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# Role of Probiotics in recovery of children with Severe Acute Malnutrition

**Submission date**
06/01/2014

**Recruitment status**
No longer recruiting

**Registration date**
15/01/2014

**Overall study status**
Completed

**Last Edited**
01/11/2021

**Condition category**
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
About 35% of global child deaths below five years of age are estimated to be caused by Undernutrition, and pneumonia and diarrhea are the two most common causes of death in undernourished children. Adding probiotics to the food of severely malnourished children may be a way to reduce the occurrence and severity of both diarrhea and airway infections in undernourished children. Studies suggest that probiotics are able to reduce the occurrence and duration of diarrhea and may reduce the risk of airway infections. Some of the probiotic studies have included mildly to moderately malnourished children, but most studies have been conducted in well-nourished populations.The main aim of the study is to measure the effect of two probiotic strains on diarrhea in children with severe acute malnutrition (SAM) when given together with the usually recommended treatment.

Who can participate?
Children aged 659 months with severe acute malnutrition.

What does the study involve?
Children with severe acute malnutrition admitted to a nutritional rehabilitation unit at a national referral hospital in Uganda will be recruited. All children are treated according to the WHO protocol for treatment of children with SAM. Children were randomly allocated to either receive a daily dose of probiotics or a dummy sachet of similar appearance and taste during the entire study period. The follow-up visits as an outpatient will last between 8 to 12 weeks depending on the recovery rate of the child. Each child will have body measurements performed at admission, discharge and at the follow-up visits every two weeks. Weight will be measured daily and height will be measured weekly during hospitalization. A thymus gland ultrasound scan will be carried out and blood and stool samples will be collected at admission, discharge and after 8 weeks follow-up. Diarrhea will be monitored closely with daily registration of stool frequency, stool consistency, vomiting and fever. Pneumonia is diagnosed by medical doctors.30 healthy children of the same age and from the same area will be included to collect reference samples of blood and feces and thymus scans.

What are the possible benefits and risks of participating?
All children will benefit from the extra attention they may get in the study especially in relation

to diarrhea and pneumonia. Children that receive the probiotics may benefit from a reduced occurrence and severity of diarrhea and pneumonia. The risk associated with treatment of children with SAM with the two probiotic strains is minimal. However, as the study population is vulnerable, an independent Data Safety Monitoring Board has been established to follow safety during the study. All the procedures carried out in the study involve no or minimal risk or discomfort to the children.

Where is the study run from?
The study takes place at Mwanamugimu Rehabilitation Nutrition Unit, National Referral, Mulago Hospital, Department of Paediatrics and Child Health, Kampala, Uganda.

When is the study starting and how long is it expected to run for?
The study will take place between March 2014 and July 2015.

Who is funding the study?
Chr. Hansen A/S and University of Copenhagen, Denmark.

Who is the main contact?
Prof. Henrik Friis
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# Contact information

### Type(s)
Scientific

### Contact name
Prof Henrik Friis

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# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
HND-IN-017

# Study information

### Scientific Title
Role of Probiotics in recovery of children with Severe Acute Malnutrition: a randomized, double-blind, placebo-controlled, parallel study

### Acronym
ProbiSAM

### Study objectives
1. Probiotics are able to reduce the duration, incidence and severity of diarrhea in children with severe acute malnutrition
2. Probiotics are able to reduce the risk and duration of respiratory tract infections in children with severe acute malnutrition
3. Probiotics are able to increase nutritional recovery in children with severe acute malnutrition
4. Probiotics are able to change the microbiota, immune response and markers of environmental enteropathy in a beneficial direction in children with severe acute malnutrition

On 12/05/2014 the overall trial start date was changed from 01/02/2014 to 01/03/2014.

On 01/09/2015 the overall trial end date was changed from 01/07/2015 to 01/10/2015.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
1. Uganda: School of Medicine Research and Ethics committee (SOMREC) at Makerere University, 7 October 2013, #REC REF 2013-132.
2. Denmark: The National Committee on Health Research Ethics, 12/02/2014

### Study design
Block-randomized double-blind placebo-controlled parallel study

### Primary study design
Interventional

### Secondary study design
Randomised controlled trial

### Study setting(s)
Hospital

### Study type(s)
Quality of life

### Participant information sheet

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

## Health condition(s) or problem(s) studied
Severe acute malnutrition (SAM)

## Interventions
Two study arms - receiving one daily dose of:
1. Probiotic sachet containing two probiotic strains (Lactobacillus and Bifidobacterium)
2. Placebo sachet
The content of one probiotic/placebo sachet will be consumed daily during the study period: from hospital admission to discharge and throughout a follow-up period of 8 weeks to 3 months depending on the recovery rate of the child.

## Intervention Type
Other

## Phase
Not Applicable

## Primary outcome measure
Current primary outcome measures as of 11/09/2015:
Duration of diarrhea during hospitalization

Previous primary outcome measures:
Duration of diarrhea episodes (days)

## Secondary outcome measures
Current secondary outcome measures as of 11/09/2015:
1. Incidence and severity of diarrhea (during hospitalization and during the outpatient treatment period, respectively) and duration of diarrhea during the outpatient treatment period
2. Incidence, severity and duration of pneumonia (during hospitalization and during the outpatient treatment period, respectively)
3. Nutritional recovery based on weight gain (during hospitalization and during the outpatient treatment period, respectively)
4. Specific changes in gut microbiota, immune response and intestinal health markers as indicated in the study protocol (at discharge and after 8 weeks outpatient treatment)

Diarrhea, pneumonia and weight gain are measured throughout the study. Diarrhea and pneumonia will be measured daily and weight gain will be measured daily during the hospitalization and fortnightly during
the follow-up period. We will include all these measurements in the statistical analyses

Previous secondary outcome measures:
1. Incidence and severity of diarrhea episodes (during hospitalization and during the outpatient treatment period, respectively)
2. Incidence, severity and duration of pneumonia episodes (during hospitalization and during the outpatient treatment period, respectively)
3. Nutritional recovery based on weight gain (during hospitalization and during the outpatient

treatment period, respectively)
4. Specific changes in gut microbiota, immune response and intestinal health markers as indicated in the study protocol (at discharge and after 8 weeks outpatient treatment)

Diarrhea, pneumonia and weight gain are measured throughout the study. Diarrhea and pneumonia will be measured daily and weight gain will be measured daily during the hospitalization and fortnightly during
the follow-up period. We will include all these measurements in the statistical analyses.

### Overall study start date
01/03/2014

### Completion date
01/10/2015

## Eligibility

### Key inclusion criteria
1. Age 6 - 59 months
2. Children with severe acute malnutrition
3. Care-taker willing to come back for follow-up
4. Written informed consent obtained by parent or care-taker

### Participant type(s)
Patient

### Age group
Child

### Lower age limit
6 Months

### Upper age limit
59 Months

### Sex
Both

### Target number of participants
400

### Total final enrolment
400

### Key exclusion criteria
1. Patients with severe conditions and diseases
1.1. Shock at admission. Once stabilized, these children may be included.
1.2. Severe respiratory difficulty at admission. Once stabilized, these children may be included.
2. Weight below 4 kg at admission
3. Obvious disability, e.g. Cerebral palsy, hydrocephalus, Downs syndrome

4. Significant congenital diseases, e.g. Congenital heart disease
5. Malignant diseases
6. Patients considered by study staff not to be able to participate in the study
7. Patients being admitted with SAM in the last 6 months
8. Patients participating in another study

### Date of first enrolment
01/03/2014

### Date of final enrolment
01/10/2015

## Locations

### Countries of recruitment
Uganda

### Study participating centre
**Mwanamugimu Rehabilitation Nutrition Unit**
National Referral
Mulago Hospital
Department of Paediatrics and Child Health
Kampala
Uganda
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## Sponsor information

### Organisation
Chr. Hansen A/S (Denmark)

### Sponsor details
Bøge Allé 10-12
Hørsholm
Denmark
2970

### Sponsor type
Industry

### Website
http://www.chr-hansen.com/

### ROR
https://ror.org/01mv6bt66

# Funder(s)

### Funder type
University/education

### Funder Name
Chr. Hansen A/S (Denmark)

### Funder Name
University of Copenhagen (Denmark)

# Results and Publications

### Publication and dissemination plan
To be confirmed at a later date

### Intention to publish date

### Individual participant data (IPD) sharing plan
Not provided at time of registration

### IPD sharing plan summary
Not expected to be made available

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | results | 01/03/2017 | | Yes | No |
| Results article | results | 01/09/2019 | 10/06/2019 | Yes | No |
| Other publications | analysis of weight and MUAC gain velocities | 18/06/2021 | 21/06/2021 | Yes | No |
| Other publications | Weight-for-Height Z-score Gain (sub study) | 25/09/2021 | 01/11/2021 | Yes | No |