1 Introduction

In this chapter acute malnutrition and nutritional products used for treatment are introduced, and the thesis objectives are presented.

Childhood malnutrition continues to be a major global health problem, and nearly half of all deaths in children less than five years are attributable to the condition (1). The term malnutrition by definition includes over-nutrition (obesity), however, for the purposes of this thesis this meaning is disregarded. Malnutrition encompasses deficiencies in micronutrients, chronic malnutrition (stunting, where children are too short) and acute malnutrition (wasting, where children are too thin). The different types of malnutrition can co-exist in the same child. Prevention and treatment play key roles towards the aim to end all forms of malnutrition by 2030 as stipulated by the United Nations (UN) as part of the new sustainable development goals (2).

The diagnosis of acute malnutrition is based on anthropometric and clinical assessment and is a continuum condition classified by severity into severe acute malnutrition (SAM) or moderate acute malnutrition (MAM) and is associated with around 13 % of all under-five child mortality accounting for 800,000 deaths annually (3). Children with SAM have a nine time higher risk of death and children with MAM a three time higher risk of death compared to well-nourished children (4). Estimates suggest that a total of 52 million children less than five years suffer from acute malnutrition with 2/3 of these suffering from MAM (3). For several reasons, this is an underestimation of the true burden: most importantly, estimates include wasted children and not children diagnosed by mid-upper arm circumference (MUAC), an omission repeated in various sources on malnutrition data (5,6). Moreover, estimates are based on prevalence, while the burden of acute conditions like acute malnutrition would be more appropriately reported with incidence figures accumulating episodes over a period of 12 months (7).

Children with SAM and MAM are currently treated separately with different food products and following different treatment guidelines. In SAM the nutritional support is well defined and diagnostic criteria are clear and endorsed by the World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNICEF) (8). Children with SAM are treated with nutritional products designed to completely replace the family diet. If accompanied by lack of appetite and medical complications children with SAM are managed as in-patients and treated initially with specially designed therapeutic milk products (i.e. F-75/F-100). Moreover, the development of ready-to-use therapeutic foods (RUTF) has made large-

scale community-based care of uncomplicated SAM possible, and specific recommendations for the nutritional composition of RUTF have been established in a United Nations (UN) joint statement (9). Nevertheless, while relative consensus exists on the overall SAM management, challenges remain in particular with regards to the medical treatment of children with complicated SAM (10). Additionally, the nutritional rehabilitation may also be further improved (11).

There has been less focus on MAM than on SAM, which is somewhat a paradox as management of children with MAM is fundamental both as a curative strategy and as a preventative strategy to halt deterioration into SAM (12). Treating acute malnutrition at an early stage, i.e. at the stage of MAM, is less costly per child and reduces morbidity and mortality. Nevertheless, key areas of management of children with MAM are not sustained by evidence and subject to ongoing debate.

The nutritional rehabilitation of children with MAM is based on a principle of improving the family diet through supplementation with fortified foods (13). These supplements, given in outpatient programs, belong to a matrix of corn-soy blend (CSB) or lipid-based nutrients (LNS). The current evidence base in supplement effectiveness is limited in particular in terms of soy quality and addition of dairy protein, and WHO recommends research to inform policy (14). Improved quality of soy with reduced levels of anti-nutrients and the addition of milk protein is believed to increase supplement effectiveness. Given the large number of children with MAM the cost-effectiveness of key factors must also be considered.

Mortality is an important outcome and therapeutic foods currently used for children with SAM have successfully proved to reduce mortality. However, in trials for children with MAM the mortality is often too low to be a meaningful outcome on supplement effectiveness. Currently, effectiveness outcomes in trials for children with MAM are based on standard anthropometric traits i.e. weight gain and derived measures of nutritional recovery. However, weight gain alone contains limited information and better outcomes based on body composition that discriminates between fat and fat-free tissue accretion have been proposed (15). Although, not backed by evidence nor put formally in writing there has been a concern that LNS supplements, with a their high content of fat, would lead to excessive fat deposition in the child.

The diagnosis of MAM is still not formally endorsed in the UN system. Based on expert opinion and humanitarian practice several malnutrition programs in Central and West Africa use a length cutoff when deciding which children are admitted for treatment by MUAC only. Apparently, short children with low MUAC are suspected to be either less than 6 months of age or stunted rather than acutely malnourished and therefore suspected not to have the rapid catch-up growth found in wasted children. A secondary concern is that short children may be harmed by prolonged treatment of supplements in particular with

LNS with excessive fat gain. At a UN technical consultation on MAM in 2010, a consensus statement recommended that more research was needed to identify the appropriate admission and discharge criteria based on MUAC for children <67 cm and ≥6 months of age (16) .

1.1 Objectives of PhD thesis

The overall objective of this thesis is to contribute to the evidence base for treatment of children with MAM.

Specific objectives include:

- To resolve methodological issues in assessment of body composition determined by stable isotope dilution technique in MAM (**Paper I**).

- To assess the effectiveness of key factors in supplementary foods in terms of body composition and anthropometry in MAM (**Paper II**).

- To assess short body length as exclusion criterion for supplementary feeding in MAM (**Paper III**).