ACTION AGAINST HUNGER

The MANGO project

CAN WE RECOVER SEVERELY MALNOUSRISHED CHILDREN BY USING A REDUCED DOSE OF NUTRITIONAL PRODUCT DURING TREATMENT ?

Burkina Faso, District of Fada N'Gourma
5 years (2015-2021)

UNIVERSITY OF COPENHAGEN

04/2021

MANGO PROJECT

MANGO

Modelling an **A**lternative **N**utritional protocol **G**eneralisable to **O**utpatient Care

MAIN OBJECTIVE

To prove, under artificially ideals conditions, the **efficacy of a reduced dose of RUTF** compared to a standard dose in the treatment of uncomplicated severe acute malnutrition (SAM) in children aged 6-59 months.

ORIGINS

The idea for the MANGO project was born out of an innovative emergency nutrition program in Myanmar between 2008 and 2009.

Due to country-specific supply difficulties, and the increased number of SAM children following the adoption of the "new" WHO standard in February 2009, AAH chose to decrease the amount of RUTF during treatment once the SAM children had regained MAM status.

Retrospective analysis of the results showed a similar recovery rate that of children previously treated with a standard dose. AAH decided to confirm these programmatic results through more solid scientific research with a control group and in a more common context of support to the Ministry of Health and not substitution.

Analyses of program data led to the design of an innovative new time-sequenced dosage while maintaining simplicity of dosing by whole sachet and weight category for ease of care delivery.

AAH partnered with leading researchers in pathophysiology of acute malnutrition and other specialists to design the MANGO project. The study was designed to avoid disruption in the supply of RUTF and other treatment inputs, with strict adherence to protocol and the highest quality of care. This was done in order to attribute the results obtained to the reduced dose while minimising the possible impacts of changes in the care protocol during the study.

GLOSSAIRE

MAM	Moderate Acute Malnutrition
MUAC	Mid Upper Arm Circumference
RUTF	Ready-to-Use Therapeutic Food
SAM	Severe Acute Malnutrition
WHZ	Weight For Height Z-score

RESEARCH OBJECTIVES

A Is the reduced dose of RUTF effective in SAM children aged 6-59 months in terms of:

1. Weight gain velocity?
2. Body Composition?
3. Vitamin A and Iron status?
4. Cost savings per child treated?
5. Nutritional and energy intake and daily needs coverage?
6. Food diversity and factors of diversity?

B More descriptively, around the reduced dose of RUTF during SAM treatment:

7. Adherence, use and perception of RUTF in families
8. Factors predicting slower recovery or non-response to treatment.

METHOD

1st step

Determining the reduced dosage and development of the research protocol.

Dosage of RUTF according to the group

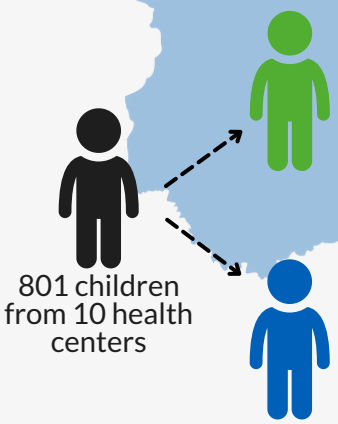
	Sachets/week			Reduction percentage (%)
	Standard dose (n=399)	Reduced dose (n=402)		
Weight (kg)	From admission to discharge	Week 1 and 2	From 3rd week onward	Between week 1-2 and week 3
3.0-3.4	8	8	7	13
3.5-4.9	10	10	7	30
5.0-6.9	15	15	7	53
7.0-9.9	20	20	14	30
10.0-14.9	30	30	14	53

2nd step

Implementing the study to test the efficacy of the established dosage.

RANDOMIZED CONTROL TRIAL IN NON-INFERIORITY
A high level of reliability (WHO)

Individual randomization



Eligibility criteria
Children from 6 to 59 months
SAM according to WHZ< -3 and/or MUAC < 115mm
Successful appetite test

Exclusion criteria
Bilateral oedemas
Medical complications at admission
Severe anaemia, malformation, allergy
Having received SAM treatment less than 6 months ago

Discharge criteria
- Recovered: WHZ ⩾ -2 and/or MUAC ⩾ 125mm (aligned with admission criteria) for two consecutive weeks
- Defaulter: absent 3 consecutive weeks
- Death: during treatment
- Non-respondent: have not reached recovered criteria after 16 weeks
- Referral : transferred to hospital due to danger signs
- Relapse: SAM again 3 months after recovery

Starting Hypothesis
There will be no or very little difference in mean weight gain velocity between the 2 groups at the end of the treatment (acceptable variation 0.5g/kg/day)

ENCOURAGING RESULTS

1/8 The reduced dose of RUTF does not affect weight gain in SAM children but does affect height gain in younger child

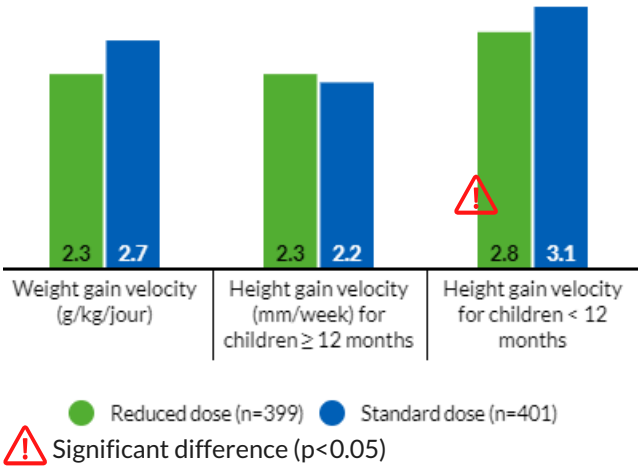
Programmatic results of SAM treatment according to the dose of RUTF

Rate in %	Reduced dose (n=399)	Standard dose (n=401)	*p*-value
Recovery	52.7	55.4	0.45
Recovery (SPHERE standards 2018)	68.0	72.0	N/A
Death	0.3	0.3	N/A
Defaulter during treatment	12.2	8.5	0.09
Referral	19.2	20.1	0.80
Non-respondant	12.7	12.5	0.95
Relapse after 3 months	2.4	1.8	0.69

There are no significant differences between the two groups of children in terms of recovery, defaulter, death, referral, non respondent, or relapse rates. The average length of stay is 56 days (8 weeks).

Weight gain and height gain velocity of SAM children treated with a reduced or a standard dose of RUTF

The weight gain velocity is not different between the two groups. Note that a reduced dose slows the height gain velocity of children under 12 months.



WHAT TO REMEMBER

Weight gain velocity → Not different for the two groups

Recovery, defaulter, death, relapse and other indicators → Not different for the two groups

Not different for the two groups → Reduced dose **efficacious** for this population in this context

Height gain velocity → Slower for children < 12 months → Reduced dose **inadequate** for younger children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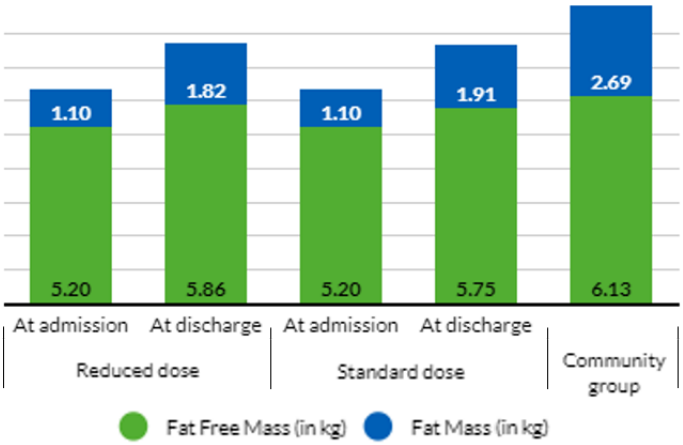
2/8 Body composition is similar in both groups of children

Body composition of SAM children treated with a reduced, with a standard dose and of a community control group



Body composition was measured twice by Bio-electrical Impedance (BiA) at admission (n=452) and discharge (n=259) and on a community control group (n=97).

Fat Free Mass (FFM) accounts for nearly half of the children's weight gain (45%) during treatment in both groups. This indicates that **the reduced dose similarly ensures the growth of fat free mass during treatment.**

However, at the end of the treatment, children who recovered from SAM still have a lower fat mass (FM) than the community group.

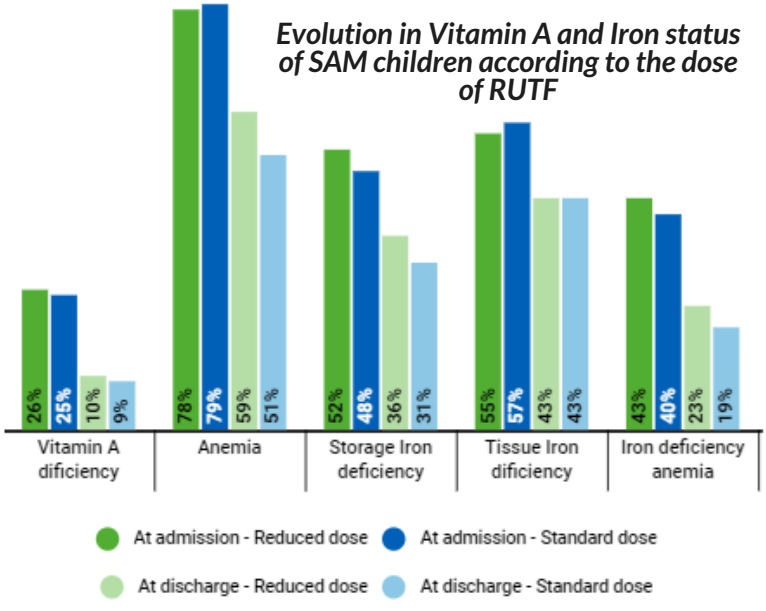
3/8 Initial Vitamin A and Iron deficiencies are reduced in both groups

Blood samples taken at admission and discharge and analyzed for 425 recovered children for anemia and 383 recovered children for other biomarkers. Among the 5 biomarkers measured, Retinol Binding Protein, Serum Ferritin and Soluble Transferrin Receptor are used to assess Vitamin A and Iron status.

No significant difference is observed in vitamin A deficiency, storage and tissue iron deficencies, and Iron deficiency anemia (IDA) between the two groups of children. However, the reduced dose group has a higher anemia (+9%) and a lower haemoglobin, althought this was marginally significant.

Recovered SAM children still show deficiencies in vitamin A and iron compared to healthy children.

Evolution in Vitamin A and Iron status of SAM children according to the dose of RUTF



4/8 The reduced dose allows net savings on the total cost per child treated

AAH opts for a societal approach for economic analyses where the costs borne by families and partners are evaluated in the same way as those of the NGO, since they contribute to the success of the treatement of malnutrition. Individual randomization allows to postulate that all costs are identical in the two groups, only the difference in intervention is evaluated.

The incremental costs for a consultation during treatment are those that were analysed in detail: HR costs, equipment costs, consumables, costs borne by the families of the treated children, and the price and costs of transporting and storing the RUTF. There is no difference in these costs except for the cost of RUTF consumed per group.

The reduced dose of RUTF for the treatment of uncomplicated SAM for 399 children represents a saving of $6,140 or 16.8% and a saving of $15.4 per child treated in the context of Burkina Faso.

In a "real life" scenario and if only the NGO costs are taken into account, the cost per child treated with a reduced dose is estimated at $36.1 and $47.6 with a standard dose.

Average costs of SAM treatment with a reduced dose and with a standard dose

Dollar (2017) using the Purchasing Power Parity (1EUR = 0.8 USD)	Reduced dose (n=399)	Standard dose (n=401)	Net savings
Per child treated	**$76.2**	**$91.6**	**$15.4**
Per consultation	$9.6	$11.6	$2
For the treatment	$30,411	$36,550	$6,140

-16.8 %
of net savings

5/8 Energy and nutritional intakes are covered in both groups

A 24-hour dietary recall was conducted with mothers at week 4 or 5 of treatment to list all foods and beverages consumed (excluding breast milk) by the child in the past 24 hours. The foods consumed were converted into nutrients using a food composition table created for the study.

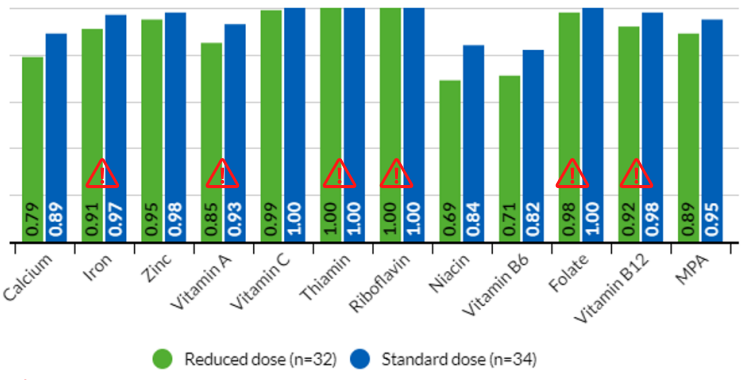
The reduced dose group has a significantly lower energy and nutrient intake ($p<0.001$) than the standard group (1321 kcal vs 1467 kcal). Nevertheless, the Recommended Nutrient Intakes (RNI) are met in both groups. Taking into account only the nutritional intake from RUTF, the reduced dose would cover 92% of the RNI.

The family and supplementary foods contribute significantly to the daily energy intake in the two groups : 40% in the reduced dose group, 35% in the standard dose group.

The mean probability of micronutrient adequacy (MPA) is similar in both groups when adjusted for energy. There is no difference in calcium, zinc, vitamin C, niacin, and vitamin B6.

It should be noted, however, that a reduced dose of RUTF leads to a decrease in the coverage of iron, vitamin A, thiamin, riboflavin and vitamin B12.

Probability of micronutrient adequacy with a reduced and a standard dose



6/8 Impact of a reduced dose of RUTF on dietary diversity of SAM children and factors of diversity

Determinants of dietary diversity score of SAM children during treatment

	DDS		
Child's sexe		Caregiver's ethnic group	
Male	3,95	Fulani	3,63
Female	4,12	Mossi	4,26
Child's age		Gourma	4,07
< 12 months	3,91	Others	4,30
≥ 12 months	4,24	Household's food security	
Child's morbidity		Food secure	4,01
No	3,97	Mid food insecurity	4,21
Yes	4,34	Moderate and severe FI	4,19
Stunting at admission		Household's wealth index	
No	4,16	Low	3,81
Yes	3,95	Medium	3,92
Caregiver's education		High	4,26
No	3,92	Household's residence	
Yes	4,41	Rural	3,98
Caregiver's age		Urban	4,37
< 25 years	4,14	Season of interview	
≥ 25 years	3,98	Rainy season	4,23
		Dry season	3,91

24-hour dietary recall conducted at week 4 or 5 of treatment among 219 children in the reduced dose group and 240 in the standard dose group. This consisted of listing and quantifying all foods and beverages consumed (excluding breast milk) in the past 24 hours.

All SAM children consumed diversified family foods outside of RUTF. The dietary diversity score is 4 food groups consumed on average in both groups of children.
Supplementary feeding practices did not differ according to the dose of RUTF received, except for the Minimum Meal Frequency (MMF) which is higher in the reduced dose group.

Some factors significantly improve DDS: children between 12 and 23 months, educated caregiver, non-Fulani cultural group, wealthy household living in urban area, child sick the week prior and rainy season.

7/8 Availability, use and consumption of RUTF prescribed to SAM children

In-depth individual interviews with caregivers at 1 month (4 weeks) and 2 months (8 weeks) of treatment. The aim was to assess the perception of the caregivers, the availability (% of children having RUTF available until the end of the week with or without leftovers) and the consumption of the nutritional product.

RUTF was available in both groups of children. At the end of the treatment, the reduced dose group consumed 82.4% (i.e. 97/117) of the sachets prescribed during the treatment compared with 80.3% (i.e. 143/175) for the standard dose group.
More than 40% of the children in the reduced dose group consumed the product at least 3 times a day compared to 82% in the standard dose group.

Side effects (diarrhea and/or vomiting) were reported in both groups: 18% in the reduced dose group and 24% in the standard dose group.

Availability, consumption and perceptions according to the dose of RUTF

	Reduced dose n=243	Standard dose n=273
RUTF availibility during week		
RUTF available (%)	95,4	99,2
Week with remains (%)	6,2	10,5
Week without remains (%) ⚠	89,2	88,7
Finished before visit (%)	4,6	0,8
RUTF quantity per week		
Prescribed, *in sachets* (n) ⚠	10,0	17,6
Consumed, *in sachets* (n) ⚠	9,3	15,9
Consumption rate (%)	95,0	92,8
RUTF frequency of consumption		
Once a day (%) ⚠	10,4	0
Twice a day (%)	47,0	17,3
Three times or more a day (%)	42,6	82,7
Perception on RUTF prescribed		
RUTF at least sufficient* (%)	92,3	97,7
More than desired (%) ⚠	1,5	7,5
Enough (%) ⚠	90,8	90,2
Less than desired (%) ⚠	7,7	2,3

*At least sufficient = More than desired + Enough

⚠ Significant difference (p<0,05)

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6/8 Predictors of time to recovery and to non-response to SAM treatment

This upcoming article will present the study (included in the MANGO project) on predictors that lengthen or shorten time to recovery and predictors of non-response to treatment.

CONCLUSIONS

Treatment with a reduced dose of RUTF is as effective as with a standard dose.

Nevertheless, a treatment with a reduced dose is insufficient in terms of :
Linear growth of children under 12 months ;
Iron, vitamin A, thiamin, riboflavin, folate and vitamin B12 intakes ;
Hemoglobin concentration and prevalence of anemia.

The treatment of SAM is not as effective as it should be, regardless of the dose. Indeed, at the end of the treatment :
Fat mass remains lower than in healthy children ;
Vitamin A and iron deficiencies are not fully corrected.

Our study does not justify a direct change in practice as it was an efficacy trial conducted under ideal conditions such as no shortage of RUTF and additional staff to provide optimal quality of care for each child.

AFTER MANGO...

1. The last 2 analyses of the MANGO project are still ongoing:
   - Predictors of time to recovery and to become non-respondent
   - Status of children in vitamin B12 from admission to discharge and under a reduced dose.

2. Our reduced dose needs to be confirmed:
   - In a routine context of health services and
   - in food insecure areas

   to be able to conclude that this reduction is safe, effective and feasible in other types of context.

3. A sub-study called "Opti'diag" nested in the MANGO project has made it possible to document the vulnerability profile of children at admission from a physiological (blood and urine biomarkers) and clinical point of view, according to various anthropometric deficits. It will provide a solid insight into which children are most vulnerable (https://doi.org/10.1542/peds.2020-027003).

4. If a reduced dose is implemented on a large scale, avoiding shortages of RUTF will remain the biggest challenge, as well as the high cost of RUTF to governments.

5. From a treatment point of vue, the current challenge in treating SAM is to achieve sustainable anthropometric and psysiological recovery, no relapse within 6 months and minimised long-term consequences in terms of morbidity and mortality.

MANGO PROJECT

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To go further

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- Nikièma V (2021), *Availability, use, and consumption practices of Ready-to-Use Therapeutic Foods prescribed to children with uncomplicated severe acute malnutrition aged 6-59 months during outpatient treatment in Burkina Faso*. **Appetite** . https://doi.org/10.1016/j.appet.2021.105751
- Bio-electrical impedance technical brief (BiA) available on our project web page: https://www.actioncontrelafaim.org/projet-mango/
- Opti'diag study - https://www.actioncontrelafaim.org/projet-optidiag/

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