and whey permeate in a lipid-based nutrient supplement (LNS) on growth in children with stunting.

Who can participate?
Children aged 12 – 59 months with stunted growth.

What does the study involve?
Participants will be randomly allocated to one of five groups. Groups 1 – 4 will receive a different LNS for 12-weeks, group 5 will not receive any supplement. Participants will be measured to assess growth over the 12 weeks as well as priding blood and stool samples.

What are the possible benefits and risks of participating?
It is expected that all children will benefit from the experimental products and/or the nutrition counselling, as well as the medical assessments and referrals, if needed. Apart from low risk of allergic reactions to milk or peanut, the products are not likely to pose any risks.

Where is the study run from?
1. Buwenge Health Centre IV, Uganda
2. Walukuba Health Centre IV, Uganda

When is the study starting and how long is it expected to run for?
January 2020 to December 2020 (updated 11/11/2020, previously: January 2021) (updated 14/07/2020, previously: September 2020)

Who is funding the study?
1. ARLA Food for Health, Denmark
2. Danish Dairy Research Foundation, Denmark
3. Nutriset, France
4. University of Copenhagen, Denmark

Who is the main contact?
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Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
D222

Study information

Scientific Title
The role of milk protein and whey permeate in the growth and development of stunted children: a randomised controlled trial in Eastern Uganda

Acronym
MAGNUS

Study objectives
1. Milk protein and whey permeate in a lipid-based nutrient supplement (LNS) increases linear growth among children with stunting
2. Milk protein and whey permeate in a LNS increases ponderal growth and fat-free mass accretion, haemoglobin, and child development among children with stunting
3. Supplementation with LNS, with or without milk ingredients, increases linear and ponderal growth, fat-free mass accretion, haemoglobin and child development in children with stunting
4. The effects of milk protein and whey permeate in LNS, or LNS itself, on linear and ponderal growth, fat-free mass accretion, haemoglobin and child development in children with stunting, are mediated by effects on markers of environmental enteric dysfunction

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/12/2019, School of Medicine Research and Ethics committee (SOMREC) at Makerere University (PO Box 7072, Kampala, Uganda; +256 414 533541; rresearch9@gmail.com), ref: 2019-013

Study design
Randomized controlled double-blind two-by-two factorial trial

Primary study design
Interventional

Secondary study design
2-by-2 factorial

Study setting(s)
Community

Study type(s)
Other

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Stunting

Interventions
Children in four study arms will receive a lipid-based nutrient supplement (LNS, 100 gram containing 530 kcal per day) with or without whey permeate and milk protein isolate using a 2-by-2 factorial design. The supplements contain similar proportions of energy, protein and carbohydrates. Each formulation contains a mineral and vitamin mix. The minerals provided by the whey permeate are in addition. The supplements have similar appearance, texture, colour and taste. Children in a fifth study arm will not be supplemented, and serve as a reference. Children in all study arms will receive nutrition counselling. The duration of the intervention is 12 weeks.

Groups:
1. LNS with whey permeate and milk protein isolate
2. LNS with whey permeate and without milk protein isolate
3. LNS without whey permeate and with milk protein isolate
4. LNS without whey permeate and without milk protein isolate
5. No supplement

In 2 and 4, milk protein isolate is replaced by soy protein isolate. In 3 and 4, whey permeate is replaced by maltodextrin.

Randomisation will be done stratified by site and using variable block size.

Intervention Type
Supplement

Primary outcome measure
Measured at baseline and 12-weeks:
1. Knee-heel length (mm)
2. Height (cm)

Secondary outcome measures
Measured at baseline and 12-weeks:
1. Mid-upper arm circumference (mm)
2. Weight (g)
3. Height-for-age z-scores (HAZ)
4. Weight-for-height z-scores (WHZ)
5. Weight-for-age z-scores (WAZ)
6. Child development index (CDI)
7. Head circumference (cm)
8. Bioimpedance: Fat mass (FM, kg), fat-free mass (FFM, kg), fat mass index (FMI, kg/m2), fat-free

mass index (FFMI, kg/m2)
9. Skin folds: triceps, subscapularis (mm)
Blood tests:
10. Haemoglobin (g/L)
11. Serum/plasma insulin-like Growth Factor-1 (IGF-1)
12. Serum/plasma insulin
13. Serum C-reactive protein
14. Serum alpha-1-acid glycoprotein
15. Plasma citrulline
16. Serum ferritin and transferrin receptors (markers of iron status)
17. Plasma cobalamin and methylmalonic acid (markers of B12 status)
18. Plasma folate
19. Serum retinol
Fecal tests:
20. Fecal myeloperoxidase
21. Fecal neopterin
22. Fecal alpha-1-antitrypsin
23. Gut microbiota

24. Morbidity (including diarrhea, pneumonia, fever, malaria), safety (deterioration to MAM or SAM and mortality) measured using patient records

Overall study start date
01/01/2018

Completion date
18/12/2020

Eligibility

Key inclusion criteria
1. Age 12 - 59 months
2. Height-age-Z < -2 according to WHO growth standards (2006)
3. Care-taker able and willing to return for follow-up visits and agrees to phone follow-up
4. Living within the catchment area
5. Written informed consent given by parent/caregiver

Participant type(s)
Other

Age group
Child

Lower age limit
12 Months

Upper age limit
59 Months

Sex

Both

Target number of participants
750

Total final enrolment
750

Key exclusion criteria
1. Severe acute malnutrition, defined as MUAC <115 mm OR WHZ<-3 OR bilateral pitting oedema
2. Medical complications requiring hospitalization
3. Obvious disability that impedes eating capacity
4. Disability that makes length/height assessment problematic
5. Participation in another study which impacts on this study or previous enrollment in this study
6. Family plans to move away from the catchment area in the next 6 months
7. History or known allergy to peanuts or milk

Date of first enrolment
31/01/2020

Date of final enrolment
30/06/2020

Locations

Countries of recruitment
Uganda

Study participating centre
Buwenge Health Centre IV
Jinja
Uganda
TBD

Study participating centre
Walukuba Health Centre IV
Jinja
Uganda
TBD

Sponsor information

Organisation

University of Copenhagen

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Sponsor type
University/education

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ROR
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Funder(s)

Funder type
Research organisation

Funder Name
ARLA Food for Health, Denmark

Funder Name
Danish Dairy Research Foundation, Denmark

Funder Name
Nutriset, France

Funder Name
University of Copenhagen, Denmark

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan
The datasets generated during 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 V5	03/12/2019	11/11/2020	No	No
Statistical Analysis Plan	version 01	16/04/2021	19/04/2021	No	No
Protocol article		24/04/2021	13/08/2021	Yes	No
Results article	results	23/05/2023	24/05/2023	Yes	No
Results article	Analysis of plasma citrulline levels and correlations	20/12/2023	27/12/2023	Yes	No
Other publications	Secondary analysis	24/01/2024	29/01/2024	Yes	No
Other publications	Correlates of body composition using baseline measurements data	05/08/2024	09/08/2024	Yes	No