Simplifying and optimising the management of uncomplicated acute malnutrition in children aged 6–59 months in the Democratic Republic of the Congo (OptiMA-DRC): a non-inferiority, randomised controlled trial

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Summary

Background Global access to acute malnutrition treatment is low. Different programmes using different nutritional products manage cases of severe acute malnutrition and moderate acute malnutrition separately. We aimed to assess whether integrating severe acute malnutrition and moderate acute malnutrition treatment into one programme, using a single nutritional product and reducing the dose as the child improves, could achieve similar or higher individual efficacy, increase coverage, and minimise costs compared with the current programmes.

Methods We conducted an open-label, non-inferiority, randomised controlled trial in the Democratic Republic of the Congo. Acutely malnourished children aged 6–59 months with a mid-upper-arm circumference (MUAC) of less than 125 mm or oedema were randomly assigned (1:1), using specially developed software and random blocks (size was kept confidential), to either the current standard strategy (one programme for severe acute malnutrition using ready-to-use therapeutic food [RUTF] at an increasing dose as weight increased, another for moderate acute malnutrition using a fixed dose of ready-to-use supplementary food [RUSF]) or the OptiMA strategy (a single programme for both severe acute malnutrition and moderate acute malnutrition using RUTF at a decreasing dose as MUAC and weight increased). The primary endpoint was a favourable outcome at 6 months, defined as being alive, not acutely malnourished as per the definition applied at inclusion, and with no further episodes of acute malnutrition throughout the 6-month observation period; the endpoint was analysed in the intention-to-treat (all children) and per-protocol populations (participants who had a minimum prescription of 4 weeks' RUTF, received at least 90% of the total amount of RUTF they were supposed to receive as per the protocol, or were prescribed RUSF rations for a minimum of 4 weeks [ie, minimum of 28 RUSF sachets], and had a maximum interval of 6 weeks between any two visits in the 6-month follow-up). The non-inferiority analysis (margin 10%) was to be followed by a superiority analysis (margin 0%) if non-inferiority was concluded. This trial is registered at ClinicalTrials.gov, NCT03751475, and is now closed.

Findings Between July 22 and Dec 6, 2019, 912 children were randomly assigned; after 16 were excluded, 896 were analysed (446 in the standard group and 450 in the OptiMA group). In the intention-to-treat analysis, 282 (63%) of 446 children in the standard group and 325 (72%) of 450 children in the OptiMA group had a favourable outcome (difference –9·0%, 95% CI –15·9 to –2·0). In the per protocol analysis, 161 (61%) of 264 children in the standard group and 291 (74%) of 392 children in the OptiMA group had a favourable outcome (–13·2%, –21·6 to –4·9).

Interpretation In this non-inferiority trial treating children with MUAC of less than 125 mm or oedema, decreasing RUTF dose according to MUAC and weight increase proved to be a superior strategy to the standard protocol in the Democratic Republic of the Congo. These results demonstrate the safety and benefits of an approach that could substantially increase access to treatment for millions of children with acute malnutrition in sub-Saharan Africa.

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For the French translation of the abstract see **Online** for appendix 1

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Introduction

In 2019, acute malnutrition affected 47 million children aged under 5 years worldwide, including 14 million with the most severe form of malnutrition,[1] and was an underlying cause of 875 000 child deaths.[2] A quarter of all children with acute malnutrition were in Africa in 2018, and as many as 2 million children with severe wasting were reported in the Democratic Republic of the Congo in the same year.[3] Global access to acute malnutrition treatment was low, with as few as 20% of all children with acute malnutrition[4] and only 30% of severe cases receiving treatment,[5] in part because of the shortcomings

Research in context

Evidence before this study

We searched PubMed on May 9, 2021, for publications in English using the search terms "acute malnutrition" AND "randomised controlled trial". There were no date restrictions. Of the 143 study results, only two reported trials comparing the standard acute malnutrition treatment strategy with a strategy integrating severe acute malnutrition and moderate acute malnutrition management with a decrease in ready-to-use therapeutic food (RUTF) dosage as the child improved. The two trials were cluster randomised.

Added value of this study

To our knowledge, this is the first individual randomised controlled trial of an integrated, simplified strategy of acute malnutrition treatment in children aged 6–59 months in the Democratic Republic of the Congo. We compared the current national standard strategy (separate protocols and products for severe acute malnutrition and moderate acute malnutrition management using RUTF at an increasing dose with increasing weight in children with severe acute malnutrition, and ready-to-use supplementary food at a fixed dose in children with moderate acute malnutrition) and the OptiMA strategy (a single protocol for severe acute malnutrition and moderate acute malnutrition management using only RUTF at a decreasing dose with increasing weight). We found that the OptiMA strategy was not only non-inferior to the standard strategy, but it was in fact superior. The rate of favourable outcome was 9% higher for the OptiMA group.

Implications of all the available evidence

These findings from an individual randomised controlled trial, together with those from two previous cluster randomised trials in South Sudan, Kenya, and Sierra Leone, suggest that it is safe, feasible, beneficial, and less expensive to treat children with a mid-upper-arm circumference (MUAC) of less than 125 mm with a single product, RUTF, at a dose adapted to the degree of acute malnutrition (ie, decreasing the dosage of RUTF as a child's MUAC and weight increase). Further studies should directly compare the different integrated and simplified protocols currently being investigated.

of the current programmes and inadequate amounts of funding.[6]

Acute malnutrition is arbitrarily divided into two categories: severe acute malnutrition and moderate acute malnutrition. This distinction results in separate programmes overseen by different UN agencies, using different protocols and products: ready-to-use therapeutic food (RUTF) for children with severe acute malnutrition and ready-to-use supplementary food (RUSF) or fortified-blended flours for children with moderate acute malnutrition. Such separation complicates case detection, delivery of care, supply chain management, and data collection, while also creating confusion and extra work for caregivers and health workers.[7]

Current definitions of severe acute and moderate acute malnutrition use a mix of different parameters: mid-upper-arm circumference (MUAC), weight-for-height Z score (WHZ score), and presence or absence of oedema. WHO defines severe acute malnutrition as a child with a MUAC of less than 115 mm, or WHZ score of less than –3, or oedema; moderate acute malnutrition is defined by WHO as a child with a MUAC between 115 mm and less than 125 mm or a WHZ score between –3 and less than –2. WHZ score alone or in combination with MUAC does not offer a clear advantage over MUAC alone for identifying children at near-term risk of death,[8] and evidence has shown that weight and MUAC gain correlate during treatment.[9–11] With basic community training, mothers can use MUAC bracelets to screen their children at home.[12] MUAC is therefore becoming a stand-alone practical tool for all phases of nutrition programmes, from screening children with malnutrition to monitoring recovery and determining discharge.

The programmes are also considered expensive and are, therefore, largely underfunded due to the cost of RUTF.[13] The current recommended RUTF dose for treating severe acute malnutrition is weight-related (130–200 kcal/kg per day), presenting a paradox in which a child receives more RUTF when nearer to recovery than at the more life-threatening stage at the start of treatment, since weight and MUAC gain are maximal during the first 2–3 weeks of supplementation.[9] Studies have demonstrated that rates of weight (g/kg per day) and MUAC (mm per day) gain are slower in children at higher absolute weight and MUAC compared with those at lower values, when provided the same ration in caloric value.[14] In a randomised clinical trial, Kangas and colleagues[15] demonstrated similar rates of weight and MUAC gain in children with severe acute malnutrition given a standard RUTF ration (175–200 kcal/kg per day) compared with a 30–50% reduced ration. The plausible biological explanation for these findings is that regaining lost weight is more energy efficient than laying down new body mass. As the aim of therapeutic feeding is the recovery of lost weight, it makes sense to taper the caloric value of the ration concomitant with the slowing of rate of weight and MUAC gain. Additionally, therapeutic feeding might be acting by means other than provision of highly fortified, energy-balanced calories. Indeed, there is new evidence on the role that therapeutic foods might have in promoting healthier microbiota in children with malnutrition.[16] Therefore, therapeutic foods might act also through the selection of more favourable intestinal flora for nutrient absorption. Tapering the RUTF dose as a child's nutritional status improves has the potential to achieve the same efficacy at a lower cost.

Therefore, integrating treatments for severe acute malnutrition and moderate acute malnutrition into a single programme using a single anthropometric criterion and decreasing the dose of RUTF as weight increases could simplify malnutrition programmes, increase treatment coverage, and optimise cost allocation with similar clinical efficacy.[17–20]

We designed a trial to assess whether an integrated severe acute malnutrition and moderate acute malnutrition strategy using gradually decreasing doses of RUTF as weight and MUAC increase was non-inferior to the current standard of care in malnourished children aged 6–59 months in the Democratic Republic of the Congo.

Methods

Study design and participants

The Optimising MAlnutrition treatment (OptiMA)-DRC trial was a two-arm, open-label, individually randomised, controlled non-inferiority trial. The study protocol was published previously.[21] The OptiMA trial protocol included two steps.

The first step was an initial non-inferiority analysis on the whole population of children with severe acute malnutrition and moderate acute malnutrition randomised in the same calendar period. The results of this step are reported in this Article.

The second step consisted of a further non-inferiority analysis restricted to the population of children presenting with the current WHO definition of severe acute malnutrition. To achieve this second analysis, we needed 476 children with severe acute malnutrition to be randomly assigned, a number not achieved for the first step. At the end of the first step, therefore, we stopped enrolling children with moderate acute malnutrition and continued to enrol children with severe acute malnutrition until we had a total of 476 participants in the severe acute malnutrition group. This continued enrolment phase and second non-inferiority analysis in children with severe acute malnutrition were done as planned. Its full results will be reported in a separate publication.

The trial was conducted in the Kamuesha health zone, in the Kasai Province of the Democratic Republic of the Congo. Kamuesha is a remote district of 500 000 people with 26 health centres and one district hospital. The trial was nested within a nutritional emergency project launched on May 1, 2018, by the Alliance for International Medical Action (ALIMA), a non-governmental organisation acting in support of the Democratic Republic of the Congo Ministry of Health. The project consisted of implementing the national Democratic Republic of the Congo protocol for severe acute malnutrition treatment for the first time and supporting paediatric care in nine health centres and the district hospital for this landlocked rural health zone, which had experienced 2 years of armed conflict, significant population displacement, and high levels of food insecurity.[22] The prevalence of acute malnutrition in this region based on MUAC was estimated at 19·7% (95% CI 14·4–26·3) and based on WHZ score or oedema at 11·0% (7·5–15·8) in 2017.[23] The OptiMA-DRC trial was conducted in four of the nine health centres participating in the nutritional emergency project. Selection of the four trial centres was based on demographic, epidemiological, and logistical criteria; they covered a catchment area of 12 000 children aged 6–59 months, spread over 60 villages.

Eligible children were identified through monthly exhaustive community-based malnutrition screenings in each of the 60 villages. Children presenting for outpatient consultations at any of the four health centres were also screened for trial eligibility. During the prerandomisation process, all children who lived in the trial catchment area, were aged between 6 and 59 months, and had a MUAC of less than 125 mm, bilateral oedema, or WHZ score of less than −3 were identified. Those who had any of the following conditions were excluded: medical conditions requiring hospitalisation; no appetite; grade 3 oedema; known allergy to milk, peanuts, or RUTFs; any chronic pathology; MUAC of 125 mm or larger with no bilateral oedema but a WHZ score of less than −3; and siblings of children already randomly assigned in the trial. Among excluded children, those with MUAC of 125 mm or larger and no oedema but a WHZ score of less than −3, and those who had a sibling already randomly assigned in the trial were compassionately followed up by the study team but not included in the analysis. Children with MUAC of 125 mm or larger and no oedema but WHZ score of less than −3 received the standard treatment. Children who had a sibling in the trial received the same treatment as their sibling.

Children were enrolled after written informed consent had been given by their caregivers. Ethical approval with annual renewal was granted by the Democratic Republic of the Congo National Ethics Committee (approval number 94/CNES/BN/PMMF/2018) and the Ethics Evaluation Committee of the French National Institute for Health and Medical Research (INSERM, approval number 18–545).

Randomisation and masking

Children were randomly assigned (1:1) to either the OptiMA group (intervention) or the standard group (following the recommended nutritional protocol of the Democratic Republic of the Congo). Randomisation was performed using specially developed software, containing lists prepared in advance by an independent statistician, and inaccessible to trial staff. Once inclusion in the trial was decided by the investigator on the basis of the verification of the eligibility criteria, they interrogated this software, which assigned the code and the corresponding treatment. After the children were assigned to a group by the software, the trial and clinic staff were informed of the assigned treatment and, therefore, became unmasked to treatment assignment. Random blocks were used (block size was kept confidential) and randomisation was

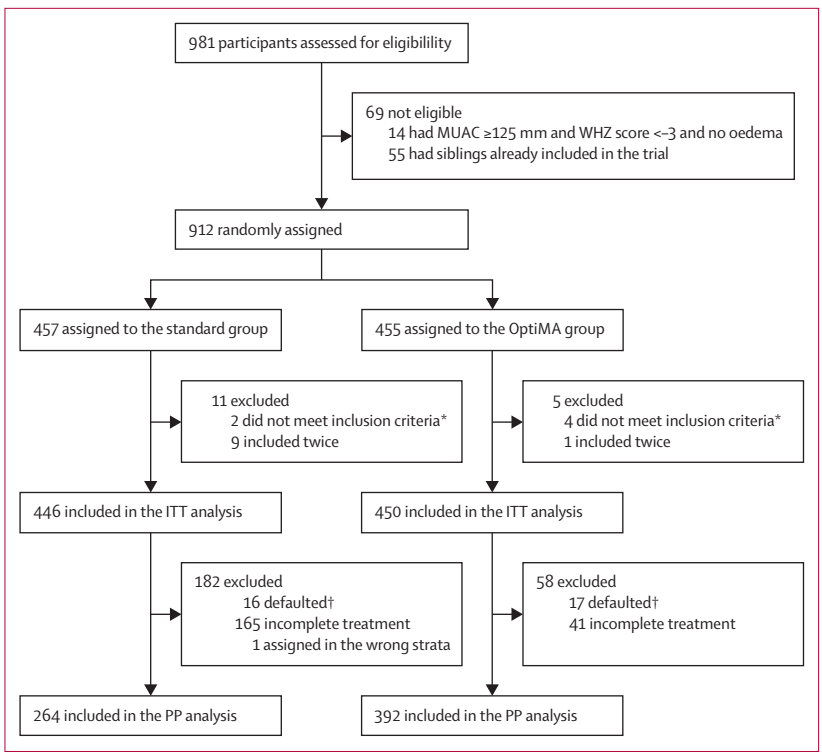

Figure 1: **Trial profile**
ITT=intention-to-treat. MUAC=mid-upper-arm circumference. PP=per-protocol. WHZ=weight-for-height Z. *Five had MUAC ≥125 mm and WHZ-score <–3 and no oedema at inclusion and one had MUAC ≥125 mm and weight-for-height Z-score ≥–3 and no oedema. †Children who defaulted were lost to follow-up or moved out of the study area with their family.

stratified by trial centre and WHO definition of severe acute or moderate acute malnutrition.

Procedures

In the OptiMA group, all children with severe acute malnutrition and moderate acute malnutrition were given RUTF at doses relative to bodyweight and MUAC category that gradually decreased as the child's weight and MUAC increased. The OptiMA dosage table provided for a daily caloric intake of 170–200 kcal/kg per day for children with MUAC of less than 115 mm, 125–190 kcal/kg per day for those with MUAC between 115 and 119 mm, and 50–166 kcal/kg per day for children with MUAC of 120 mm or larger (appendix 2 p 1). Children with oedema and MUAC of 115 mm or larger received the same RUTF dosage as children with MUAC of less than 115 mm until the oedema was resolved, and thereafter the RUTF dosage for children with MUAC of 115 mm or larger.

See Online for appendix 2

In the standard group, children with severe acute malnutrition and moderate acute malnutrition followed two different treatment protocols as per national Democratic Republic of the Congo guidelines. Children with severe acute malnutrition were given RUTF supplements at gradually increasing doses as the child's weight increased. The standard dose table provided for a daily caloric intake of 150–200 kcal/kg per day (appendix 2 p 1). Children with moderate acute malnutrition were given one sachet of RUSF supplement per day (500 kcal per day) every 2 weeks until they recovered. RUTF stock and delivery were managed by ALIMA. RUSF stock and delivery were managed by another local Ministry of Health nutrition partner.

RUTF and RUSF treatments were stopped in both groups when recovery was reached. The definition of recovery included all of the following criteria: treatment for a minimum duration of four weeks; axillary temperature of less than 37·5°C; absence of bipedal oedema; and anthropometric recovery for 2 consecutive weeks. Anthropometric recovery was defined as MUAC of 125 mm or larger in the OptiMA group and MUAC of 125 mm or larger or WHZ score of –1·5 or higher in the standard group (appendix 2 p 1). Since anthropometric recovery corresponds to the end of treatment criteria specific to each strategy, we retained the definition used by each strategy (ie, based on MUAC only with the OptiMA strategy and based either on MUAC or on WHZ score with the standard one).

Children in both groups were monitored for 6 months from inclusion. Children in both groups receiving RUTF were asked to visit the trial centre once a week for those living in villages less than 14 km from the health centre, and once a fortnight for those living more than 14 km away. At each visit, the following data were collected: MUAC and weight; whether any RUTF had been provided; whether a rapid diagnostic test for malaria was needed, with artemisinin-based combination therapy provided for those who tested positive; and whether any clinical symptoms were present. Children were referred to the hospital as indicated. Height was measured once a month. Children not receiving RUTF (ie, those in either group for whom RUTF was stopped after recovery, and those in the standard group who never started RUTF) were visited every 2 weeks in their village until 6 months after inclusion. During home visits in the village, a nurse research officer assisted by one or two community health workers monitored the anthropometric and clinical status of the children. At each visit, the following data were collected: MUAC and weight; a rapid diagnostic test for malaria was administered if indicated and artemisinin-based combination therapy was provided as needed; and whether any clinical symptoms were present. Any child who needed nutritional or medical care was referred to either the trial centre or the Kamuesha general hospital. Height was measured once a month.

All children in both groups were given vitamin A and an anthelmintic. A rapid malaria test was done at inclusion for all children, and at follow-up visits for children with signs or symptoms of malaria; if positive, an artemisinin-based combination therapy was prescribed. All children with severe acute malnutrition were given amoxicillin 50–100 mg/kg per day for 7 days.

	Standard group (n=446)	OptiMA group (n=450)
Sociodemographic characteristics		
Sex		
Male	255 (50%)	221 (49%)
Female	221 (50%)	229 (51%)
Age, months		
Median (IQR)	17 (11 to 29)	16 (9 to 27)
6–24	278 (62%)	290 (64%)
Currently breastfed	284 (64%)	297 (66%)
Number of siblings	3 (1 to 4)	3 (1 to 5)
Birth order	3 (2 to 5)	3 (2 to 6)
First-born child	85 (19%)	71 (16%)
Caretaker was illiterate	393 (88%)	388 (86%)
Mother as caretaker	372 (83%)	374 (83%)
Maternal age*, years	26 (21 to 32)	27 (21 to 32)
Number of births per mother	4 (2to 6)	4 (2 to 6)
Health centre's distance from the village >14 km	44 (10%)	53 (12%)
Anthropometric characteristics		
MUAC, mm	120 (114 to 123)	120 (114 to 122)
Median (IQR)		
<115	119 (27%)	123 (27%)
Nutritional oedema	43 (10%)	35 (8%)
Weight, kg	7·5 (6·4 to 8·7)	7·2 (6·2 to 8·6)
Height, cm	72·5 (66·8 to 79·0)	72·0 (65·8 to 78·3)
WHZ score†	−2·0 (−2·6 to −1·4)	−2·1 (−2·6 to −1·5)
<−3	69 (17%)	67 (16%)
<−2	195 (48%)	223 (54%)
WAZ score†	−3·1 (−3·8 to −2·3)	−3·0 (−3·7 to −2·3)
<−3	209 (52%)	199 (48%)
<−2	336 (83%)	353 (85%)
HAZ score	−2·9 (−3·9 to −1·8)	−2·7 (−3·7 to −1·6)
<−3	202 (45%)	182 (40%)
<−2	311 (70%)	296 (66%)

(Table 1 continues in next column)

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	Standard group (n=446)	OptiMA group (n=450)
Medical and nutritional characteristics		
Temperature axillary >37·4°C	30 (7%)	32 (7%)
Had a malaria rapid antigen test	416 (93%)	421 (94%)
Malaria rapid antigen positive	234/416 (56%)	234/421 (56%)
ACT received	216/234 (92%)	207/234 (88%)
Diarrhoea	16 (4%)	16 (4%)
Respiratory infection	2 (0%)	3 (1%)
Children with severe acute malnutrition	200 (45%)	198 (44%)
RUTF treatment initiated	200/200 (100%)	198/198 (100%)
Amoxicillin received	200/200 (100%)	198/198 (100%)
Children with moderate acute malnutrition	246 (55%)	252 (56%)
RUTF treatment initiated	0	252/252 (100%)
RUSF supplementation initiated	65/246 (26%)	0 (0%)

Data are n (%), n/N (%), or median (IQR). Severe acute malnutrition is defined as MUAC<115 mm, or WHZ score <−3 or oedema. Moderate acute malnutrition is defined as MUAC 115–124 mm and WHZ score ≥−3. ACT=artemisinin-based combination therapy. HAZ=height-for-age Z. MUAC=mid-upper-arm circumference. RUSF=ready-to-use supplementary food. RUTF=ready-to-use therapeutic food. WAZ=weight-for-age Z. WHZ=weight for-height Z. *Calculation excludes five deceased mothers and one with missing data. †Calculation excludes children with nutritional oedema.

Table 1: **Baseline characteristics**

Outcomes

The primary endpoint was a favourable outcome 6 months after inclusion. A favourable outcome was defined as satisfying all three of the following criteria: MUAC of 125 mm or larger, WHZ score of −3 or higher, and absence of bilateral oedema. Children who died, were lost to follow-up, or moved out of the study area with their families during the 6-month follow-up, and those who had a new episode of acute malnutrition within the period (ie, relapse), were considered as having an unfavourable outcome, including those who recovered from the initial episode before the 6 months. Relapse was defined as a MUAC of less than 125 mm, or a WHZ score of less than −3 or the presence of bilateral oedema after the child had met the criteria for a favourable outcome (ie, MUAC of 125 mm or larger and WHZ score of −3 or worse without oedema) at a previous visit, regardless of whether RUTF or RUSF had previously been prescribed.

Secondary endpoints were: MUAC, WHZ score, weight-for-age Z score (WAZ score) and height-for-age Z score (HAZ score) at 6 months, change in weight and MUAC between inclusion and 6 months, hospitalisation, amount and cost of RUTF and RUSF provided between inclusion and 6 months, and time to nutritional improvement. Nutritional improvement was defined as MUAC of 125 mm or larger without oedema at two consecutive follow-up visits with a maximum of 15 days between visits.

Statistical analysis

A non-inferiority analysis was planned to compare the OptiMA and standard groups in terms of favourable outcome rates at 6 months, in the intention-to-treat (ITT) and per-protocol (PP) populations. ITT analysis included all participants. PP analysis included participants who had a minimum prescription of 4 weeks' RUTF, received at least 90% of the total amount of RUTF they were supposed to receive as per the protocol (appendix 2 p 2), or were prescribed RUSF rations for a minimum of 4 weeks (ie, minimum of 28 RUSF sachets), and had a maximum interval of

	Standard group	OptiMA group	Difference (95% CI)
Intention-to-treat analysis			
Number of patients	446	450	..
Favourable outcome*	282 (63%)	325 (72%)	–9·0% (–15·9 to –2·0)
Unfavourable outcome			
New episode of acute malnutrition resolved at 6 months	98 (22%)	96 (21%)	..
New episode of acute malnutrition unresolved at 6 months	37 (8%)	4 (1%)	..
Initial acute malnutrition episode unresolved at 6 months	12 (3%)	7 (2%)	..
Discontinued trial†	16 (4%)	17 (4%)	..
Death	1 (<1%)	1 (<1%)	..
Per-protocol analysis‡			
Number of patients	264	392	..
Favourable outcome*	161 (61%)	291 (74%)	–13·2% (–21·6 to –4·9)
Unfavourable outcome			
New episode of acute malnutrition resolved at 6 months	64 (24%)	93 (24%)	..
New episode of acute malnutrition unresolved at 6 months	27 (10%)	3 (1%)	..
Initial acute malnutrition episode unresolved at 6 months	11 (4%)	5 (1%)	..
Death	1 (<1%)	1 (<1%)	..

Data are n (%), unless stated otherwise. Acute malnutrition is defined as mid-upper-arm circumference <125 mm or nutritional oedema. *Assessed 6 months after inclusion: child alive, not acutely malnourished (mid-upper-arm circumference ≥125 mm, no bilateral nutritional oedema, and weight-for-height Z score ≥–3), and not having experienced any new episode of acute malnutrition throughout the 6-month observation period. †Family moved out of study area or children were lost to follow-up. ‡Per-protocol definition: minimum prescription of 4 weeks of ready-to-use therapeutic food, children received at least 90% of the total amount of ready-to-use therapeutic food they were supposed to receive as per protocol (appendix 2 p 2), or were prescribed ready-to-use supplementary food rations for a minimum of 4 weeks (ie, minimum of 28 ready-to-use supplementary food sachets), and a maximum interval of 6 weeks between any two visits in the 6-month follow-up.

Table 2: **Favourable outcome at 6 months (primary outcome)**

6 weeks between any two visits in the 6-month follow-up. The OptiMA strategy was to be considered non-inferior to the standard strategy if the upper bound of the 95% CI for the difference between standard and OptiMA groups was lower than 10%, both in the ITT and PP analyses. Assuming a 6-month favourable outcome rate of 55% in the standard group and a one-sided type I error of 2·5%, we calculated that 772 participants would provide 80% power to demonstrate non-inferiority of the OptiMA strategy. The sample size was set at 887 participants to account for a loss to follow-up of 15%.

Where non-inferiority was demonstrated, superiority analyses were planned to compare the OptiMA and standard groups in terms of primary and secondary endpoint rates. The OptiMA strategy was to be regarded as superior to the standard strategy for the primary endpoint if the upper bound of 95% CI difference between the standard and OptiMA groups was lower than 0%, both in the ITT and PP analyses. For the secondary endpoints analyses, we performed superiority analyses using Student's *t* test or Wilcoxon's test and χ^2 or Fisher's exact tests. We also did a time-to-failure Kaplan-Meier analysis and log-rank test to compare the probability of occurrence of nutritional improvement over time. Secondary analyses were done in the overall populations, then stratified according to nutritional status at baseline (MUAC <115 mm or oedema *vs* MUAC ≥115 mm without oedema, the threshold considered at higher risk of death by some authors,[24]) by random assignment group. The stratified analyses were post hoc. For each secondary analysis, a p value of less than 0·05 was considered significant. We compared nutritional improvement rate at 12 weeks, the threshold routinely used as maximum length of RUTF and RUSF treatment in the Democratic Republic of the Congo, and at 16 weeks, the one used in some other countries, post hoc. All statistical analyses were done with the R software, version 4.1.2.

The trial was overseen by an independent data safety monitoring board and registered at ClinicalTrials.gov (NCT03751475).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between July 22 and Dec 6, 2019, 912 children were randomly assigned to the trial, of whom 16 (2%) were excluded and 896 (98%) included in the ITT analysis (446 in the standard group and 450 in the OptiMA group; figure 1).

Baseline sociodemographic, anthropometric, and clinical characteristics were similar in both groups (table 1). The median age was 17 months (IQR 10–28), 450 (50%) children were girls, 312 (35%) had a MUAC of less than 115 mm, oedema, or both, and 468 (52%) had confirmed malaria. In the standard group, all children with severe acute malnutrition started RUTF and 65 (26%) of 446 children with moderate acute malnutrition started RUSF. In the OptiMA group, all children started RUTF.

During follow-up (appendix 2 p 3), two children died (one in each group), three were lost to follow-up (two in the standard group *vs* one in the OptiMA group), 30 moved out of the study area with their families (14 *vs* 16), and 861 completed the 6 months of follow-up (429 *vs* 432). Overall, there were 12 532 trial visits (6064 *vs* 6468), including 5221 visits at the trial centre (2122 *vs* 3099) and 7311 home visits (3942 *vs* 3369). During the trial, 882 (98%) of 896 caregivers of the children in the two groups were trained to detect acute malnutrition at home with MUAC bracelets.

In the ITT analysis, 282 (63%) children in the standard group and 325 (72%) children in the OptiMA group had a favourable outcome (difference –9·0%, 95% CI –15·9 to –2·0; table 2). In the PP analysis, 161 (61%) of 264 children in the standard group and 291 (74%) of 392 children in the OptiMA group had a favourable outcome (–13·2%, –21·6 to –4·9). The main cause of unfavourable outcomes was relapse, which occurred in 235 participants in the ITT population (135 in the

standard group *vs* 100 in the OptiMA group). Of these 235 episodes, 194 were resolved within 6 months (98 *vs* 96) and 41 were still unresolved at 6 months (37 *vs* four).

Compared with children in the standard group, children in the OptiMA group had increased weight gain, MUAC gain, and height gain between inclusion and 6 months, which resulted in higher WAZ and HAZ scores at 6 months (table 3). The median time to reach nutritional improvement was 8 weeks (IQR 5–12) in the standard group and 5 weeks (3–8) in the OptiMA group (p<0·0001). The probability of reaching nutritional improvement by week 12 was 64·3% (95% CI 59·5–68·5) in the standard group and 87·0% (83·4–89·8) in the OptiMA group (log-rank p<0·0001, figure 2A). Nutritional improvement rates at 16 weeks are shown in table 3.

In the standard group, 315 (71%) of 446 children received RUTF, RUSF, or both, with a median of 133 (IQR 65–84) sachets received. In the OptiMA group, all children received RUTF, with a median of 64 (47–98) sachets received (table 3). Consequently, the overall cost and number of sachets were higher in the standard group (45 637 sachets, US$12 753) than in the OptiMA group (37 035 sachets, $10 374; appendix 2 p 4), despite the number of children treated being 29% higher in the OptiMA group.

The results of the analysis comparing the rates of primary and secondary endpoints in the standard and OptiMA groups, separating children with MUAC of less than 115 mm or oedema (severe stratum based on MUAC) at baseline from those with a baseline MUAC of 115 mm or more and no oedema (moderate stratum based on MUAC) are shown in appendix 2 (pp 5–9). Significant differences between the standard and OptiMA groups for the rate of favourable outcome were found in both strata (severe 59% *vs* 70%, p=0·0005; moderate 65% *vs* 73%, p=0·0048), because a higher rate of new episodes of acute malnutrition was observed in the standard group compared with the OptiMA group. There was a significant difference in terms of time to nutritional improvement, however, between the severe and moderate strata in the standard and OptiMA groups. In the severe stratum, the median time to reach nutritional improvement was 6 weeks (IQR 5–10) in the standard group versus 7 weeks (5–10) in the OptiMA group (p=0·74); the probability of reaching nutritional improvement by week 12 was 77·2% (95% CI 69·5–82·9) versus 78·2% (70·4–83·9; log-rank p=0·79; figure 2B). In the moderate stratum, the median time to reach nutritional improvement was 9 weeks (5–13) in the standard group versus 4 weeks (3–6) in the OptiMA group (p<0·0001), and the probability of reaching nutritional improvement by week 12 was 57·3% (51·2–62·7) versus 91·5% (87·5–94·1; log-rank p<0·0001, figure 2C). Between inclusion and 6 months, children with moderate acute malnutrition at inclusion according to the WHO definition (ie, those with a MUAC between 115 and 124 mm, WHZ score between –3 and –2, or both) were more likely to deteriorate to severe acute malnutrition in the standard group compared with the OptiMA group (40 [16%] of 246 children *vs* 12 [5%] of 252 children; p=0·0001; appendix 2 pp 10–11).

Discussion

Our primary hypothesis was that the OptiMA strategy for children with moderate or severe acute malnutrition

	Standard group (n=446)	OptiMA group (n=450)	p value
Anthropometric parameters at 6 months			
Height, cm	74·8 (69·0 to 80·9)	74·0 (68·8 to 81·0)	0·71
Weight, kg	9·0 (8·0 to 10·3)	9·0 (8·0 to 10·5)	0·51
MUAC, mm	130 (126 to 135)	131 (128 to 135)	0·050
<125	54 (12%)	18 (4%)	<0·0001
<115	5 (1%)	6 (1%)	1·00
WHZ score	–0·4 (–1·2 to 0·5)	–0·2 (–0·9 to 0·6)	0·046
<–3	5 (1%)	2 (0·4%)	0·29
<–2	43 (10%)	36 (8%)	0·45
WAZ score*	–2·3 (–3·1 to –1·5)	–2·0 (–2·8 to –1·4)	0·0032
<–3*	119 (27%)	81 (18%)	0·0022
<–2*	259 (59%)	219 (49%)	0·0049
HAZ score*	–3·8 (–4·7 to –2·9)	–3·6 (–4·5 to –2·6)	0·024
<–3*	313 (71%)	289 (65%)	0·057
<–2*	393 (89%)	383 (86%)	0·17
Change in anthropometric parameters between inclusion and 6 months			
Weight gain, g	1600 (1000 to 2200)	1700 (1200 to 2400)	0·0035
MUAC gain, mm	12 (8 to 16)	13 (9 to 18)	0·016
Height gain, cm	1·9 (1·3 to 3·2)	2·0 (1·5 to 3·3)	0·015
Daily weight gain†, g/kg per day	1·1 (0·7 to 1·6)	1·3 (0·8 to 1·9)	0·0025
Weekly MUAC gain, mm per week	0·5 (0·3 to 0·6)	0·5 (0·3 to 0·7)	0·020
Nutritional improvement‡			
Time to reach nutritional improvement by 6 months‡, weeks	8 (5 to 12)	5 (3 to 8)	<0·0001
Children who reached nutritional improvement by 12 weeks	284 (64%)	386 (86%)	<0·0001
Improvement by 16 weeks			
Children with improvement	334 (75%)	413 (92%)	<0·0001
Children alive with no improvement	106 (24%)	29 (6%)	..
Defaulted§	5 (1%)	7 (2%)	..
Deceased	1 (<1%)	1 (<1%)	..
Nutritional treatment distributed			
Children receiving RUTF, RUSF, or both	315 (71%)	450 (100%)	<0·0001
Amount of RUTF or RUSF distributed¶, sachets	133 (65 to 184)	64 (47 to 98)	<0·0001
RUTF or RUSF treatment duration¶, days	49 (35 to 70)	42 (35 to 70)	0·27
Children receiving RUTF	238 (53%)	450 (100%)	<0·0001
Amount of RUTF distributed‖, sachets	147 (120 to 210)	64 (47 to 98)	<0·0001
RUTF treatment duration‖, days	56 (42 to 77)	42 (35 to 70)	<0·0001
Children receiving RUSF	94 (21%)	0	..
Amount of RUSF distributed**, sachet	30 (15 to 30)	0	..
RUSF treatment duration**, days	15 (0 to 16)	0	..

(Table 3 continues on next page)

	Standard group (n=446)	OptiMA group (n=450)	p value
(Continued from previous page)			
Hospitalisation during follow-up			
Children with at least one follow-up visit with indication for reference to hospital	59 (13%)	83 (18%)	0·046
Main reason for reference to hospital: stagnant or weight loss	42 (71%)	62 (75%)	0·66
Children hospitalised at least once	32 (7%)	43 (10%)	0·24
Main diagnosis			0·43
Malaria or respiratory infection†	24 (75%)	26 (61%)	
Stagnant or weight loss†	4 (13%)	6 (14%)	..
Other diagnosis†	3 (9%)	10 (23%)	..
Vital prognosis engaged†	1 (3%)	1 (2%)	..
MUAC†, mm	110 (105 to 115)	115 (106 to 120)	0·037
80≥MUAC<115†	27 (84%)	25 (58%)	0·029
115≥MUAC<180†	5 (16%)	18 (42%)	..
Nutritional oedema†	2 (6%)	1 (2%)	0·57
Length of therapeutic milk F-75 received†, days	3 (2 to 4)	2 (2 to 3)	0·21
Length of therapeutic milk F-100 received†, days	1 (1 to 4)	2 (1 to 2)	0·78
Length of RUTF received†, days	3 (3 to 6)	4 (2 to 5)	0·97
MUAC at the end of hospitalisation†, mm	115 (110 to 120)	116 (112 to 122)	0·18
Length of hospitalisation†, days	5 (4–7)	5 (3 to 6)	0·28

Data are median (IQR) or n (%). F-75 milk provides 75 calories per 100 ml of reconstituted milk. F-100 milk provides 100 calories per 100 ml of reconstituted milk. HAZ=height-for-age Z. MUAC=mid-upper-arm circumference. RUSF=ready-to-use supplementary food. RUTF=ready-to-use therapeutic food. WAZ=weight-for-age Z. WHZ=weight-for-height Z. *11 children aged more than 59 months were excluded from this analysis. †Calculated at first hospitalisation of the 75 children hospitalised at least once (32 in the standard group and 43 in the OptiMA group), ‡Improvement of the initial acute malnutrition episode (MUAC ≥125 mm without oedema during two consecutive follow-up visits with a maximum of 15 days between them); 818 children (386 in the standard group and 432 in the OptiMA group) reached nutritional improvement by 6 months. §Children who defaulted did not recover and withdrew from trial follow-up before 12 weeks. ¶Calculated among children receiving RUTF, RUSF, or both. ||Calculated among children receiving RUTF. **Calculated among children receiving RUSF.

Table 3: **Secondary endpoints (intention-to-treat analysis)**

would be non-inferior to the standard strategy currently applied in the Democratic Republic of the Congo, but we showed that the OptiMA strategy was superior to the standard strategy, with a 9% higher rate of favourable outcome. Secondary analyses showed that the OptiMA strategy also shortened the time to nutritional improvement and reduced the amount and cost of treatment needed.

We report a low coverage of moderate acute malnutrition supplementation with RUSF in the standard group. This finding reflects real-life conditions of nutritional programming, where funding for moderate acute malnutrition is separate from severe acute malnutrition programmes, is often limited to conflict zones or zones assessed as more food insecure, and is routinely provided for shorter intervention periods than is severe acute malnutrition. This trial was nested in an emergency programme, in which the European Civil Protection and Humanitarian Aid Operations funded RUTF through the non-governmental organisation ALIMA, whereas the World Food Programme funded RUSF through another non-governmental organisation. We conducted a pragmatic trial to evaluate the OptiMA strategy against these standard field operating conditions. Our results suggest that an integrated strategy allowing the same operator to treat both severe acute malnutrition and moderate acute malnutrition at the same time and optimising the distribution of supplementation products could benefit more children.

Our study was conducted at community level and has several strengths. First, despite the challenging post-conflict context and complex, landlocked, rural environment, the retention in follow-up and compliance to protocol were excellent, in terms not only of the nutritional intervention tested under this trial but also associated measures, such as administration of vitamin A, anthelmintic drugs, and amoxicillin. The involvement of community representatives and of health workers, and the frequency of home visits are likely to have contributed to the low default rate and allowed us to use individual randomisation, which was preferable to cluster randomisation when it can be conducted in such conditions.

Second, we monitored the children for 6 months—ie, approximately 4 months longer than the mean time to recovery. We were thus able to compare rates of relapse between the two strategies. The rate of relapse into acute malnutrition being higher in the standard group confirmed that the OptiMA strategy was more effective than the standard strategy after the initial weeks of nutritional intervention.

Third, we compared a strategy that combined the treatment of moderate acute malnutrition and severe acute malnutrition in a single programme using a single product, with the current standard strategy separating the treatment of moderate acute malnutrition and severe acute malnutrition into two different programmes using different nutritional products. In our study, all children with severe acute malnutrition in both groups were given RUTF, whereas the percentage of children with moderate acute malnutrition who were given RUSF or RUTF was 47% in the standard group and 100% in the OptiMA group (RUTF only). These findings are a reflection of a current global situation where moderate acute malnutrition programmes are partially functional, resulting in very low moderate acute malnutrition treatment coverage. In this study, 16% of children with moderate acute malnutrition in the standard group deteriorated to severe acute malnutrition within 6 months, compared with 5% in the OptiMA group. These children then require more intensive RUTF supplementation. This standard group rate is higher than the 9·3% of children with moderate acute malnutrition in a study in Ethiopia,[25] who received no supplementation and deteriorated to severe acute malnutrition. The findings suggest that the OptiMA strategy not only allows more children to be successfully treated but might also prevent severe acute malnutrition cases from developing.

Finally, the overall cost of RUTF—a major cost driver in malnutrition treatment programmes—in the OptiMA group was 19% lower than the combined cost of RUTF and RUSF in the standard group ($10 374 *vs* $12 753). In addition to the individual benefits for children in terms of a higher rate of favourable outcome, the OptiMA strategy appears to hold major advantages from a programming perspective as it allows more children to access treatment at a lower cost.

Our findings are consistent with those of other recent studies. The ComPAS study,[18] a cluster randomised trial in South Sudan and Kenya, used similar MUAC and oedema criteria for admission and cessation of nutritional programme, and another simplified reduced dose regimen for RUTF (two sachets per day for children with MUAC <115 mm or oedema, one sachet per day for children with MUAC between 115 mm and 125 mm). This strategy was shown to be non-inferior to the standard protocol in terms of recovery; there was no difference in terms of death, time to recovery, or average daily weight gain among children who recovered; and better overall cost-effectiveness.[18] An earlier cluster randomised trial in Sierra Leone,[17] which tested a similar MUAC and oedema programme with a weight-based reduced RUTF dose regimen against the national protocol, with separate foods for children with severe acute malnutrition and moderate acute malnutrition, found similar recovery rates in both groups and lower RUTF costs in the intervention group. Non-inferiority was also demonstrated in a randomised controlled trial in Burkina Faso, which tested a reduced RUTF dosage regimen for children who met the current WHO definition of severe acute malnutrition.[26] At 6 months, we found significantly better weight and height gain with the OptiMA strategy but similar median weight and median height between both groups. Indeed, children allocated to the standard group were slightly older at baseline. It is, therefore, not surprising that we observed no significant difference in median weight and height between both groups but better WAZ and HAZ scores in the OptiMA group. Of note, the number of children achieving MUAC of 125 mm or larger for 2 weeks by week 12, daily weight gain, and RUTF consumption in our trial were similar to those found in an earlier single-arm proof-of-concept trial conducted in Burkina Faso.[19] In terms of rates of new episodes of acute malnutrition, comparisons with other studies are difficult due to variations in the definition of new acute malnutrition episodes and relapse.[27] However, two studies comparing the incidence of relapse after treatment with different reduced RUTF dosage strategies compared with standard protocols found similar rates of severe acute malnutrition relapse across both groups.[15,28]

Our study had some limitations. First, the study was open label, which could introduce bias. However, a review of 146 meta-analyses that included 1346 trials with a wide range of interventions and outcomes concluded that there was little evidence of bias in open-label trials that compared objectively assessed outcomes.[29] We believe our primary outcome combining survival and anthropometric measurements was objectively assessed. Moreover, this was a pragmatic trial assessing a new

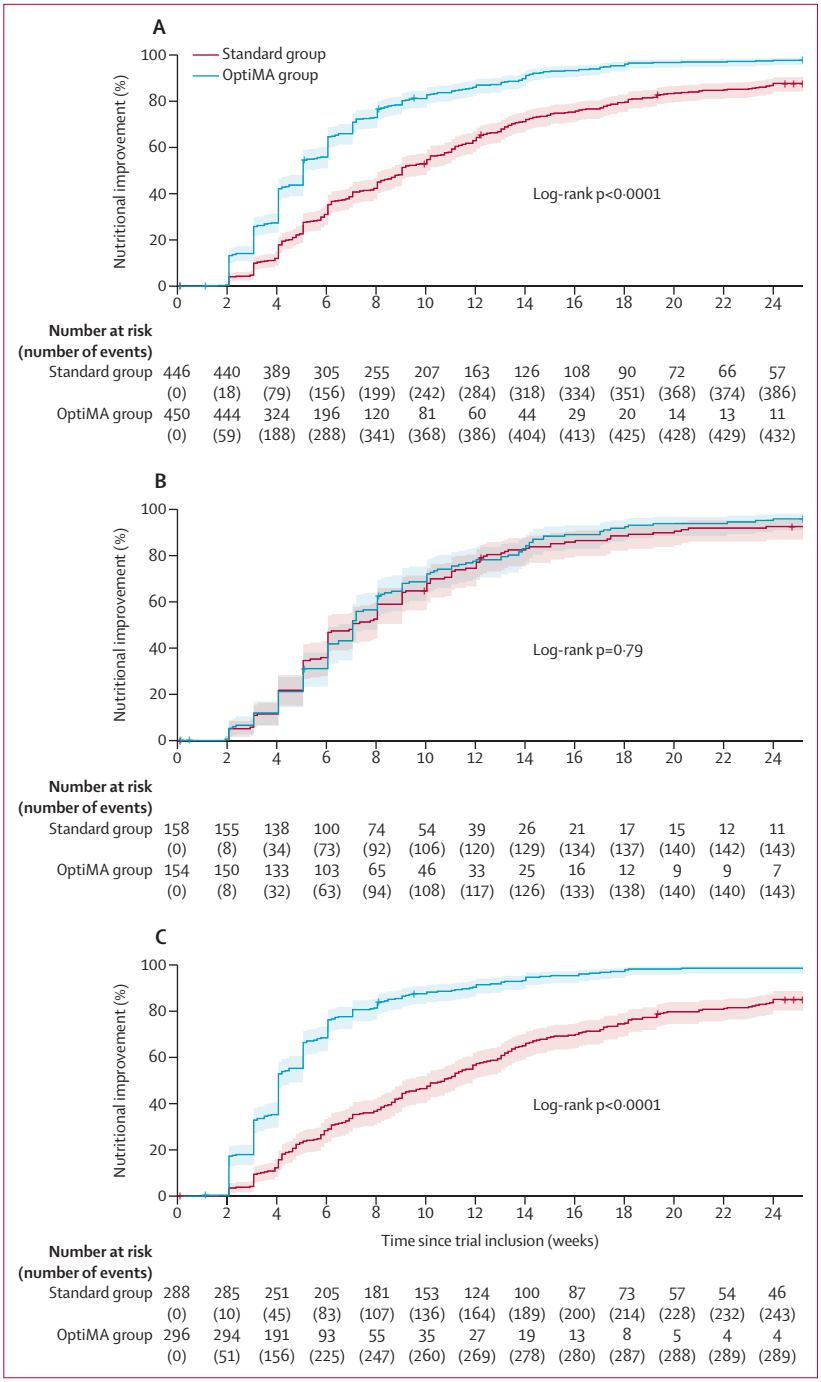

Figure 2: **Cumulative probability of reaching nutritional improvement (MUAC ≥125 mm and no oedema during two consecutive visits) according to randomisation groups (n=896)**
(A) Overall population. (B) Children with MUAC of less than 115 mm or oedema at baseline. (C) Children with MUAC of 115 mm or larger and no oedema at baseline. MUAC=mid-upper-arm circumference.

intervention in real-life conditions, which include the perception of a new intervention by caregivers. However, we cannot entirely exclude the possibility that the open status might have affected the assessment of the efficacy and safety outcomes, and the ongoing management of the children. Second, randomisation does not 100% prevent confounding bias, even if it generally ensures that the groups are comparable. Potential confounders might be residual and concern variables that might not have been recorded during the study. Third, the definitions of adherence that we used in the PP analysis differed between the two groups. Basing these groups on postrandomisation behaviours might create biases. Fourth, we decided a priori that statistical tests made for the secondary analysis would not be adjusted for multiplicity. Multiple tests might lead to increase in type I error, and should therefore be interpreted with caution. Fifth, even if there are true benefits of the OptiMA strategy in terms of weight gain, it might not replete the children in terms of key micronutrients important for haemopoiesis and brain development. Further studies should explore this point. Sixth, the pattern of acute malnutrition, including the proportion of children with moderate acute malnutrition and severe acute malnutrition and the frequency of oedema, differs across geographical areas. It might not be appropriate, therefore, to generalise our conclusions for all contexts. A three-arm trial comparing the ComPAS, OptiMA, and national standard strategies is underway in Niger (NCT04698070)[30] and will allow not only for testing the OptiMA strategy in another context but also for putting it in perspective with the ComPAS strategy. Finally, only part of the population meeting the current WHO definition of moderate acute malnutrition and severe acute malnutrition was included in the trial. Children with MUAC of 125 mm or larger and WHZ score between −3 and −2 (meeting the definition of moderate acute malnutrition) and those with MUAC of 125 mm or larger and WHZ score of less than −3 (meeting the definition of severe acute malnutrition) were not eligible for randomisation. However, WHZ score measurement was part of the screening process for the prerandomisation phase, and children with a MUAC of 125 mm or larger and WHZ score of less than −3 represented a very small fraction (19 [2%] of 981 children) of the overall population of children with acute malnutrition.

In conclusion, the OptiMA malnutrition treatment protocol was superior to the current Democratic Republic of the Congo national protocol in terms of favourable outcomes at 6 months after inclusion. Compared with the national protocol, OptiMA treated 29% more children using 19% less RUTF and RUSF, with significantly better weight and MUAC gain over 6 months. This study therefore suggests that it is safe, feasible, and beneficial to treat children with a MUAC of less than 125 mm or oedema with RUTF as a single nutritional supplement, adapting the initial dosage to the degree of acute malnutrition by progressively decreasing the dose as MUAC and weight increase. These findings could have substantial individual and public health implications, especially at this time when disruptions caused by COVID-19 could simultaneously increase the burden of acute malnutrition and reduce treatment coverage.[31]

Contributors

SS and RB developed the clinical and methodological study concept. RB, CC, XA, DG, MD, AA, KP, and SS designed the study methodology and wrote the protocol. CC, VH, HB, RA, and MK coordinated the study teams. LIB, BKT, TT, and GTS coordinated the Ministry of Health of the Democratic Republic of the Congo staff working in the trial. CC, VH, HB, LIB, GTS, AK, CY, and RB organised and supervised data collection. CY created the software tool for randomisation and developed the database. CC, DG, XA, SS, and RB developed the statistical analysis strategy. CC performed the statistical analysis and all coauthors interpreted the results. CC wrote the first draft of the manuscript with substantial inputs from KP, SS, XA and RB. SS and RB were primarily responsible for the final content of the manuscript. All authors critically reviewed the first draft and made substantial writing contributions to the development of the final manuscript. All authors had full access to all the data in the study. DG and RB verified the underlying data of the study. The principal investigators (RB and SS) had final responsibility for the decision to submit the manuscript for publication.

Declaration of interests

KP serves on the Social Purposes Advisory Commission of Nutriset, a main producer of lipid-based nutrient supplement products. All other authors declare no competing interests.

Data sharing

A data sharing plan is available in the ClinicalTrials.gov registry (NCT03751475). In accordance with the International Committee of Medical Journal Editors, the data generated by the trial will be made available starting 6 months and ending 36 months following the Article publication. After this timepoint, the data will be available upon request to the corresponding author to researchers who can demonstrate a methodologically sound proposal and whose proposed use of the data has been approved by an independent review committee.

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primarily on improving maternal and child health outcomes. A board of directors defines the scientific policy of the CORAL partnership, along with the supervision of research projects and dissemination of results. It consists of senior representatives from both ALIMA and INSERM: Renaud Becquet (INSERM, Bordeaux, France), Susan Shepherd (ALIMA, Dakar, Senegal), Augustin Augier (ALIMA, Paris, France), Moumouni Kinda (ALIMA, Dakar, Senegal), Marie Jaspard (ALIMA and INSERM, Abidjan, Côte d'Ivoire), Claire Levy-Marchal (ALIMA, Paris, France), and Xavier Anglaret (INSERM, Bordeaux, France, and Abidjan, Côte d'Ivoire). The CORAL research platform meets annually with an external scientific advisory board to review projects and strategic orientation. Finally, we thank the members of the data safety monitoring board for the OptiMA-DRC trial: Yves Martin-Prevel (chair, French National Institute for Sustainable Development, MoISA team, University of Montpellier, Montpellier, France), Matthew Coldiron (Epicentre, New York, NY, USA), and Katia Castetbon (statistician, School of Public Health, Université Libre de Bruxelles, Bruxelles, Belgium).

References

1 UNICEF, WHO, World Bank Group. Levels and trends in child malnutrition. Key findings of the 2020 edition. Geneva: World Health Organization, 2020.

2 Black RE, Victora CG, Walker SP, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet* 2013; **382:** 427–51.

3 UNICEF. UNICEF DRC humanitarian situation report March, 2018. https://reliefweb.int/report/democratic-republic-congo/unicef-drc-humanitarian-situation-report-march-2018 (accessed Feb 22, 2022).

4 No Wasted Lives. Accelerating action for children with acute malnutrition. 2018. https://static1.squarespace.com/static/58da81cdd1758e39ca705526/t/5a7adf8171c10b8aa3b4462f/1518002053092/No+Wasted+Lives+Brochure+2018.pdf (accessed Feb 22, 2022).

5 No Wasted Lives Coalition. The state of acute malnutrition. https://acutemalnutrition.org/en/countries (accessed Feb 22, 2022).

6 World Bank Group, Shekar M, Kakietek J, Eberwein JD, Walters D. An investment framework for nutrition: reaching the global targets for stunting, anemia, breastfeeding, and wasting. Washington, DC: The World Bank, 2017.

7 Rogers E, Myatt M, Woodhead S, Guerrero S, Alvarez JL. Coverage of community-based management of severe acute malnutrition programmes in twenty-one countries, 2012–2013. *PloS One* 2015; **10:** e0128666.

8 Briend A, Maire B, Fontaine O, Garenne M. Mid-upper arm circumference and weight-for-height to identify high-risk malnourished under-five children. *Matern Child Nutr* 2012; **8:** 130–33.

9 Goossens S, Bekele Y, Yun O, Harczi G, Ouannes M, Shepherd S. Mid-upper arm circumference based nutrition programming: evidence for a new approach in regions with high burden of acute malnutrition. *PLoS One* 2012; **7:** e49320.

10 Roberfroid D, Hammami N, Lachat C, et al. Utilization of mid-upper arm circumference versus weight-for-height in nutritional rehabilitation programmes: a systematic review of evidence. Geneva: World Health Organization, 2013.

11 Binns P, Dale N, Hoq M, Banda C, Myatt M. Relationship between mid upper arm circumference and weight changes in children aged 6–59 months. *Arch Public Health* 2015; **73:** 1–10.

12 Alé FGB, Phelan KPQ, Issa H, et al. Mothers screening for malnutrition by mid-upper arm circumference is non-inferior to community health workers: results from a large-scale pragmatic trial in rural Niger. *Arch Public Health* 2016; **74:** 38.

13 Isanaka S, Menzies NA, Sayyad J, Ayoola M, Grais RF, Doyon S. Cost analysis of the treatment of severe acute malnutrition in west Africa. *Matern Child Nutr* 2017; **13:** e12398.

14 Chase RP, Kerac M, Grant A, et al. Acute malnutrition recovery energy requirements based on mid-upper arm circumference: secondary analysis of feeding program data from 5 countries, Combined Protocol for Acute Malnutrition Study (ComPAS) Stage 1. *PLoS One* 2020; **15:** e0230452.

15 Kangas ST, Salpéteur C, Nikièma V, et al. Impact of reduced dose of ready-to-use therapeutic foods in children with uncomplicated severe acute malnutrition: a randomised non-inferiority trial in Burkina Faso. *PLoS Med* 2019; **16:** e1002887.

16 Chen RY, Mostafa I, Hibberd MC, et al. A microbiota-directed food intervention for undernourished children. *N Engl J Med* 2021; **384:** 1517–28.

17 Maust A, Koroma AS, Abla C, et al. Severe and moderate acute malnutrition can be successfully managed with an integrated protocol in Sierra Leone. *J Nutr* 2015; **145:** 2604–09.

18 Bailey J, Opondo C, Lelijveld N, et al. A simplified, combined protocol versus standard treatment for acute malnutrition in children 6–59 months (ComPAS trial): a cluster-randomized controlled non-inferiority trial in Kenya and South Sudan. *PLoS Med* 2020; **17:** e1003192.

19 Daures M, Phelan K, Issoufou M, et al. New approach to simplifying and optimising acute malnutrition treatment in children aged 6–59 months: the OptiMA single-arm proof-of-concept trial in Burkina Faso. *Br J Nutr* 2020; **123:** 756–67.

20 Defourny I, Seroux G, Abdelkader I, Harczi G. Management of moderate acute malnutrition with RUTF in Niger. *Field Exchange* 2007; **31:** 2.

21 Cazes C, Phelan K, Hubert V, et al. Simplifying and optimising management of acute malnutrition in children aged 6 to 59 months: study protocol for a community-based individually randomised controlled trial in Kasaï, Democratic Republic of Congo. *BMJ Open* 2020; **10:** e041213.

22 World Food Programme. Evaluation approfondie de la sécurité alimentaire en situation d'urgence dans les provinces du Kasai, Kasai central, Kasai oriental, Lomami et du Sankuru, République Démocratique du Congo. 2017. https://docs.wfp.org/api/documents/WFP-0000023449/download/ (accessed Feb 22, 2022).

23 Action Contre la Faim. Résumé exécutif des résultats clés de l'enquête nutritionnelle et de mortalité retrospective. Aires de santés affectées par la crise humanitaire dans les zones de santé de Kalonda Ouest et Kamuesha, Province Kasaï, RDC. 2017. https://www.humanitarianresponse.info/sites/www.humanitarianresponse.info/files/assessments/acf_kasai-smart_resume_executif_kalonda_ouest-kamuesha_2017.pdf (accessed Feb 22, 2022).

24 Myatt M, Khara T, Dolan C, Garenne M, Briend A. Improving screening for malnourished children at high risk of death: a study of children aged 6–59 months in rural Senegal. *Public Health Nutr* 2019; **22:** 862–71.

25 James P, Sadler K, Wondafrash M, et al. Children with moderate acute malnutrition with no access to supplementary feeding programmes experience high rates of deterioration and no improvement: results from a prospective cohort study in rural Ethiopia. *PLoS One* 2016; **11:** e0153530.

26 Kangas ST, Salpéteur C, Nikièma V, et al. Impact of reduced dose of ready-to-use therapeutic foods in children with uncomplicated severe acute malnutrition: a randomised non-inferiority trial in Burkina Faso. *PLoS Med* 2019; **16:** e1002887.

27 Schaefer R, Mayberry A, Briend A, et al. Relapse and regression to severe wasting in children under 5 years: a theoretical framework. *Matern Child Nutr* 2021; **17:** e13107.

28 Lelijveld N, Musyoki E, Adongo SW, et al. Relapse and post-discharge body composition of children treated for acute malnutrition using a simplified, combined protocol: a nested cohort from the ComPAS RCT. *PLoS One* 2021; **16:** e0245477.

29 Wood L, Egger M, Gluud LL, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ* 2008; **336:** 601–05.

30 Daures M, Hien J, Phelan K, et al. Simplifying and optimising management of acute malnutrition in children aged 6 to 59 months: study protocol for a 3 arms community-based individually randomised controlled trial in decentralised Niger. *Trials* 2022; **23:** 89.

31 Roberton T, Carter ED, Chou VB, et al. Early estimates of the indirect effects of the COVID-19 pandemic on maternal and child mortality in low-income and middle-income countries: a modelling study. *Lancet Glob Health* 2020; **8:** e901–08.