RECOVERY, RELAPSE AND EPISODES OF DEFAULT IN THE MANAGEMENT OF ACUTE MALNUTRITION IN CHILDREN IN HUMANITARIAN EMERGENCIES

About this systematic review

This is an independent systematic review commissioned by the Humanitarian Evidence Programme, a partnership between Oxfam GB and Feinstein International Center at the Friedman School of Nutrition Science and Policy, Tufts University. It was funded by aid from the United Kingdom (UK) government through the Humanitarian Innovation and Evidence (HIEP) Programme at the Department for International Development. The views and opinions expressed herein are those of the authors and do not necessarily represent those of Oxfam, Feinstein International Center or the UK government.

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The initial database and website searches took place between 1 November 2015 and 31 March 2016.

Citation

Akparibo, R., Lee, A.C.K. and Booth, A. (2017). *Recovery, relapse and episodes of default in the management of acute malnutrition in children in humanitarian emergencies: A systematic review*. Humanitarian Evidence Programme. Oxford: Oxfam GB.

Acknowledgments

We wish to thank Oxfam GB, Feinstein International Center and the UK Department for International Development for funding this review. Our sincere thanks go to the revision team and everyone who contributed thoughts, reviewed drafts and shared documents during the development of this review. We particularly want to thank Tanya Khara for her technical advice and Eleanor Ott, Roxanne Krystalli and Lisa Walmsley for providing editorial support. We would also like to thank the organizations and individuals who responded to our requests for their programme reports.

Series editors

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ABBREVIATIONS

CASP	Critical Appraisal Skills Programme
CBTC	Community-based therapeutic care
CMAM	Community-based management of acute malnutrition
CRED	Centre for Research on the Epidemiology of Disasters
CSB	Corn/soy blend
CTC	Community therapeutic care
DFID	Department for International Development
FBF	Fortified blended food
FS	Fortified spread
GAM	Global acute malnutrition
GNC	Global Nutrition Cluster
HEP	Humanitarian Evidence Programme
ICRC	International Committee of the Red Cross
IMAM	Integrated management of acute malnutrition
LNS	Lipid-based nutrition supplement
MAM	Moderate acute malnutrition
MSF	Médecins Sans Frontières
MUAC	Mid-upper arm circumference
NCHS	National Centre for Health Statistics
OTP	Outpatient therapeutic feeding programme
RCT	Randomized controlled trial
RUF	Ready-to-use food
RUSF	Ready-to-use supplementary food
RUTF	Ready-to-use therapeutic food
SAM	Severe acute malnutrition
SFP	Supplementary feeding programme
TFC	Therapeutic feeding centre
TSFP	Targeted supplementary feeding programme
UNICEF	United Nations Children's Fund
WHO	World Health Organization
WHZ	Weight-for-height z-score

EXECUTIVE SUMMARY

This systematic review, commissioned by the Humanitarian Evidence Programme (HEP) and carried out by a research team from the University of Sheffield, represents the first attempt to apply systematic review methodology to establish the relationships between recovery and relapse and between default rates and repeated episodes of default or relapse in the management of acute malnutrition in children in humanitarian emergencies in low- and middle-income countries.¹

Definitions and scope

Severe acute malnutrition (SAM, or severe wasting) and moderate acute malnutrition (MAM, or moderate wasting) affect 52 million children under five years of age around the globe. This systematic review seeks to establish whether there is a relationship between recovery and relapse or a relationship between default rates and/or repeated episodes of default or relapse following treatment for SAM and MAM in children aged 6–59 months in humanitarian emergencies. The review also seeks to determine the reasons for default and relapse in the same population.

For the purposes of this review:

- **Definitions of SAM and MAM** are based on the National Centre for Health Statistics (NCHS) child growth standard where studies are published before or during 2006, and the World Health Organization (WHO) Child Growth Standards where published after 2006.
- Humanitarian emergencies are defined as major incidents that threaten human life and public health (GNC, 2014; UNICEF, 2014), including protracted conflicts, flooding, earthquakes and other natural disasters. The team used data from ReliefWeb and the Centre for Research on the Epidemiology of Disasters (CRED) to identify the existence of a 'humanitarian' context, which might include seasonal spikes in malnutrition, a declared food crisis, natural disasters or disease outbreaks that affected nutritional status.
- **Recovery rate** means the proportion of children who are cured through treatment in acute malnutrition programmes.
- **Default rate** means the proportion of children absent from treatment for two consecutive sessions.
- **Absence and/or repeated absence** means the proportion of children who were absent from treatment/the number of absences recorded.
- **Return default rate/repeated default episodes** means the proportion of children who re-enrolled into treatment after defaulting/the number of times they re-enrolled.
- **Relapse rate/repeated relapse episodes** means the proportion of children who re-enrolled after they had recovered and been discharged.
- **Time to recover** means length of time between admission and discharge.

The research team:

- mapped and documented existing research;
- synthesized the evidence in response to two key research questions:
 - the relationship between recovery and relapse; and the relationship between relapse and default or return default/episodes of default
 - the reasons for default and relapse or return defaults/episodes of default; and
- identified gaps in existing research and knowledge.

What evidence was eligible for review?

The research team identified a total of 9,574 articles, studies and programme reports relating to acute malnutrition in its initial search of databases and websites. Following the removal of duplicates, screening and quality appraisal, 24 articles were eligible for review. Of the 24 eligible studies, 23 focused on sub-Saharan Africa: eight were conducted in Malawi, five in Ethiopia, three in Niger, three in Sudan and the remaining four in Angola, Chad, Kenya and Sierra Leone. One study focused on Afghanistan. Most studies and programme reports reported on quantitative outcomes and two contained both quantitative and qualitative outcomes. The 22 quantitative studies included eight clinical efficacy and effectiveness trials using randomized controlled designs, seven observational cohort studies and seven programme evaluation reports.

¹ HEP is a partnership between Oxfam GB and Feinstein International Center at the Friedman School of Nutrition Science and Policy, Tufts University. It is funded by the United Kingdom government's Department for International Development (DFID) through the Humanitarian Innovation and Evidence Programme (HIEP).

What are the findings?

What is the relationship between recovery and relapse, and between relapse and default or return default/episodes of default?

Six of the 24 studies included in this review addressed the issue of relapse and/or reported relapse rates (Bahwere et al., 2014; Ciliberto et al., 2005; Linneman et al., 2007; Querubin, 2006; Taylor, 2002; UNICEF, 2012). Figure 0.1 presents the relapse and default rates reported for each of these studies. None of the studies addressed the relationship between relapse and default or return default. This may be partly attributable to the relatively short duration of most interventions and the fact that most of the studies did not include post-intervention follow-up.

Figure 0.1: Relapse rates and relationship between relapse and default

Study	Country	Type	Quality	Findings
Bahwere et al. (2014)	Malawi	Randomized controlled clinical effectiveness trial	High	Briefly mentions relapse but does not report rate.
Ciliberto et al. (2005)	Malawi	Clinical effectiveness trial	Medium	Higher default rate (9.8 percent) and lower relapse/mortality rate (8.7 percent) reported for children receiving home-based care vs. those receiving standard therapy (8.1 percent and 16.7 percent respectively).
Linneman et al. (2007)	Malawi	Observational cohort study	High	Average default rates of 7 percent for children with SAM and 8 percent for children with MAM reported. Relapse rates not reported separately from non-recovery rates (3 percent and 4 percent for children with SAM and MAM respectively).
Querubin (2006)	Sudan	Programme evaluation report	Low	Default rate of 7 percent and no cases of relapse reported for children in home treatment group.
Taylor (2002)	Sudan	Programme evaluation report	Low	Average default rate of 10.1 percent reported. Readmission rate approximately 1 percent of total admissions.
UNICEF (2012)	Kenya	Programme evaluation report	Low	Default rate of 12.9 percent and relapse rate of 3.2 percent reported for outpatient SAM treatment. Default rate of 1.4 percent and relapse rate of 6.1 percent reported for inpatient SAM treatment. Default rate of 14.4 percent and relapse rate of 3.7 percent reported for MAM treatment.

What are the reasons for default and relapse or return defaults/episodes of default?

Default data was reported in each of the 24 included studies, but reasons for default were not always cited (see Figure 0.2). Relapse was reported in six of the included studies – but only one study discussed possible reasons for relapse. A UNICEF programme evaluation report of an integrated management of acute malnutrition (IMAM) programme in Kenya (2012; low quality) suggests that the lack of a follow-up system to track children treated for SAM or MAM, together with a lack of encouragement to return for outpatient treatment, may have contributed to relapses, as well as the sharing of ready-to-use therapeutic food (RUTF) among siblings and other non-admitted children.

Figure 0.2: Reasons for default reported in studies

Study	Country	Type	Quality	Family illness	Other household priorities	Travel distance	Poor community sensitization	Poor follow-up	Other issues	No reason for default offered or not applicable
Amthor et al. (2009)	Malawi	Observational cohort study	High							X
Bahwere et al. (2014)	Malawi	Randomized controlled trial	High							X
Belachew and Nekatibeb (2007)	Ethiopia	Mixed methods study	Medium			X	X		X	
Chaiken et al. (2006)	Ethiopia	Observational cohort study	Low							X
Ciliberto et al. (2005)	Malawi	Randomized controlled trial	Medium							X
Collins and Sadler (2002)	Ethiopia	Observational cohort study	Medium							X
Deconinck (2004)	Ethiopia	Programme evaluation report	Low							X
Flax et al. (2009)	Malawi	Mixed methods study	Medium	X						
Gaboulaud et al. (2007)	Niger	Observational cohort study	Low							X
Grellety et al. (2012)	Niger	Observational cohort study	High							X
Huybregts et al. (2012)	Chad	Randomized controlled trial	Medium							X
Isanaka et al. (2009)	Niger	Randomized controlled trial	Medium							X
Karakochuk et al. (2012)	Ethiopia	Randomized controlled trial	High							X
Lagrone et al. (2010)	Malawi	Observational cohort study	Medium		X					
Linneman et al. (2007)	Malawi	Observational cohort study	High	X*						
Lurqin (2003)	Afghanistan	Programme evaluation report	Low	X	X				X	
Matilsky et al. (2009)	Malawi	Randomized controlled trial	High							X
Maust et al. (2015)	Sierra Leone	Randomized controlled trial	Medium							X
Morgan et al. (2015)	Angola	Programme evaluation report	Low							X
Oakley et al. (2010)	Malawi	Randomized controlled trial	High							X**
Querubin (2006)	Sudan	Programme evaluation report	Low							X
Taylor (2002)	Sudan	Programme evaluation report	Low		X					
UNICEF (2012)	Kenya	Programme evaluation report	Low					X		
Walker (2004)	Sudan	Programme evaluation report	Low			X				

* Authors indicated that high default rates at two study locations could be attributable to undiagnosed HIV infection.

** Authors did not find sufficient evidence to determine the contribution to default rates of taste/colour differences between products.

What is the state of the evidence on acute malnutrition?

This review found little evidence on the impact of programmes implemented to manage MAM and SAM in emergencies, which can be partly explained by the nature of interventions conducted in humanitarian settings. Also, it found few studies that explored the issue of relapse.

There is considerable heterogeneity in the evidence base owing to the diversity of study types, types of intervention and settings in which the programmes were delivered. The quality of the published literature, however, varies markedly:

- Generally, the grey literature reports and qualitative studies included in the review lacked crucial detail, such as details of their recruitment strategies.
- The review of articles did identify the presence of significant barriers relating to the acceptability of the intervention and implementation issues.
- The detail presented in the mixed methods studies offers a more nuanced understanding of the precise context and, indeed, suggests that some factors are generic and others, even though present, may not have the same relative importance in a different context.

The **lack of qualitative data on acute malnutrition in humanitarian contexts** is striking, with only two mixed methods studies eligible for inclusion in this review (Belachew and Nekatibeb, 2007; Flax et al., 2009). However, it is possible that qualitative studies related to treatment of acute malnutrition are better represented in nutritional emergencies, and were therefore left out of this review. It is possible that nutritional emergencies exist in non-humanitarian settings, often as a result of inequities related to poverty. For example, India has the highest number of acutely malnourished children under five in the world – 25,461,000 – but this is not considered a humanitarian emergency.

Child-level **data, disaggregated by age and gender**, is routinely collected in the management of acute malnutrition programmes, although this was not reported in the included studies. This is a gap in understanding how management of acute malnutrition may result in default and/or relapse differently in boys compared with girls. Given that boys are more likely to be wasted than girls in humanitarian emergency settings (Wamani et al., 2007), there could be a different type of programming modality for boys versus girls at certain ages. Also, the lack of age breakdown is a gap in this review, since children aged 6–23 months are often the most wasted age group (UNICEF, 2013). Age category analysis can inform how programmes can adapt to age-specific diet and psychosocial needs in order to mitigate relapse and default, and improve recovery. Evidence on the relationship between recovery and relapse following management of acute malnutrition in humanitarian emergencies is sparse.

Overall conclusions

This review identified 24 publications and programme reports that reported recovery, relapse and default and reasons for recovery and default in the management of acute malnutrition in humanitarian emergencies. Assessment of these publications did not provide sufficient information for conclusions to be drawn in relation to the review questions.

- The relationship between recovery and relapse; and between relapse and default or return default/episodes of default: **The evidence related to this theme is inconclusive.**
- Reasons for default and relapse or return defaults/episodes of default: **The strength of evidence relating to this theme is limited.**

This review provides further confirmation that RUTF used in an outpatient setting is effective at promoting recovery from SAM and reducing mortality. It could not be established whether default rates reported were lower according to the WHO 2013 protocol, which formally included the community-based treatment of acute malnutrition using RUTF, compared with other methods to treat acute malnutrition. Data relating to relapse is limited.

Similarly, as reported in the studies, the use of ready-to-use supplementary foods (RUSFs) to treat MAM, compared with other supplementary foods such as fortified blended foods (FBFs) or corn/soy blends (CSBs), has the potential to improve nutritional recovery in children suffering from MAM. However, the weight gain reported for children given RUSFs or CSBs was small. No significant differences in mortality rates were reported for children who received RUSF compared with children in CSB groups. It could not be concluded whether RUSF could potentially improve relapse and default rates or reduce mortality as there was insufficient robust data available to undertake this analysis.

Little evidence was found on the long-term impact of programmes implemented to manage MAM and SAM in emergencies. Due to the nature of humanitarian emergencies, it is difficult to conduct longitudinal data collection and trace the same children once they have been discharged. The mortality rates reported in these studies ranged from 0.007 percent (Isanaka, 2009) to 18.9 percent (Gaboulaud, 2006). Low mortality and relapse rates were associated with access to skilled medical care, availability of essential drugs, greater parental awareness of the consequences of illness and the need to seek available health services early.

While reasons for default were sometimes cited – including distance to travel to sites, family illness and other commitments, other household priorities, poor community sensitization and household follow-up – none of the studies included in the review focused on defaulted children as an objective.

Barriers to successful completion of acute malnutrition treatment were multi-factorial and included geographic, cultural and socioeconomic obstacles to care (Guerrero et al., 2013). For successful implementation of the WHO protocols for community-based management of acute malnutrition (CMAM), emergency nutrition workers need to be able to adapt protocols to each context.

Programmatic issues and operational challenges also vary between settings and are powerful determinants of the efficacy of programmes. Additional factors for efficacious programme implementation included the degree of integration into existing health systems, the extent of service coverage, staff training and alignment of inpatient treatment with WHO guidelines. However, there were pervasive problems such as resource constraints, the lack of adequate supervision and monitoring, lack of adequate outreach to identify the most vulnerable, dependence on external technical support, weak pipelines for specialized nutritious foods and logistical constraints.

A number of research gaps were identified during this review. In particular, there is a need for more evidence on default and relapse post-treatment; for in-depth analysis of contexts where default and/or relapse rates have been historically high; for observational studies on care practices for malnourished children during and after treatment; and for studies to examine the long-term effects of SAM treatment, in particular the relationship between wasting and stunting.

1 INTRODUCTION

1.1 BACKGROUND

Acute malnutrition is a major contributor to deaths in children under five years of age worldwide (WHO and UNICEF, 2009; UNICEF, 2014). According to current estimates, approximately 17 million children under the age of five suffer from severe acute malnutrition (SAM) and 33 million from moderate acute malnutrition (MAM) globally (UNICEF, WHO and World Bank, 2016). Nearly two-thirds of the burden of acute malnutrition is borne by South-East Asia and sub-Saharan Africa (UNICEF, WHO and World Bank, 2012). South Sudan has the highest level of global acute malnutrition (GAM) (23 percent) and SAM (10 percent), with a GAM level of 15 percent regarded as the threshold for defining an emergency (UNHCR, WFP, 2011).

Defining acute malnutrition in children aged 6–59 months

The classification of acute malnutrition has evolved, with improved evidence to define optimal growth. The World Health Organization (WHO) Child Growth Standards were published in 2006 and were based on a global sample of optimally fed infants from birth through five years of age. Before 2006, interventions implemented to manage acute malnutrition classified children as acutely malnourished based on the US-based National Centre for Health Statistics (NCHS) child growth standard or on the presence of bilateral pitting oedema (WHO, 1999). These reference standards compared children under five with a reference population, many of whom were artificially fed. The 2006 WHO Child Growth Standards are now used to identify a child as being malnourished (WHO, 2013). The table below outlines the differences between the two systems of classification. Mid-upper arm circumference (MUAC) was added as an independent admission criterion in the 2013 update.

Classification	Severe acute malnutrition (SAM)	Moderate acute malnutrition (MAM)
NCHS	<70% median <-3 z-score Oedema	<80% median >=-3 and <-2 z-score Oedema
WHO, 2013	<-3 z-score or oedema MUAC: <115mm	>=-3 and <-2 z-score or oedema MUAC: <125mm

MUAC is more predictive of mortality and tends to select more children who are younger, stunted and female (Isanaka et al., 2015). MUAC has been effectively used in most community-based management of acute malnutrition (CMAM) programmes to screen and refer children for appropriate treatment (Myatt et al., 2006). MUAC is also increasingly used as an independent admission criterion for treatment and discharge. The studies included in this review may use different indicators to define acute malnutrition, depending on when they were conducted. This may have implications for study outcomes, but whenever possible comparisons have been made between equivalent indicators.

In the aftermath of a humanitarian emergency, a breakdown in health services, destruction of food sources and markets and loss of infrastructure can result in an increase in acute malnutrition (Bagchi et al., 2004). Humanitarian emergencies may also disrupt cultivation and harvest, negatively impacting the food security status of an affected population. The risk of disease outbreaks increases with displacement, overcrowding and a breakdown in sanitation and hygiene, which also increases the risk of undernutrition (Brundtland, 2000). Compromised infant and young child feeding practices, resulting from displacement, stress/trauma, lack of complementary foods and a breakdown in social structure, are also common during a humanitarian emergency. Nutritional emergencies can also exist in non-humanitarian settings, often as a result of inequities related to poverty. For example, India has the highest number of acutely malnourished children aged under five in the world – 25,461,000 – but this is not considered a humanitarian emergency. Most of the world's acutely malnourished children (33.9 million) live in Asia (UNICEF, WHO and World Bank, 2015). The UN has highlighted that 'the wasting rate in Southern Asia is approaching a critical public health emergency', at 14.1 percent GAM in its most recent estimate (UNICEF, WHO and World Bank, 2016).

The WHO Guideline, 'Management of severe malnutrition: a manual for physicians and other senior health workers', was first published in 1999 (WHO, 1999) and has guided the inpatient management of acute malnutrition in hospital or specialized nutrition rehabilitation wards since then. In 2013, WHO published updates on the management of SAM in infants and children

(WHO, 2013), which include CMAM interventions for children without medical complications. There are no global guidelines for the management of MAM, but there are country-level national guidelines for acute malnutrition which incorporate the treatment of MAM and a Global Nutrition Cluster (GNC) guidance document from the MAM taskforce (Force, 2012). CMAM programmes exist in over 70 countries worldwide (UNICEF, 2014) and are the standard intervention for responding to acute malnutrition during a humanitarian crisis.

Management of acute malnutrition

The WHO guideline, 'Management of severe malnutrition: a manual for physicians and other senior health workers', published in 1999, outlines the phases of inpatient care for children: initial stabilization (Phase I), nutritional rehabilitation (Phase II) and follow-up. Phase I requires the use of F-75 therapeutic milk and the treatment of life-threatening conditions such as shock and dehydration. Phase II involves continued nutritional rehabilitation with F-100 therapeutic milk until the discharge weight is achieved. After discharge, health workers are supposed to conduct regular follow-up visits to the homes of treated children to support and counsel their care-givers, with the aim of preventing relapse (WHO, 1999).

The CMAM model was introduced to address both SAM and MAM at the community and household levels. Different terminologies have been used to describe the CMAM model, including community therapeutic care (CTC), integrated management of acute malnutrition (IMAM), community-based therapeutic care (CBTC) and ambulatory care for the treatment of acute malnutrition. This review uses CMAM to refer to the community management of acute malnutrition. CMAM programmes use essential medicines and RUTFs to treat SAM in outpatient therapeutic feeding centres and maintain stabilization centres for children who have SAM with medical complications and require 24-hour care.

Another component of CMAM is the treatment of MAM. While MAM treatment is not included in the WHO 2013 protocol, there are different approaches in national guidelines. MAM treatment through targeted supplementary feeding programmes (TSFPs) employs fortified blended foods (FBFs), such as corn-soy blends (CSBs) or SuperCereal Plus, which are fortified with micronutrient pre-mixes and may include vegetable oil, whey or skimmed milk powder (Webb et al., 2011). Ready-to-use supplementary foods (RUSFs) have now been designed as an alternative to FBFs to treat MAM (UNICEF, 2014). These are energy-dense fortified foods that are packaged in a convenient way and are ready for use, i.e. they do not require cooking or preparation at home before use, unlike FBFs (Nutraset, 2008).

The CMAM model was developed in the late 1990s and early 2000s, and early CMAM programmes achieved nutritional recovery rates of almost 80 percent, with low case fatality rates of <5 percent (Collins et al., 2006). Other clinical trials (Diop et al., 2004; Manary et al., 2004; Ndekha et al., 2005) as well as descriptive studies (Webb et al., 2014) conducted in emergency nutrition situations have all demonstrated that the CMAM approach can achieve successful outcomes in nutritional recovery and promote child survival.

Performance of CMAM is measured through four main indicators: recovery – the proportion of children aged 6–59 months who successfully recover; died – the proportion of children who die during treatment; default – the proportion of children who default from (do not complete) treatment; relapse – the proportion of children who complete treatment, but develop SAM and are readmitted for further treatment. The recovery rates reported in most studies have been within the Sphere Project's Minimum Standards or indicators for therapeutic effectiveness (Sphere, 2011).

Sphere Project: minimum standards for measuring programme effectiveness

Indicators	Proportions
Proportion of children who die in the programme	<10%
Proportion of children who recover in the programme	>75%
Proportion of children who default from the programme	<15%
Minimum rate of weight gain (g/kg/person/day)	>8

Source: Sphere Project (2011)

1.2 RATIONALE AND PURPOSE

Previous systematic reviews have investigated the effectiveness of interventions to manage acute malnutrition in children aged 6–59 months. Some have focused on comparing the inpatient model with the community model (Lenters et al., 2013; Schooness et al., 2013; Ashworth, 2006); some have assessed the appropriateness and efficacy of routine first-line antibiotics provided during outpatient care for children with uncomplicated SAM (Alcoba et al., 2013); and others have examined the effect of different ready-to-use foods (RUFs), including cost-effectiveness (Bhutta et al., 2008; Gera, 2010). Picot and colleagues (2012) reviewed various intervention studies that have been designed to treat infants and children aged under five years with SAM. The most recent review (Suri et al., 2016) focusing on the management of MAM compared RUTFs and FBFs to determine whether the inclusion of dairy products modifies their comparative effectiveness.

Emergency intervention studies focusing on SAM treatment (Kerac et al., 2009; Giugliani et al., 2010; Aguayo, 2013; Puett et al., 2013; Puett and Guerrero, 2015; Dale et al., 2013; Burza et al., 2015), as well as the management of SAM and MAM (UNICEF, 2012; Somassè et al., 2015), have reported high rates of default and relapse. Evidence is sparse on the extent to which children who recover during treatment for acute malnutrition in humanitarian emergencies subsequently relapse. Further, little is known about how operational realities, such as insecurity and access to a population, affect both the implementation of programmes to treat acute malnutrition and research conducted on programme performance.

1.3 RESEARCH QUESTIONS

This systematic review was undertaken to examine outcomes beyond recovery. Specifically, the review team sought to better understand how relapse and default are affected during CMAM programmes in order to determine how programmes can be modified to improve overall quality in humanitarian emergencies. A further aim was to synthesize findings from qualitative research studies to explore the contexts in which acute malnutrition management programmes have been implemented, in order to identify and describe how the implementation context influences success or relapse and/or default.

The review investigated:

- the relationship between recovery and relapse; and between relapse and default or return default/episodes of default in children aged 6–59 months affected by humanitarian emergencies
- reasons for default and relapse or return defaults/episodes of default in children aged 6–59 months affected by humanitarian emergencies.

The findings of this review are expected to contribute to the growing literature on interventions used to treat acute malnutrition in emergency settings, with the ultimate aim of better informing programme and policy decisions.

0.1 POPULATION, INTERVENTION, CONTROL AND OUTCOME (PICO) PARAMETERS

Population

The review included studies if they targeted children aged 6–59 months of age with treatment of acute malnutrition in humanitarian emergencies. Studies that focused on the management of acute malnutrition in infants less than six months of age and pregnant women or lactating mothers were not included. Because of the different definitions and classification criteria that have been used to identify children with acute malnutrition (see Section 1.2), only studies that used ‘standard and accepted’ definitions (Picot et al., 2012) of SAM and MAM were included: i.e. definitions for MAM and SAM used by the authors should be based on the NCHS child growth standard if studies were published before or during 2006 and on the WHO Child Growth Standards if studies were published after 2006.

Interventions/issues

The interventions considered for this review are those for the treatment of SAM or MAM delivered in humanitarian emergencies. Humanitarian emergencies are defined as major incidents that threaten human life and public health (WHO, 2010). These include protracted conflicts, flooding, earthquakes and other natural disasters. Interventions provided to manage/treat SAM in humanitarian emergencies should include inpatient care using therapeutic milks such as F-75 or F-100 and RUTFs, and outpatient care using RUTFs. Interventions provided to manage/treat MAM in humanitarian emergencies include those that used FBFs e.g. SuperCereal, SuperCereal Plus, CSBs and/or oil-based RUSFs. Studies that were based on blanket supplementary feeding provided to children to prevent MAM from progressing to SAM were not considered. However, where studies state that the aim of the

supplementary feeding programme was to manage rather than prevent MAM they were included in the review.

Comparison

This review compared relapse rates and default rates in children aged 6–59 months in the management of acute malnutrition programmes in humanitarian emergencies.

Outcomes

- **Recovery rate:** the proportion of children who are cured through treatment of acute malnutrition programmes – as defined by the authors based on standard criteria.
- **Default rate:** the proportion of children who were absent from treatment for two consecutive sessions.
- **Absence and/or repeated absence:** the proportion of children who were absent from treatment/the number of absences recorded.
- **Return default rate/repeated default episodes:** the proportion of children who re-enrolled into treatment after defaulting/number of times they re-enrolled.
- **Relapse rate/repeated relapse episodes:** the proportion of children who re-enrolled after they had recovered and been discharged.
- **Time to recover:** the length of time between admission and discharge.

2 METHODS

2.1 PROTOCOL DEVELOPMENT

A protocol was developed and used to guide the review (Akparibo et al., 2016), setting out the problem and the rationale for the review. It also provides a complete description of the proposed methods for the review. The protocol was peer-reviewed and revised before the review began. The full review protocol is available online at: <http://fic.tufts.edu/assets/OX-HEP-Malnutrition-Print.pdf>

2.2 IMPLEMENTATION OF THE SEARCH STRATEGY

This systematic review used a mixed methods systematic literature review approach to identify and include various types of literature: quantitative, qualitative and mixed methods studies, as well as grey literature such as programme reports. The search was conducted in the following databases: Medline and Medline In-Process; Embase; CINAHL; Science Citation Index Expanded, Conference Proceeding Citation Index – Science, and Book Citation Index – Science (all via Web of Science); regional literature databases: African Index Medicus, Index Medicus for the Eastern Mediterranean Region (IMEMR), Latin American and Caribbean Health Sciences Literature (LILACS), the Western Pacific Regional Index Medicus (WPRIM) and Index Medicus for the South-East Asian Region (IMSEAR); the Cochrane Central Register of Controlled Trials (CENTRAL) and BIOSIS. In addition, the research team used cluster-searching techniques (Booth et al., 2013) to enable the retrieval of ‘sibling’ studies (those closely associated with previously identified randomized controlled trials (RCTs) and observational studies) to broaden the collective understanding of the context in which these studies were conducted.

Grey literature, including programme reports, was identified from websites of relevant governments and non-governmental organizations (NGOs), via Google Scholar and by engaging with stakeholders in the nutrition field. Grey literature was also collected by contacting humanitarian organizations or individuals to ask if they had unpublished reports relevant to the review.

Studies published prior to 1980 were excluded, as were any not published in English. The rationale for the date limitation was that the standardized diagnostic criteria for classifying SAM and MAM for treatment, as well as the development of tailored interventions to address these conditions, occurred in the early 1980s. Very few of these studies fall within the framework of humanitarian emergencies caused by protracted conflicts, flooding and earthquakes. We emailed the authors of studies that were unclear to ask them to clarify whether these were humanitarian emergency or non-humanitarian emergency studies.

2.3 MODIFICATIONS FROM THE PUBLISHED PROTOCOL

The first modification from the original protocol was the decision made, in consultation with the review commissioners, not to address one of its specific objectives through the systematic review process – ‘the effect of treatment on mortality risk among children suffering from SAM and/or MAM’ (Akparibo et al., 2016). It was suggested in peer reviews and by the systematic review expert board that this question had already been sufficiently addressed. Previous reviews (Lenters et al., 2013; Ashworth et al., 2006) have highlighted that the 1999 inpatient guidelines have resulted in improved nutritional recovery rates (compared with non-standard care) and have led to significant reductions in mortality rates (Briend et al., 1999; Collins, 2004).

Revisions following peer review

The second modification was a re-screening of included articles for a stricter application of including only studies that were conducted in humanitarian emergencies. The protocol defined humanitarian emergencies as:

major incidents that threaten human life and public health. These include protracted conflicts, flooding, earthquakes and other natural disasters, and nutrition emergencies when prevalence rates of malnutrition have reached a crisis level ($\geq 15\%$), according to the WHO crisis classification using global acute malnutrition. The latter in particular may include government-led interventions designed to manage acute malnutrition in such a crisis situation. (Akparibo et al., 2016)

Peer review feedback indicated that not all selected studies were from humanitarian emergencies. To address this feedback, studies were also included if they did not take place in a humanitarian setting but their objectives explicitly stated that the research was intended to improve management of acute malnutrition programmes in humanitarian emergencies. Following peer review, two sources (ReliefWeb and the Centre for Research on the Epidemiology of Disasters (CRED)) were used to verify that a humanitarian emergency was occurring at the time data was collected for each study. These databases were also used to verify if the study had an objective to improve humanitarian response in the study area. Considerations for the search in the databases included seasonal spikes in malnutrition, a declared food crisis and natural disasters or disease outbreaks that affected nutrition status. Articles that did not meet these criteria were not included in the review. It was determined that 24 out of 69 studies referred to strictly humanitarian emergency settings.

2.4 DOCUMENT SCREENING

Guided by the inclusion or eligibility criteria, as well as purpose-specific checklists, all the studies identified during the search were screened in two stages.

Stage 1

One reviewer screened all the titles of the studies initially identified for potentially relevant studies, and a subject specialist checked this.

Stage 2

Four reviewers then conducted a further screening of the abstracts and executive summaries of articles selected after initial screening in Stage 1 ($n=1,521$), based on the article titles. The four reviewers were paired, and each pair was assigned a test set of 25 papers and reports to review in order to establish a consensual selection process.

The relevance of each paper was coded and cross-checked by a subject specialist. Further, the quality of each study was thoroughly assessed and graded using standard checklists. To minimize inter-observer variability in the screening and coding process, several measures were instituted. For instance, before any coding was started, the subject specialist gave the review team an orientation tutorial on the management of MAM and SAM in humanitarian emergencies and the type of information required to address the review question. The review team drew upon training materials developed by UNICEF, as well as a PowerPoint presentation received from a nutrition specialist as resource or reference materials. We held team meetings to resolve uncertainties or disagreements between reviewers, where necessary.

2.5 EVIDENCE APPRAISAL

From the outset, we anticipated that studies to be included in the review would be based on different methodological designs. The review team followed the Cochrane guidance for the critical appraisal of qualitative research and selected the Critical Appraisal Skills Programme (CASP) checklist for qualitative studies (CASP, 2013). CASP checklists (www.casp-uk.net) were used to assess the quality of quantitative and systematic review studies as there are separate checklists for these study types. Two reviewers applied CASP checklists to assess and grade the quality of the included studies. They screened the full text of the filtered sets of quantitative articles, and another two reviewers cross-checked their selections. The studies were graded as high, moderate, low or very low quality. In accordance with recent empirical research, we decided that the quality assessment process would not lead to the exclusion of papers. Instead, it would be used to moderate the strength of evidence for the thematic findings (Carroll et al., 2011). During revision, ReliefWeb and CRED databases were used to classify articles from the search by context, either humanitarian or development. Those articles that did not meet the revised, stricter interpretation of the review criteria were omitted from the final review.

Figure 2.1: CASP checklist questions

CASP checklist for RCT quality assessment questions	CASP checklist for cohort study quality assessment questions	CASP checklist quality assessment questions for qualitative studies
<ul style="list-style-type: none"> Clearly focused issue Randomized Patients/study personnel/health workers blinded Groups similar at start of trial Treated equally Results precise Can results be applied? Clinically important outcomes Benefits worth harms/cost 	<ul style="list-style-type: none"> Clearly focused issue Recruitment acceptable Exposure accurately measured Outcomes accurately measured Confounders identified Follow-up long enough Rates or proportions reported Results precise Results believable Can results be applied? Fits with other evidence Provides implications for practice 	<ul style="list-style-type: none"> Clear statement of aims Qualitative methodology appropriate Appropriate research design Appropriate recruitment strategy Appropriate data collection Relationship between researcher and participants Ethical issues considered Data analysis rigorous Findings clear Value of research

2.6 DATA EXTRACTION AND EVIDENCE SYNTHESIS

Methods of quantitative data synthesis were largely informed by the nature and type of studies identified and included in the review. We did not conduct a meta-analysis of included homogenous studies, since previous reviews (Gera, 2010; Schooness et al., 2013; Lenters et al., 2013) have already done this. Instead, a narrative synthesis of the data was performed, with a tabulation of the results.

3 RESULTS

3.1 SEARCH RESULTS

The PRISMA diagram presented in Figure 3.1 illustrates the screening process. A total of 9,574 studies and programme reports were retrieved. After duplicates were removed, 7,693 citations were left to be screened. An initial title screening resulted in 6,172 citations being excluded. An abstract screening resulted in the exclusion of 1,419 additional studies. A full text review was conducted of the remaining 102 studies, which resulted in the exclusion of 33 studies. To address peer review feedback, 45 studies that did not meet the humanitarian crisis criteria were excluded. A total of 24 studies were therefore included in the review.

Figure 3.1: PRISMA diagram of included studies

3.2 CHARACTERISTICS OF INCLUDED STUDIES

A total of 24 articles were included in the review, based on the criteria set out in Section 2. One study was conducted in Afghanistan and 23 were conducted in sub-Saharan Africa: eight in Malawi, five in Ethiopia, three in Niger, three in Sudan and one each in Angola, Chad, Kenya and Sierra Leone.

Of the 24 studies/programme reports eligible for inclusion, 22 reported on quantitative outcomes and two on both quantitative and qualitative outcomes (mixed methods). The quantitative studies were clinical efficacy and effectiveness trials using randomized controlled designs (n=8), observational cohort studies found in journal articles (n=7) and programme evaluation reports found in grey literature (n=7). The sample sizes ranged from 170 to 5,799 children for studies focusing on SAM, 1,038 to 23,865 children for studies focusing on MAM and 7,028 to 97,692 children for studies focusing on both SAM and MAM.

The mixed methods studies examined issues relating to the implementation and acceptability of programmes to combat acute malnutrition. Data collection methods employed in the mixed methods studies included interviews (Belachew and Nekatibeb, 2007; Flax et al., 2009) and documentary analysis, focus groups and observations (Belachew and Nekatibeb, 2007). We identified five reviews, but only extracted data from their included papers if they were relevant to our review.

3.3 ASSESSMENT OF STUDY QUALITY

The studies were evaluated based on various CASP checklists (CASP, 2013). Overall, the included studies were categorized as high, medium, or low quality based on these checklists (see Appendix 2). The observational cohort studies (n=7) and programme evaluation reports (n=7) were evaluated based on the CASP Cohort Study Checklist. Three of the observational studies were assessed to be of high quality (Amthor et al., 2009; Grellety et al., 2012; Linneman et al., 2007); two were assessed to be of medium quality (Collins and Sadler, 2002; Lagrone et al., 2010); and two were assessed to be of low quality (Chaiken et al., 2006; Gaboulaud et al., 2006). All seven of the programme evaluation reports were assessed to be of low quality (Deconinck, 2004; Lurqin, 2003; Morgan et al., 2015; Querubin, 2006; Taylor, 2002; UNICEF, 2012; Walker, 2004). The quality of the RCTs (n=8) was evaluated based on the CASP RCT Checklist. Four of these studies were assessed to be of high quality (Bahwere et al., 2014; Karakochuk et al., 2012; Matilsky et al., 2009; Oakley et al., 2010) and four were assessed to be of medium quality (Ciliberto et al., 2005; Huybregts et al., 2012; Isanaka et al., 2009; Maust et al., 2015). The qualitative component of the mixed methods studies (n=2) was evaluated based on the CASP Qualitative Checklist and was assessed to be of medium quality (Belachew and Nekatibeb, 2007; Flax et al., 2009).

Particular concerns related to the adequacy of descriptions of the recruitment strategy used in the included studies. The extent to which participants expressed the range of opinions held by the population in general was unclear. Little detail was provided of ethical considerations with, at best, a cursory mention of ethical approval being sought. For the two mixed methods studies, assessing the individual components separately may not have captured the added value of integrating them as complementary.

Notwithstanding these reservations, the objectives of most studies were clear and they offered some justification for the use of either quantitative or qualitative methods. The specific methods chosen seemed appropriate to the research questions posed by the included studies, and mixed quantitative and qualitative methods were utilized to offer a wider frame for evaluation in two studies. Overall it is difficult to assess the value of the grey literature studies, either individually or collectively as a body of evidence. The characteristics of the included studies and their findings are presented in Appendix 3.

3.4 NARRATIVE SYNTHESIS OF RESULTS

This section is organized according to the research questions introduced earlier in the review.

Relationship between recovery and relapse; relationship between relapse and default or return default/episodes of default

Of the 24 studies included in this review, only six addressed the issue of relapse and/or reported relapse rates (Bahwere et al., 2014; Ciliberto et al., 2005; Linneman et al., 2007; Querubin, 2006; Taylor, 2002; UNICEF, 2012), and none addressed the relationship between relapse and default or return default. This may be partly attributed to the relatively short duration of most interventions and the fact that most of the studies did not include post-intervention follow-up.

The first of the six studies that addressed relapse was a randomized controlled clinical effectiveness trial conducted by Bahwere et al. (2014; high quality), comparing the effectiveness of a whey protein-based RUTF with a standard peanut-based RUTF for

treating SAM in central Malawi. The article briefly mentioned that children included in the intervention who then relapsed were not eligible to be readmitted to the programme, although the rate of relapse was not reported. A second clinical effectiveness trial conducted by Ciliberto et al. (2005; medium quality) compared the effectiveness of home-based therapy using RUTFs with standard inpatient therapy using F-75 and F-100 for treating SAM in southern Malawi. Recovery and relapse or death rates were reported as the primary outcomes of the study. The authors found that children with SAM who received the home-based therapy were more likely to achieve a WHZ > -2 compared with those who received the standard therapy (79 percent compared with 46 percent; $p < 0.001$) and were less likely to relapse or die (8.7 percent compared with 16.7 percent; $p < 0.001$). The authors reported a default rate of 9.8 percent for children who received the home-based therapy and 8.1 percent for those who received the standard therapy. The authors did not identify specific reasons for relapse or default among those children included in the intervention, nor did they attempt to draw a relationship between relapse and default.

A prospective cohort study was conducted by Linneman et al. (2007; high quality) to study the outcomes of home-based therapy with RUTF to treat both children with SAM and children with MAM in an operational setting in southern Malawi. Of the 2,131 severely malnourished children included in the intervention, an average of 89 percent recovered, 3 percent failed to recover or relapsed, 1 percent died and 7 percent defaulted across the 12 rural centres studied. Of the 806 moderately malnourished children included in the intervention, 85 percent recovered, 4 percent failed to recover or relapsed, 2 percent died and 8 percent defaulted on average across the 12 rural centres. The authors did not report relapse rates separately from non-recovery rates or identify reasons for relapse among the study population.

Three programme evaluation reports identified in the grey literature addressed the issue of relapse. One of these reports evaluated an ACF-USA therapeutic feeding programme to treat SAM in South Sudan (Querubin, 2006; low quality). All children included in the intervention began treatment at a therapeutic feeding centre (TFC) utilizing F-75 for the first phase of their treatment; they either continued to receive inpatient care utilizing F-100 for the second phase of the programme (28 percent) or transitioned to home treatment utilizing RUTF (72 percent). Of those children in the home treatment group, 81 percent recovered and 7 percent defaulted. The author reported that there were no cases of relapse among the children in the home treatment group. A second programme report evaluated an outpatient therapeutic feeding programme (OTP) to treat SAM and MAM in 10 rural council areas in North Darfur, Sudan (Taylor, 2002; low quality). Children with SAM included in the intervention were treated with RUTF and children with MAM were treated with RUSF over a five-month period in 2001. A supplementary feeding programme (SFP) targeting children and pregnant and lactating women was also established. The average rate of discharge from the OTP to the SFP was 81.4 percent, the average rate of default was 10.1 percent, the average rate of mortality was 2.9 percent and the average rate of transfer to a TFC, hospital or dispensary was 5.6 percent across the 10 rural councils. The authors reported that readmission rates were approximately 1 percent of total admissions.

The third programme report evaluated four components of an integrated management of acute malnutrition (IMAM) programme in Kenya, including community outreach, outpatient treatment for SAM cases without medical complications, inpatient treatment for SAM cases with medical complications and management of MAM (UNICEF, 2012; low quality). UNICEF reported that outpatient SAM treatment utilizing RUTF resulted in a recovery rate of 80.7 percent, a mortality rate of 1.5 percent, a default rate of 12.9 percent and a relapse rate of 3.2 percent. Inpatient SAM treatment for children with medical complications utilizing F-75 and F-100 resulted in a recovery rate of 84.6 percent, a mortality rate of 8.7 percent, a default rate of 1.4 percent and a relapse rate of 6.1 percent. Treatment for children with MAM utilizing supplementary foods resulted in a recovery rate of 80.5 percent, a mortality rate of 0.4 percent, a default rate of 14.4 percent and a relapse rate of 3.7 percent (note: these rates were averaged across eight districts).

Reasons for default and relapse or return defaults/episodes of default

All 24 of the studies included in this review provided data about rates of default. Reasons for default were often cited, including distance to travel to sites, family illness and other commitments, other household priorities and poor community sensitization and household

follow-up. As related above, few studies reported relapse rates and only one identified possible reasons for relapse within the context of the study. The UNICEF programme evaluation report (2012; low quality) suggested that the lack of a follow-up system to track children treated for SAM or MAM and encourage them to return for outpatient treatment may have contributed to the relapse rate, as well as the sharing of RUTFs among siblings and other non-admitted children. Improved community outreach was identified as a mechanism for addressing these issues.

A mixed methods study of an OTP for SAM treatment in Ethiopia conducted by Belachew and Nekatibeb (2007; medium quality) identified several reasons for a 44.8 percent default rate in one administrative region (Oromia), including a lack of supplies, attrition of trained staff and poor community mobilization, all of which caused interruptions in service. The authors also attributed the default rate to the long distances that mothers and children had to travel for follow-up services, and recommended that two weeks' worth of RUTF be provided at a time and that the programme be decentralized to community health posts in order to reduce opportunity costs for participants and their families. Another mixed methods study comparing maternal attitudes towards supplementary foods, specifically CSBs and lipid-based nutrient supplements (LNSs), to treat MAM in Malawi found that, while mothers had positive attitudes towards both, they were likely to stop giving LNS if children were sick because the LNS was considered sweet in taste (Flax et al., 2009; medium quality).

Of the observational cohort studies included in the review (n=7), two offered reasons for default. Lagrone et al. (2010; medium quality) studied the effectiveness of using a locally produced soy/peanut RUSF to treat MAM in southern Malawi and suggested that a relatively low default rate (4 percent) compared with similar interventions utilizing CSB may be due to lower opportunity costs incurred by mothers, who had to gather firewood and prepare food in order to utilize CSB. Linneman et al. (2007; high quality, observational cohort study) indicated that high default rates at two rural centres located near border areas along a major truck route may have been caused in part by undiagnosed HIV infection among children in these centres. The authors suggested that routine HIV testing and home health visits by village health workers might be added to interventions in these communities.

A programme evaluation report from an outpatient SAM treatment intervention conducted in Afghanistan identified four possible reasons for a relatively high default rate of 23.8 percent, based on interviews with mothers: illness of the child or mother; children accompanying mothers to cultivate land; insufficient food distributed at the centres; and problems at home (Lurqin, 2003; low quality). Taylor (2002; low quality, programme evaluation report) attributed a high default rate of 34 percent in one rural council area in Darfur to children from pastoralist families being in town for only a few days at a time. A programme evaluation report of an outpatient programme conducted in South Sudan identified TFCs being cut off by heavy rains and mothers having to walk with food and a child for four hours as reasons for a default rate of 15 percent (Walker, 2004; low quality). Default rates for outpatient treatment in some districts involved in UNICEF's Kenya intervention were partly attributed to weak household follow-up (UNICEF, 2012; low quality).

A randomized controlled clinical effectiveness trial conducted by Oakley et al. (2010; high quality) compared a standard RUTF made with 25 percent milk powder with one made with a 10 percent milk powder/soy blend. The authors addressed the possibility of higher default rates in the 10 percent milk powder RUTF group due to subtle differences in taste or colour, but did not find sufficient evidence either to confirm this or rule it out (based on a 3 percent default rate for both intervention groups).

4 CONCLUSION

This review identified 24 publications and programme reports that reported recovery, relapse and default and reasons for recovery and default in the management of acute malnutrition in humanitarian emergencies. Assessment of these publications did not provide sufficient information for conclusions to be drawn in relation to the review questions.

- The relationship between recovery and relapse; and between relapse and default or return default/episodes of default: **The evidence related to this theme is inconclusive.**
- Reasons for default and relapse or return defaults/episodes of default: **The strength of evidence relating to this theme is limited.**

This review provided further confirmation that RUTF used as part of the WHO 2013 protocol is effective in promoting recovery from SAM and reducing mortality. We could not establish whether default rates reported were lower according to the WHO 2013 protocol. We also found limited data related to relapse. Similarly, as reported in previous reviews, we found that the use of RUSF to treat MAM, compared with other supplementary foods such as FBFs or CSBs, has the potential to improve nutritional recovery for children suffering from MAM. However, the weight gain reported by studies for children given RUSF or CSB was small. There were no substantial differences in mortality rates reported for children who received RUSF compared with children in CSB groups.

The review found very little evidence on relapse from programmes implemented to manage MAM and SAM in emergencies. Due to the nature of humanitarian emergencies, it is difficult to conduct longitudinal data collection and trace the same children once they have been discharged, except in refugee camp settings. Low mortality and relapse rates were associated with access to skilled medical care, availability of essential drugs, greater parental awareness of the consequences of illness and the need to seek available health services early.

Reasons for default were often cited and included travel distance to sites, family illness and other commitments, other household priorities, and poor community sensitization and household follow-up. However, none of the included studies focused on defaulted children as an objective.

We found that the challenges to successful completion of acute malnutrition treatment were multi-factorial and included geographic, cultural and socioeconomic obstacles to care (Guerrero et al., 2013). For successful implementation of the WHO protocols for CMAM, emergency nutrition workers need to be able to adapt protocols to different contexts. Programmatic issues and operational challenges also vary between settings and are powerful determinants of the efficacy of programmes. Additional factors were the degree of integration into existing health systems, the extent of service coverage, staff training and alignment of inpatient treatment with WHO guidelines. However, there were pervasive problems such as resource constraints, the lack of adequate supervision and monitoring, lack of adequate outreach to identify the most vulnerable children, dependence on external technical support, weak pipelines for specialized nutritious foods and logistical constraints.

4.1 LIMITATIONS OF THE REVIEW

There is considerable heterogeneity in the evidence base owing to the diversity of study types, types of intervention and the settings in which programmes are delivered. In addition, the quality of the published literature varies markedly. Generally, the grey literature reports and qualitative studies included in the review lacked crucial detail, such as details of their recruitment strategies. Review articles did identify the presence of significant barriers relating to the acceptability of the intervention and implementation issues. These qualitative insights also highlight the importance of the context in which malnutrition treatment programmes are implemented and the challenges encountered, as illustrated by the variability of effect of seemingly similar interventions based on identical guidelines and protocols. This suggests that interventions cannot simply be copied from one setting and

implemented in another, but that some local adaptation is required. The detail presented in the mixed methods studies offers a more nuanced understanding of the precise context and, indeed, suggests that some factors are generic and that others, although present, may not have the same relative importance in a different context. The three main limitations of this review are outlined below.

One major limitation is the lack of qualitative data, as only two mixed methods studies were eligible for inclusion following peer review feedback (Belachew and Nekatibeb, 2007; Flax et al., 2009). It was assumed during the protocol development that the search would yield more qualitative studies, but this was not the case. Upon applying the stricter interpretation of humanitarian emergencies, most of the 22 qualitative studies were judged not to derive from humanitarian emergencies and therefore they were excluded from the review. However, it is possible that qualitative studies related to treatment of acute malnutrition in humanitarian emergencies are part of larger response documents, and therefore more difficult to find given the search strings employed. Also, it was expected that practitioners in the field of malnutrition in humanitarian emergencies would be able to provide studies to the review team. While efforts were made to contact experts, the pool of experts was limited to only five organizations – Concern Worldwide, Action Contre La Faim (ACF), Médecins Sans Frontières (MSF), the International Committee of the Red Cross (ICRC) and KEMRI-Wellcome Trust – and two universities (Washington University in St. Louis, USA and the Université Catholique de Louvain in Belgium).

4.2 INFLUENCE OF OPERATIONAL REALITIES ON PROGRAMMING AND RESEARCH

Few of the studies cited challenges relating to operational realities affecting programmes to manage acute malnutrition. While context was given in relation to types of population (i.e. pastoralists, other migrating populations), security and access were rarely mentioned. Few details were provided about how studies were interrupted or affected by ongoing humanitarian emergencies. For example, we would have expected to see more information related to weaknesses in supply chain management in relation to specialized nutritious foods. This highlights an important gap in the literature, since understanding of how humanitarian emergencies affect the provision of services is important to document.

4.3 AGE AND SEX DATA

While child-level data disaggregated by sex and age is routinely collected in the management of acute malnutrition programmes, this data was not reported in the included studies. This creates a gap in understanding how the management of acute malnutrition may result in default and/or relapse differently in boys versus girls. Given that boys are more likely to be wasted than girls in humanitarian emergency settings (Wamani et al., 2007), there could be a different type of programming modality for boys compared with girls at certain ages. The lack of age breakdown also represents a gap in this review, since children aged 6–23 months are often the most wasted age group (UNICEF, 2013). Age category analysis can inform how programmes can adapt to age-specific diet and psychosocial needs in order to mitigate relapse and default and improve recovery.

4.4 RECOMMENDATIONS FOR FUTURE RESEARCH

This review found few studies that explored the issue of relapse. In order to understand the relationship between relapse and recovery, more research on default and relapse post-intervention is needed. A first step would be to conduct secondary analysis on existing programme data (individual-level databases on SAM and MAM performance are managed by nutrition clusters/sectors during humanitarian emergencies) and identify which countries have the highest levels of default and relapse. With this prioritization, specific geographic areas could be further researched with follow-up studies.

Additionally, to build the evidence base, prospective research could focus on one country with quality programme data and high default and/or high relapse rates and follow-up studies

could be conducted of children who have defaulted or relapsed. Such studies will allow for an improved understanding of why treatment outcomes were not maintained after discharge. This may have implications related to guideline modifications: dosage, minimum length of stay; sanitation and hygiene situation in the household leading to repeated illnesses; complementary food adequacy in the household; household sharing of specialized nutritious foods; etc.

Future studies should also examine how engagement with community members and care-givers through the implementation of nutrition education activities, counselling and home visits contributes to successful programme delivery and improvement of intervention outcomes, particularly default and relapse. High-quality longitudinal observational studies are needed to investigate the long-term impact on children of treatment for acute malnutrition. Post-discharge follow-ups are needed to assess long-term growth and development differences, mortality and relapse.

There are studies ongoing which examine the linkages between wasting and stunting (Khara and Dolan, 2014). These analyses examine the implications of a child's nutritional status, i.e. being stunted, before experiencing an episode of wasting, and the long-term morbidity and mortality effects of wasting.

APPENDIX 1: DATABASE SEARCH STRATEGY STRINGS

INITIAL SEARCH STRATEGY/OUTPUTS OF SCOPING SEARCH

Database: Ovid Medline In-process and other non-indexed citations and Ovid Medline <1946 to Present>

Search strategy

#	Searches
1	malnourish\$ or undernourish\$ or malnutrition or undernutrition or kwashiorkor or marasmus).ti,ab. (39065)
2	Malnutrition/ (7780)
3	exp Protein-Energy Malnutrition/ (8495)
4	1 or 2 or 3 (44198)
5	Child, Preschool/ or Infant/ (1023482)
6	child\$ or baby or babies or infant\$.ti,ab. (1300841)
7	5 or 6 (1772685)
8	(humanitarian\$ or conflict\$ or famine\$ or disaster\$ or emergency relief or sub-saharan africa or south-east asia or latin america\$.ti,ab. (130391)
9	Relief Work/ or Disaster Planning/ or Starvation/ (22503)
10	8 or 9 (146588)
11	Child Nutrition Disorders/ (2457)
12	10 and 11 (122)
13	4 and 7 (16526)
14	10 and 13 (813)
15	or 14 (851)

FINAL SEARCH STRATEGY

#	Search strategy
1	(malnourish\$ or undernourish\$ or under-nutrition or under-nourish or mal-nutrition or malnutrition or undernutrition or wasting or kwashiorkor or marasmus or SAM or severe-acute-malnutrition).ti,ab.
2	Malnutrition/
3	exp Protein-Energy Malnutrition/
4	1 or 2 or 3
5	Child, preschool/ or Infant/
6	(child\$ or baby or babies or infant\$ or pre-school or preschool).ti,ab.
7	5 or 6
8	4 and 7
9	Child Nutrition Disorders/ or Infant Nutrition Disorders/
10	8 or 9
11	(humanitarian\$ or conflict\$ or famine\$ or disaster\$ or emergency or emergencies or Developing countr\$ or sub-saharan africa or south-east asia or latin america\$ or Ethiopia or Malawi or South Sudan or Niger or Pakistan or India or Bangladesh or Kenya or Nepal or Afghanistan or Angola or Armenia or Azerbaijan or Bosnia-Herzegovina or Burkina Faso or Burundi or Republic of Congo or Democratic Republic of Congo or El Salvador or Eritrea or Gambia or Georgia or Guatemala or Haiti or Honduras or Indonesia or Iraq or Korea DPR or Laos or Liberia or Mauritania or Mongolia or Mozambique or Nicaragua or Panama or Papua New Guinea or Rwanda or Senegal or Sierra Leone or Somalia or Tajikistan or Tanzania or Uganda).ti,ab.

#	Search strategy
12	Developing Countries/ or Africa South of the Sahara/ or Asia, Southeastern/ or Latin America/ or Ethiopia/ or Malawi/ or Sudan/ or Niger/ or Pakistan/ or India/ or Bangladesh/ or Kenya/ or Nepal/ or Afghanistan/ or Angola/ or Armenia/ or Azerbaijan/ or Bosnia-Herzegovina/ or Burkina Faso/ or Burundi/ or Democratic Republic of the Congo/ or Congo/ or El Salvador/ or Eritrea/ or Gambia/ or Georgia (Republic)/ or Guatemala/ or Haiti/ or Honduras/ or Indonesia/ or Iraq/ or Democratic People's Republic of Korea/ or Laos/ or Liberia/ or Mauritania/ or Mongolia/ or Mozambique/ or Nicaragua/ or Panama/ or Papua New Guinea/ or Rwanda/ or Senegal/ or Sierra Leone/ or Somalia/ or Tajikistan/ or Tanzania/ or Uganda/
13	Relief Work/ or Disaster Planning/ or Starvation
14	11 or 12 or 13
15	((community adj3 care) or (home adj3 care) or (therapeutic\$ adj3 food\$) or (therapeutic\$ adj3 diet\$) or (enrich\$ adj3 food\$) or (enrich\$ adj3 diet\$) or therapy or management or feeding or fortified food\$ or Plumpy'nut or F-100 or F-75 or nutritional or rehabilitation or outpatient\$ or dietary intervention\$ or Ready-to-Use Therapeutic Food or RUTF).ti,ab.
16	Food, Fortified/ or Food Services/ or Community Health Services/ or Food, Formulated/ or Dietary Supplements/ or Outpatients/
17	15 or 16
18	10 and 14 and 17

GREY LITERATURE SEARCH

Action Against Hunger
Centre for Reviews and Dissemination (CRD)
Concern Worldwide
Coverage Monitoring Network
DFID R4D
ELDIS
Emergency Nutrition Network (ENN)
Enhancing Learning and Research for Humanitarian Assistance (ELRHA)
European Commission Humanitarian Aid and Civil Protection Department
EvidenceAid
Feinstein International Center and Friedman School of Nutrition Science and Policy, Tufts University
Food and Nutrition Bulletin
Free from Hunger
Global Alliance for Improved Nutrition
Harvard Humanitarian Initiative (HHI)
Health Technology Assessment Group
Helen Keller International
Humanitarian Policy Group (HPG)
Humanitarian Practice Network
Humanitarian Social Network
International Association of Professionals in Humanitarian Assistance and Protection (PHAP)
International Initiative for Impact Evaluation (3ie)
International Medical Corps
Médecins Sans Frontières (MSF)
Nutritional Causal Analysis
Overseas Development Institute (ODI)
Oxfam Policy Development and Evaluation Service
ReliefWeb
Save the Children
The CMAM Forum
The Network on Humanitarian Actions
The World Bank
UNICEF
USAID
Valid International
WHO Global Health Library
World Food Programme

APPENDIX 2: ASSESSMENT OF INCLUDED STUDIES

QUALITY ASSESSMENT OF INCLUDED QUANTITATIVE CASE CONTROL AND OBSERVATIONAL STUDIES AND GREY LITERATURE

Publication	Clearly focused issues	Recruitment acceptable	Exposure accurately measured	Outcomes accurately measured	Confounders identified	Follow-up long enough	Rates or proportions reported	Results precise	Results believable	Can results be applied?	Fits with other evidence	Provides implications for practice	Grade
Amthor et al. (2009)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	H
Chaiken et al. (2006)	Y	?	Y	?	N	?	Y	?	?	?	Y	Y	L
Collins and Sadler (2002)	Y	Y	Y	Y	N	Y	Y	Y	?	?	Y	Y	M
Deconinck (2004)	Y	?	?	N	N	N	N	?	?	?	N	Y	L
Gaboulaud et al. (2006)	Y	N	Y	?	N	?	Y	?	?	N	?	Y	L
Grellety et al. (2012)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	H
Linneman et al. (2007)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	H
Lagrone et al. (2010)	Y	Y	Y	Y	?	Y	Y	?	?	?	Y	Y	M
Lurquin (2003)	Y	?	N	N	N	N	Y	N	N	N	Y	N	L
Morgan et al. (2015)	Y	?	N	N	N	N	Y	N	N	N	Y	N	L
Querubin (2006)	Y	Y	N	N	N	N	Y	?	?	N	Y	N	L
Taylor (2002)	Y	?	?	N	N	N	Y	?	?	N	Y	N	L
UNICEF (2012)	Y	Y	?	?	N	?	Y	?	?	N	Y	Y	L
Walker (2004)	Y	?	?	?	N	?	Y	?	?	N	Y	N	L

Abbreviations and symbols: Y= Yes, N = No, ? = Not sure/unclear, H = High, M = Medium, L = Low

QUALITY ASSESSMENT OF INCLUDED QUANTITATIVE RCTS AND GREY LITERATURE

Publication	Clearly focused issues	Randomized	Patients/study personnel/health workers blinded	Groups similar at start of trial	Treated equally	Results precise	Can results be applied?	Clinically important outcome	Benefits worth harms/cost	Grade
Bahwere et al. (2014)	Y	Y	Y	Y	Y	Y	Y	Y	Y	H
Ciliberto et al. (2005)	Y	N	N	Y	Y	?	?	Y	Y	M
Huybregts et al. (2012)	Y	Y	N	Y	?	?	?	Y	Y	M
Isanaka et al. (2009)	Y	Y	N	Y	Y	?	?	Y	Y	M
Karakochuk et al. (2012)	Y	Y	N	Y	Y	Y	Y	?	Y	
Matilsky et al. (2009)	Y	Y	Y	Y	Y	Y	Y	Y	Y	H
Maust et al. (2015)	Y	Y	N	Y	Y	?	?	Y	Y	H
Oakley et al. (2010)	Y	Y	Y	Y	Y	Y	Y	Y	Y	M

Abbreviations and symbols: Y = Yes, N = No, ? = Not sure/unclear, H = High, M = Medium, L = Low

QUALITY ASSESSMENT OF INCLUDED QUALITATIVE STUDIES AND GREY LITERATURE

Publication	Clear statement of aims	Qualitative methodology appropriate	Appropriate research design	Appropriate recruitment strategy	Appropriate data collection	Relationship between researcher and participants	Ethical issues considered	Data analysis rigorous	Findings clear	Value of research	Grade
Belachew and Nekatibeb (2007)	Y	Y	Y	?	Y	?	?	?	Y	?	M
Flax et al. (2009)	Y	?	?	?	Y	?	Y	Y	?	Y	M

Abbreviations and symbols: Y = Yes, N = No, ? = Not sure/Unclear, H = High, M = Medium, L = Low

APPENDIX 3: INCLUDED PUBLICATIONS – REPORTED RESULTS

CHARACTERISTICS OF INCLUDED MIXED METHODS AND OBSERVATIONAL COHORT STUDIES

Author/year	Country/study population	Study design	Description of intervention	Main findings
Belachew and Nekatibeb (2007) (journal article)	Ethiopia, children 6–59 months old with SAM (n=355) plus 36 key informants and 30 focus groups	Mixed methods study	The intervention was community-based management of children with SAM using RUTF in three districts. All children received RUTF and were followed weekly until recovery, death or default. Duration of project was 5–13 weeks.	The proportion of children who achieved the recovery target (33 percent) at the end of 13 weeks was low; 44 percent defaulted and 0.8 percent died.
Flax et al. (2009) (journal article)	Malawi	Mixed methods study	This research studied attitudes of 504 Malawian mothers to LNS and CSB via exit interviews completed at the end of three 12-week clinical trials, and compared differences between the groups.	Both supplements were said to be highly acceptable, children learned to eat them within two weeks, and mothers were willing to use them again.
Amthor et al. (2009) (journal article)	Malawi, children 6–60 months old with SAM (n=826)	Observational cohort study	Each child received 200kcal of RUTF. The children were followed weekly until recovery, default or death. Total duration of treatment was eight weeks or earlier if they met the discharge criteria (attainment of WHZ >100 percent).	The proportion of children who recovered was 93.7 percent, and 1.8 percent remained malnourished. Default and death rates were 3.6 percent and 0.9 percent respectively. Mean ($\pm$ SD) rate of weight gain was 2.7 ± 3.7 g/kg/d. The proportion of severe malnutrition before and after was significantly less ($p < 0.001$).
Chaiken et al. (2006) (journal article)	Ethiopia, children 6–59 months old with SAM (n=5,799)	Observational cohort study	All children received a daily dose of 200kcal/kg/d RUTF per their body weight. They were monitored weekly till eight weeks or discharge if early recovery, or death. In addition CSBs were provided to minimize sharing and as a supplement to RUTF at home.	An 87 percent recovery rate was reported; 2.3 percent defaulted and fewer than 1 percent died. Under-five mortality and SAM before the intervention were 1.47/10,000 and 1.0 percent; after the intervention these rates improved to 0.45/10,000 and 0.6 percent (95 percent CI, 0.2–0.9).
Collins and Sadler (2002) (journal article)	Ethiopia, children 6–120 months old with SAM (n=170)	Observational cohort study	WHO endorsed interventions to manage SAM: a daily dose of RUTFs, providing 733kJ/kg/d per body weight. Followed up until recovery or death or default. At home, Famix + RUTF given in addition to Vitamin A (100,000 IU for children <12 months and 200,000 IU if older) plus 5mg folic acid fortnightly.	Eighty-five percent recovered, 4 percent died and the default rate was 5 percent. Median rate of weight gain was 3.2g/kg/d (95 percent CI, 1.9–5.6).
Gaboulaud et al. (2006) (journal article)	Niger, children 6–59 months old with SAM (n=1,937)	Observational cohort study	A total of 660 children from the three cohorts received care exclusively in hospital (inpatient care). 937 children were initially treated at TFCs and then completed treatment at home, and 340 children were exclusively treated at home.	Defaults from treatment were reportedly high: 28.1 percent, 16.8 percent and 5.6 percent respectively for TFC only, TFC + home and home only. The overall case fatality for the entire programme was 6.8 percent. Case fatality rates were higher in TFC only (18.9 percent) compared with TFC + home (1.7 percent) and home only (0 percent).

Author/year	Country/study population	Study design	Description of intervention	Main findings
Grellety et al. (2012) (journal article)	Niger, children 6–23 months old with MAM (n=2,238)	Observational cohort study	Children were registered in the programme to receive monthly distributions of RUSF (Plumpy'Doz).	The absolute rate of wasting was 4.71 events per child-year in the intervention group and 4.98 events per child-year in the comparison group. The intervention group had a small but higher weight-for-length Z-score gain (-0.2z vs. -0.3z) and less loss of MUAC than the comparison group (-2.8 vs. -4.0mm). Mortality was lower for children whose households received the intervention than those who did not (adjusted HR 0.55, 95 percent CI, 0.32–0.98).
Lagrone et al. (2010) (journal article)	Malawi, children 6–59 months old with MAM (n=2,417)	Observational cohort study	Each child received 65kcal/kg/d of locally produced soy/peanut RUSF. Anthropometry measurements were taken every two weeks and additional RUSFs were distributed at this time if the child remained wasted. Study duration: eight weeks.	RUTF (milk-peanut and soy-peanut fortified spread (FS)) resulted in greater weight than CSB (p = 0.01). Children who received either milk-peanut FS or soy-peanut FS also gained weight faster than children receiving CSB. Eight percent of children developed oedema.
Linneman et al. (2007) (journal article)	Malawi, children 6–60 months old with SAM (n=2,131) and MAM (n=806)	Observational cohort study	Outcomes of severely malnourished children were compared with a moderately malnourished group (control). Each child received a daily dose of RUTF, providing 733kJ/kg/d energy, and was monitored for eight weeks or until early recovery or death.	Recovery rate in the severely malnourished group was 89 percent vs. 85 percent in the moderately malnourished group. The death rate for severely malnourished children was 1 percent vs. 2 percent for the moderately malnourished (p < 0.01). RWG was 3.5 ± 4.1 (severe) vs. 4.6 ± 4.1 (moderate) g/kg/day. Default rate in the severely malnourished group was 7 percent vs. 8 percent in the moderately malnourished group.

CHARACTERISTICS OF INCLUDED GREY LITERATURE PROGRAMME EVALUATION REPORTS

Author/year	Country/study population	Study design	Description of intervention	Main findings
Deconinck (2004) (grey literature)	Ethiopia, children 6–59 months old with SAM (n=1,470) and MAM (n=5,558)	Programme evaluation report	Children enrolled with SAM received RUTF. Children enrolled with MAM received supplementary foods in line with WHO recommendations.	Programme treating SAM achieved 86.6 percent recovery rate. Defaulting and mortality rates were 4 percent and 0.6 percent respectively. Outcomes for children treated for MAM were not reported.
Lurqin (2003) (grey literature)	Afghanistan, children 6–59 months old with SAM (n=635)	Programme evaluation report	Each SAM child was provided with an average of 200kcal of RUTF – Plumpy'Nut and BP100, supplied weekly. They were monitored until recovery, death or default or discharge at the end of the programme.	Proportions of children who died in the programme or defaulted were 6 percent and 23 percent respectively. The proportion that achieved nutritional recovery was not reported. The rate of weight gain reported was 6.1g/kg/day.
Morgan et al. (2015) (grey literature)	Angola, children 6–59 months old with SAM (n=23,865) and MAM (n=53,229)	Programme evaluation report	Children were treated based on WHO guidelines. Children with SAM received RUTF based on their body weight. Children with MAM received RUSF each day.	The programme had a high cure rate. The SAM cure rate was 93.8 percent, and the MAM cure rate 96.7 percent. Mortality and default rates were 4.8 percent and 1.0 percent respectively for SAM, and 2.9 percent and 0.2 percent respectively for MAM.
Querubin (2006) (grey literature)	Sudan, children 6–59 months old with SAM	Programme evaluation report	Children received systematic medical treatment, plus F-75 therapeutic milk, which provided 135ml/kg body weight/day in Phase 1. In Phase 2, children received F-100 therapeutic milk, which provided 200kcal/kg/day, plus porridge. Duration of treatment: four weeks.	Average recovery rate reported was 81 percent. Average weight gain was 9g/kg/day. Overall defaulting from TFC was low at 12 percent.
Taylor (2002) (grey literature)	Sudan, children 6–59 months old with SAM (n=836) and MAM (n=24,000)	Programme evaluation report	SAM cases with medical complication were first treated in hospital stabilization centres using F-75 plus medication. They were transferred to outpatient care and received RUTF when complications were resolved. Children enrolled with MAM received RUSF.	Recovery rate for children treated for SAM was 81.4 percent. The proportions of children who died while on treatment and those who defaulted from treatment were 2.9 percent and 10.1 percent respectively. Readmission rate or relapse was 1.0 percent. Supplementary feeding outcomes were not reported.
UNICEF (2012) (grey literature)	Kenya, children 6–59 months old with SAM (n=18,509) and MAM (n=79,183)	Programme evaluation report	Children received standard treatment: 1) F-75 and F-100 at inpatient care, and RUTF at outpatient care for those admitted with SAM, and 2) supplementary foods endorsed by WHO for the treatment of MAM.	The high default rates were explained partly by weak household follow-up, whereas the greater length of stay was often due to social pressures from parents and community members who wanted children to benefit from RUTF for as long as possible. Inadequate tracking of weight gain was an additional reason. Inpatient treatment of SAM achieved a recovery rate of 84.6 percent, a death rate of 8.7 percent, a default rate of 1.4 percent and an overall relapse rate of 6.1 percent. Outpatient treatment of SAM achieved an 80.7 percent recovery rate, 1.5 percent death rate and 13 percent default rate in two districts sampled. Default rates were high in Kisumu district (17.3 percent) and Nairobi district (19.3 percent). The average relapse rate was low (3.2 percent). Interventions delivered to manage MAM achieved an 80.5 percent recovery rate, 0.4 percent death rate and 14.5 percent default rate. Relapse was not reported for MAM.
Walker (2004) (grey literature)	Sudan, children 6–59 months old with SAM (n=726)	Programme evaluation report	The children were treated in line with WHO recommendations. Children with medical conditions were treated at hospital stabilization centres while children with no such complications were admitted directly into outpatient treatment programmes.	Stabilization centre management of SAM achieved 93.5 percent recovery, 2.6 percent mortality and 0 percent default rates. In the outpatient programme phase, the proportions of children who recovered, died and defaulted were 81.8 percent, 3.1 percent and 15 percent respectively.

CHARACTERISTICS OF INCLUDED RANDOMIZED CONTROLLED TRIALS

Author/year	Country/study population	Study design	Description of intervention	Main findings
Bahwere et al. (2014) (journal article)	Malawi, children 6–59 months old with SAM (n=600)	Randomized controlled trial	The children were evenly randomized to either WPC-RUTF (n=292 in intervention group) or P-RUTF (n=308 in an active control group). The children in both groups were treated according to Malawian national guidelines for the management of SAM. Children with medical complications were referred to hospital stabilization centres for inpatient care, and were only eligible when they were referred back.	The proportions of children who recovered, died and/or defaulted in the intervention group (WPC-RUTF) were 84.8 percent, 1.6 percent and 12.2 percent respectively. For children in the controlled treatment group (P-RUTF) the recovery, mortality and default rates were 84.2 percent, 0.7 percent and 12.2 percent respectively. The average rate of weight gain was low at 3.1g/kg/d; 4g/kg/day (in the intervention group) and 2.9 g/kg/day (in the control group).
Ciliberto et al. (2005) (journal article)	Malawi, children 6–59 months old with SAM (n=1,178)	Randomized controlled trial	The children were systematically allocated to either standard treatment (n=186) or home-based therapy with RUTF (n=992).	The average recovery rate was 83 percent, the death rate was 5 percent and drop-out was 4 percent. The children who received home-based therapy with RUTF were more likely to achieve a WHZ > -2 than those who received standard therapy (93 percent recovery rate compared with 46 percent; $p < 0.001$). The overall relapse rate was 8.2 percent. Children in the RUTF group were also less likely to relapse (3.5 compared with 2.0g/kg/d).
Huybregts et al. (2012) (journal article)	Chad, children 6–36 months with MAM (n=1,038)	Randomized controlled trial	Intervention group received a monthly quantity of RUSF (Plumpy'Doz), representing a daily dose of 46g (~247kcal/d). All participating care-givers in both groups received a monthly food package. Study duration: four months.	Adding RUSF to a package of monthly household food rations for households containing a child assigned to the intervention group did not result in a reduction in cumulative incidence of wasting (incidence risk ratio: 0.86; 95 percent CI: 0.67, 1.11; $p = 0.25$). However, the intervention group had a modestly higher gain in height-for-age (+0.03 Z-score/mo; 95 percent CI: 0.01, 0.04; $p < 0.001$).
Isanaka et al. (2009) (journal article)	Niger, children 6–60 months old with MAM (n=3,533)	Randomized controlled trial	One packet per day of RUTF (Plumpy'Nut) versus no intervention.	Reduction in wasting and severe wasting; impact greater during the period of documented food shortage; no effect on mortality.
Karakochuk et al. (2012) (journal article)	Ethiopia, children 6–60 months old with MAM (n=1,125)	Randomized controlled trial	Children were randomly assigned to one of two foods. Children received CSB or RUSF bi-weekly. Study duration: 16 weeks.	The recovery rate was higher in the RUSF group (73 percent) than in the CSB group (67 percent), but no significant difference was found ($p = 0.056$). The overall HR for CSB was 0.85 (95 percent CI, 0.73–0.99), which indicates that the CSB group had a 15 percent lower overall recovery rate ($p = 0.039$). Defaulting and death rates were low and non-response rates were high. Neither group met the Sphere standards for recovery.
Matilsky et al. (2009) (journal article)	Malawi, children 6–60 months old with MAM (n=1,326)	Randomized controlled trial	Children were assigned to one of three diets: A) milk/peanut FS, B) soy/peanut FS (RUTF) and C) corn/soy blends (CSBs). They were assessed weekly until recovery or for the eight-week duration of the programme.	Each RUSF (milk-peanut and soy-peanut FS) resulted in greater weight gain than CSB ($p = 0.01$). Children who received either milk-peanut FS or soy-peanut FS gained weight faster than children receiving CSB. Eight percent of children developed oedema.

Author/year	Country/study population	Study design	Description of intervention	Main findings
Maust et al. (2015) (journal article)	Sierra Leone, children 6–59 months old with SAM (n=857) and MAM (n=1,100)	Randomized controlled trial	Children were assigned to two treatment groups: 1) integrated management of MAM and SAM; 2) standard management of MAM and SAM. In 1) children with SAM received RUTF plus amoxicillin at 175 kcal/kg/d, while children with MAM received only RUTF at 175 kcal/kg/d. In 2) SAM children received RUTF (120kcal/kg/d) plus medication, while MAM children received FBFs. Care-givers received nutrition information to prevent malnutrition. SAM follow-up was weekly until recovery or end of intervention. MAM follow-up was every 14 days. There was no limit to the duration of the intervention.	Average recovery rate in the integrated management group (including MAM and SAM children) was 83 percent compared with 79 percent. Proportions of children who died while receiving treatment were 4 percent for both integrated management and standard management groups. The default rate was 8 percent for both groups. Rates of weight gain during the first four weeks of treatment were $3.0 \pm 0.2\text{g/kg/d}$ and $3.8 \pm 0.2\text{g/kg/d}$.
Oakley et al. (2010) (journal article)	Malawi, children 6–59 months old with SAM (n=1,874)	Randomized controlled trial	Random allocation of children to receive two locally produced RUTFs, one containing 25 percent milk (n=945) and the other containing 10 percent milk (n=929). The children were followed until the end of the project (eight weeks) or early recovery, death or default.	The recovery rate among children receiving 25 percent milk RUTF was greater than for children receiving 10 percent milk RUTF, starting from 64 percent compared with 57 percent after four weeks, and 85 percent compared with 81 percent after eight weeks ($p < 0.18$). Children receiving 25 percent milk RUTF also had a higher rate of weight gain ($2.4 \pm 2.8\text{g/kg/day}$) compared with those receiving 10 percent milk RUTF ($1.9 \pm 2.7\text{g/kg/day}$) ($p < 0.001$).

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Published by Oxfam GB under ISBN 978-0-85598-914-9 in March 2017. DOI: 10.21201/2017.9149.
Oxfam GB, Oxfam House, John Smith Drive, Cowley, Oxford, OX4 2JY, UK.

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