Optimising acute malnutrition treatment is non-inferior to standard protocol in uncomplicated severely wasted children: main secondary outcome of a randomised controlled trial in Democratic Republic of Congo.

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Introduction and Methods

Introduction The Optimising MAlnutrition treatment (OptiMA) strategy aims to simplify current malnutrition treatment protocols by enrolling children with mid-upper arm circumference (MUAC)<125mm or oedema and supplementing with one product—ready-to-use therapeutic food (RUTF)—at gradually reduced doses as a child's weight and MUAC increases.

Objective To determine whether the recovery rate of children with uncomplicated severe acute malnutrition (SAM) according to the current WHO definition (ie, MUAC <115 mm or weight-for-height Z-score, WHZ, <–3 or bilateral oedema) managed under the OptiMA protocol is non-inferior to that of the national standard protocol during trial follow-up.

Methods

- Non-inferiority individually randomized controlled trial
- Nested in a post-conflict emergency program in Kasai province
- 4 health centres, 60 villages, one district hospital included
- Children aged 6-59 months with MUAC <115 mm OR WHZ<-3 OR bipedal oedema (+,++) without medical complications
- 6 months follow-up post-inclusion, follow-up visits in the village twice a month after discharge from health centre or in case of absence during outpatient weekly visits.

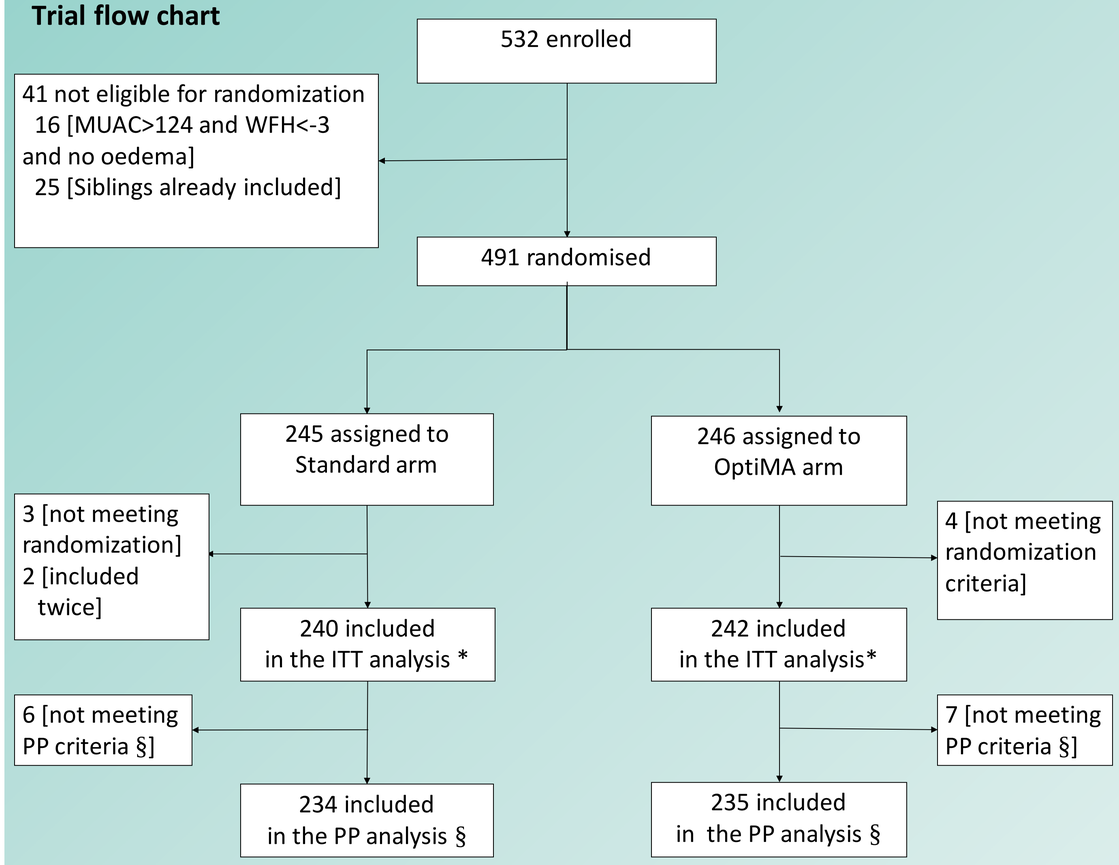
Ethics Approved by the National Health Ethics Committee, DRC, and by the Ethics Evaluation Committee of Inserm, the French National Institute for Health and Medical Research (Paris, France).

Main secondary outcome

Recovery over the trial follow-up **-> 480 participants needed**	- 4 week minimum duration of RUTF treatment **and** - Temperature <37.5°C **and** - Absence of bipedal oedema **and** - For OptiMA arm : MUAC > 124 mm - For Standard arm: MUAC > 124 mm **or** WHZ ≥-1.5 (2 weeks)
Main analysis	- **Non-inferiority analysis** comparing both arms on an **intention-to-treat (ITT) and per-protocol (PP)** basis - Non-inferiority demonstrated **if the upper-bound of the 95% confidence interval (CI) of the difference** between standard and OptiMA arms is **<10%** (one-sided test, α =2·5%, 1-β=80%).
Secondary outcomes	- Anthropometric changes, quantity and length of RUTF treatment among the children who recovered - Recovery rate and time to recover with the same recovery definition applied in both arms (standard definition, OptiMA definition).

Results

Trial flow chart



** ITT: whatever the RUTF treatment dosage received and the interval between two visits treatment or at village over the 6 months follow-up In the trial*
§ Per Protocol: minimum 4 weekly rations RUTF prescribed in accordance with the dosage table of the respective randomization arm and ration received was minimum 90% of the correct number in accordance with the dosage table of the respective randomization arm and maximum interval between two visits was 6 weeks.

Main secondary outcome	Standard	OptiMA	Difference (95% CI)
Intention-to-treat analysis	(N=240)	(N=242)	
Recovered over the trial follow-up	**234 (97·5%)**	**231 (95·5%)**	**2·0% (95% CI- -2·0% to 6·4%)**
MUAC<125	0 (0·0%)	3 (1·2%)	
MUAC<125 or WFH<-1.5	3 (1·2%)	0 (0·0%)	
Recovered 1 visit only	0 (0·0%)	1 (0·4%)	
RUTF received less than 28 days	0 (0·0%)	1 (0·4%)	
Death during the 6 months follow-up	0 (0·0%)	1 (0·4%)	
Discontinued trial	3 (1·2%)	5 (2·1%)	
Per-protocol analysis	(N=234)	(N=235)	
Recovered over the trial follow-up	**230 (98·3%)**	**228 (97·0%)**	**1·3% (95% CI- -2·3% to 5·1%)**
MUAC<125	0 (0·0%)	5 (2·1%)	
MUAC<125 or WFH<-1.5	4 (1·7%)	0 (0·0%)	
Recovered 1 visit only	0 (0·0%)	1 (0·4%)	
Death during the 6 months follow-up	0 (0·0%)	1 (0·4%)	

Non-inferiority shown on ITT and PP analysis
(upper bound of 95% IC is < 10%)

Secondary outcomes at recovery visit	Standard N=234	OptiMA N=231	p value
MUAC <125 mm	71 (30%)	0 (0%)	<0·001
Weight gain (g), median (IQR)	1220 (825-1600)	1400 (1000-1800)	<0·001
Daily weight gain (g/kg/d) , median (IQR)	4·5 (2·8-6·4)	4·0 (2·6-5·7)	0·054
MUAC gain (mm), median (IQR)	11 (8-13)	14 (8-16)	<0·001
RUTF distributed (sachet), median (IQR)	112 (98-140)	74 (57-105)	<0·001
RUTF length of treatment (weeks) , median (IQR)	35 (35-49)	49 (35-63)	<0·001

Same recovery definition applied in both arms	Standard N=240	OptiMA N=242	p value
Time to recover (weeks) - standard def., *median [IC95%]*	4·0 [4·0-5·0]	5·0 [4·1-5·0]	0·750
Recovered ≤ 12 weeks - standard def.	216 (90%)	215 (89%)	0·791
Time to recover (weeks) with OptiMA def., *median [IC95%]*	6·0 [6·0-7·0]	6·4 [6·0-7·0]	0·750
Recovered by 12 weeks with OptiMA def.	190 (79%)	194 (80%)	0·874

Baseline characteristics	Standard N=240	OptiMA N=242
Girl	124 (52%)	119 (49%)
Age (months), median	17 (IQR 10-30)	16 (IQR 9-29)
MUAC (mm)	114 (IQR 110-121)	114 (IQR 111-120)
Nutritional oedema	49 (20%)	38 (16%)
WHZ<-3 §	-3.6 (1·0)	-3.5 (1·0)
HAZ <-3	-3.0 (1·7)	-2.9 (1·7)
Malaria confirmed and treated	116 (48%)	114 (47%)
Diarrhoea	7 (3%)	7 (3%)
Amoxicillin received	240 (100%)	242 (100%)

Follow-up characteristics	Standard N=240	Optima N=242
Complete 6 months follow-up	232 (96·7%)	228 (94·2%)
House moving or lost to follow-up	7 (2·9%)	13 (5·4%)
Death	1 (1·4%)	1 (0·4%)
Outpatient visits, mean (SD)	8 (5)	8 (5)
Home follow-up visits, mean (SD)	8 (3)	8 (3)
At least one hospitalization	28 (12%)	27 (11%)

Data are n (%) – median (Q1-Q3)- mean (standard deviation). MUAC= mid-upper-arm circumference. WHZ= weight for-height z-score. HAZ= height-for-age z-score. § the calculation excludes children with nutritional oedema..

Conclusion

Progressive RUTF dose reduction in children with SAM according to OptiMA strategy is not inferior to standard DRC RUTF dosage. Children under the OptiMA protocol who recovered presented better MUAC status, total weight and MUAC gain at the recovery visit, compared to their peers under standard DRC protocol. These findings could have substantial individual and public health implications.

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