Technical Briefing Paper

The relationship between wasting and stunting, policy, programming and research implications

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Emergency Nutrition Network

USAID FROM THE AMERICAN PEOPLE

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About the ENN

The ENN enables nutrition networking and learning to build the evidence base for nutrition programming. Our focus is communities in crisis and where undernutrition is a chronic problem. Our work is guided by what practitioners need to work effectively.

- We capture and exchange experiences of practitioners through our publications and online forum
- We undertake research and reviews where evidence is weak
- We broker technical discussion where agreement is lacking
- We support global level leadership and stewardship.

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Contents

M Myatt, Ethiopia, 2007

Introduction

This paper is a narrative review of the available literature on the relationship between wasting and stunting. It was born out of previous work carried out by the ENN which illustrated the divide at programme, policy and financing level between wasting and stunting. This divide ultimately has profound implications for how children worldwide receive nutrition interventions and services and, may well contribute to the lack of nutritional impact seen in programmes only addressing one part of the undernutrition problem. Gaining a clearer and common understanding of the relationship between wasting and stunting has the potential to help governments and supporting organisations to better justify, design and evaluate programmes to improve childhood nutrition. This paper aims to contribute to that clearer and common understanding.

A draft version of this paper was produced in advance of a TIG meeting held in London on February 27th 2014. The discussions and conclusions of that meeting along with resources and comments provided by members of the TIG were used to revise and finalise this document.

This paper is organised into seven sections. Section 1 provides the background to why this reviews was undertaken. Section 2 describes the methods for the review, Section 3 explores the evidence of shared causes and effects, Section 4 examines the patterns of association, evidence from cross sectional and longitudinal studies, and the role of catch-up growth. The physiological mechanisms that may link these two manifestations of undernutrition are explored in Section 5 and in Sections 6 and 7, the conclusions and programme and policy implications are outlined.

Anne Yzebe, Niger, 2005

1 Background

Childhood wasting and stunting affect large numbers of children globally (see Box 1). Both are important risk factors for illness and death yet, despite the fact that these conditions share common risk factors and are often seen in the same child, they are commonly portrayed as relatively distinct manifestations of undernutrition. Nutrition researchers have tended to focus on one form of undernutrition, or the other. This is apparent in both the 2008 and 2013 Lancet series on maternal and child undernutrition where wasting and stunting are presented as distinct problems, contributing separately to mortality and the burden of disease (see Box 1) and where interventions were assessed in terms of efficacy to address one or the other problem only (Martorell and Young 2012, Guesdon, Aissa et al. 2013). Equally, some practitioner communities tend to focus on prevention of stunting while others focus on the recuperative treatment of wasting.

This 'divide' in interests can in turn lead to a separation in policies and programming. For example humanitarian policy and practice focusses on wasting targets (Sphere 2011), the Millennium Development Goal's (MDGs) set underweight targets (a combination of wasting and stunting) and the World Health Assembly (WHA) Global Targets for 2025 include separate targets for both wasting and stunting linked to separate policy actions and frameworks (de Onis, Dewey et al. 2013). There is little understanding of how interventions need to consider and capitalise on the overlap of these manifestations of undernutrition (Menon and Stoltzfus 2012).

While much has been written about the causes and effects of stunting and of wasting in general, the relationship and associations between wasting and stunting remain poorly understood. Little is known about how one may predispose to the other, or the pathways which modulate a child experiencing one or the other, or simultaneously both, as a child grows older (ibid).

There is broad agreement that both wasting and stunting are the result of multifaceted processes in which the body responds to particular factors/ circumstances, at the individual and societal level, to which it is exposed. The process is mediated via a complex web of interactions at the molecular and microbiological level of the individual, the cultural and socioeconomic features of societies (Heikens, Amadi et al. 2008) and the physical environment. In this paper we aim to summarise the current evidence for associations between wasting and stunting, and explore the potential convergence of these multifaceted processes and factors from which they result.

A recognition of the negative implications of the current separation between wasting and stunting led to the holding of a symposium by the American Society for Nutrition in 2012 'Building

Convergence in Science, Programs, and Policy Actions on Child Undernutrition', to review and debate the issue. The background reviews conducted for this symposium have been used to inform this paper.

In 2013, the "Promoting healthy growth and preventing childhood stunting" project linked to the WHA targets for stunting reduction, commissioned nine papers for a supplement in the Maternal and Child Nutrition Journal. One paper (Stewart, Iannotti et al. 2013) mentioned the potential consequences of wasting on linear growth[2], particularly in situations where there is insufficient food availability to promote recovery after an episode of infection. No recommendations were, however, linked to this finding.

The separation between wasting and stunting is also reflected in the humanitarian and development architecture, with wasting programmes still largely funded and implemented under the 'humanitarian' remit, while stunting resides under 'development'. A recent ENN study into the financing arrangements for scaling up Community-based Management of Acute Malnutrition (CMAM), found wasting to be commonly viewed as a short term emergency problem, and stunting as a chronic development problem. The review found very little convergence in policy, financing or programmatic thinking about the possible relationship between these two manifestations of undernutrition (Shoham, Dolan et al. 2013). The findings from this review provided the conceptual basis for the ENN USAID/OFDA grant to carry out the review of the links between wasting and stunting which culminated in the production of this paper.

Box 1 Global burden of wasting and stunting

Current global estimates are that there are:

- 165 million stunted children under-five years of age at any given point in time (26%), more than 90% of which live in Africa and Asia.
- 52 million wasted children under-five years of age at any given point in time (8%), more than 70% of which live in Asia..
- There are no global estimates of the number of children both stunted and wasted con currently

(UNICEF, WHO et al. 2012)

It is important to note that these estimates are based on the prevalence of wasting and stunting at a point in time during the year. Particularly for wasting, which has a relatively shorter duration than stunting and is also highly variable seasonally, these figures may miss a relatively large proportion of incident wasting cases occurring over time and, depending on the timing of the survey on which they are based, seasonal peaks may also be missed. This means that the current global estimates underestimate the actual annual wasting burden.

[2] Growth in length or height

Hailu Sitotaw, Ethiopia, 2010

2 Methods

The search for articles was conducted on PubMed using the terms 'stunting', 'wasting', 'association', 'seasonal', 'catch-up growth', 'SGA and growth'. Additional articles were sourced by review of reference lists and contributed to by members of the TIG. This paper represents a short narrative review of available published material only. Sections (in particular section 5.) are drawn from a paper lead authored by André Briend on the subject which in particular, explores the roles of fat and muscle mass in defining the relationship between wasting and stunting. The Briend paper (co-authored by Tanya Khara and Carmel Dolan) was produced for the 'International Symposium on Understanding Moderate Malnutrition in Children for Effective Interventions' in Vienna, Austria in May 2014.

Two additional analyses on existing datasets were conducted to inform this paper. The first analysis was conducted in order to investigate the question arising from discussions amongst the TIG, of whether Mid-upper Arm Circumference (MUAC) identifies stunting (as well as wasting) in children. This analysis was conducted on a database of 560 cluster nutrition survey datasets from a range of countries in Africa and Asia. The correlations (Pearson's correlation coefficients) between MUAC and wasting (defined by low weight-for-height z-score) and between MUAC and stunting (defined by height-for-age z-score) were investigated for children aged 6-59 months without oedema at the individual level (using paired complete observations only). Relative risks of being classified as wasted or stunted according to category of MUAC (moderately low, severely low) were also calculated and chi-squared test of significance applied. The results are presented in Box 5.

The second analysis was conducted in order to investigate the question arising from the review of the literature and discussions amongst the TIG, of whether wasting treatment supports a restarting or acceleration of linear growth. This analysis was conducted by Paluku Bahwere (Valid International) on existing cohort data from research studies investigating the effects of CMAM treatment on children with SAM, including how they grow after discharge. The height data from 593 children receiving treatment for SAM in CMAM programmes (supported by the Ministry of Health and Concern Worldwide) in Dowa District of Malawi (2002-2004) and 133 children with SAM admitted into the standard RUTF arm of an alternative RUTF trial conducted by Valid International in DRC (2013) was analysed. Both cohorts were analysed separately to see if there was any improvement in height-for-age zscores either during or after SAM treatment. The results are presented in Box 7.

ACF, Peru, 2010

3 Wasting and stunting evidence of shared causes and effects

3.1 Clarifying terms

Before discussing the associations between wasting and stunting it is important to define and clarify terms and some of the issues involved in their use. In general, there is a common assumption that wasting is synonymous with acute malnutrition (i.e. occurring acutely over a short period) and stunting with chronic malnutrition (occurring over a longer period); although what constitutes 'short' and 'long' is rarely defined. It should be noted here that in this paper we do not deal with nutrition oedema (or Kwashiorkor) which is classified as a severe form of acute malnutrition. The causality of nutritional oedema and its relationship with both wasting and stunting is also the subject of various research projects and is an area where many questions are unanswered. However this was felt to be a large area beyond the scope of this review.

Linear growth retardation is generally considered to reflect long-term exposure to nutritional stresses, including an inadequate diet and a high burden of infections, from which catch-up growth is insufficient (Allen 1994), that takes time to develop and is completely reversed only by a change in the conditions in which the child is living (Golden 1994, Martorell, Khan et al. 1994).

Wasting on the other hand is commonly viewed as developing over a short period and reversible with short term intervention.

This assertion is partly supported by a recent re-analysis of 8 longitudinal studies (from Africa, Asia and Latin America) with anthropometric measures made at 3, 6, 9 and 12 months in which nearly 80% of the children identified as stunted at 3, 6, or 9 months were still stunted at 12 months, whereas 70% of the children with wasting at 3, 6, or 9 months were not wasted at 12 months of age. (Richard, Black et al. 2012). However, work investigating the duration of wasting (Garenne, Willie et al. 2009, Isanaka, Grais et al. 2011) indicates that the average duration of untreated severe wasting may be between 1.5 and 7.5 months, depending on context. In all these studies there is a large range of experiences, with some children exposed to short episodes of wasting from which they quickly recover, to those experiencing much longer periods spanning a number of months. Similarly, repeated (e.g. seasonal) bouts of wasting occurring year after year should not be viewed as a short term issue.

A number of intervention trials of mass distribution with lipid based nutrient supplements (LNS) aimed

at addressing seasonal peaks in wasting and stunting have found modest gains in height-for-age as well as weight-for-height with short term (3-6 months) interventions (Isanaka, Nombela et al. 2009, Isanaka, Roederer et al. 2010, Huybregts, Houngbé et al. 2012). In addition, as will be shown below, a child may undergo a period of stunting or cessation of linear growth whilst wasted, which is rapidly caught up as they recover without ever reaching the category of 'stunted'. In conclusion it is important, if using the terms 'acute' and 'chronic' malnutrition to describe wasting and stunting, to do so with awareness of their limitations.

Other issues around terms and definitions relevant for the below discussion are covered in Box 2 below.

Box 2 Considering the use of terms

Wasted and Stunted

The terms wasted and stunted were introduced in the early 70's by John Waterlow to differentiate among underweight children; those who had a low weight in relation to their height (wasted), from those who were small for their age (stunted) (Waterlow 1972). The terms were therefore, at their inception, used to classify children by comparing them to a derived anthropometric reference standard rather than to any biological or physiological function or condition. However, one of the aims of the definition was to allow practitioners to identify those children in need of immediate treatment due to a heightened risk of mortality (wasted children)(Waterlow 1974). Since 2006 the standards used for this comparison have been the WHO growth standards derived from the growth of optimally breastfed children living in 'healthy environments' (WHO 2006). A wasted child is commonly defined as one who has fallen beneath -2SD of the WHO growth standard population weight-for-height. A stunted child is commonly defined as one who has fallen beneath or is growing beneath -2 SD of the WHO growth standard population height-for-age. Waterlow also recognised that 'in practice, in a great many undernourished children both processes will be at work' (Waterlow 1973, McDonald, Olofin et al. 2013) and that in his clinical experience children both stunted and wasted were at particular risk (Waterlow 1974).

Low MUAC

As a result of evidence that it identifies children at high risk of death, and its appropriateness for use in large scale decentralised services, mid-upper arm circumference (MUAC) has gained in importance for referal and admission to therapeutic feeding over the last 10 yrs (see Box 4).

Wasting and Stunting

The terms wasting and stunting differ from the above in that they refer specifically to a process rather than a category, despite often being used interchangeably. Stunting is a slowing or halting of linear growth – or 'linear growth faltering'. This is commonly identified by a child falling off the standard growth trajectory described by the WHO growth standards. Wasting is a reduction or loss of body weight (or ponderal growth) in relation to height. This is commonly identified by a loss of weight in relation to height and therefore a fall in the weight-for-height index.

Underweight

This is a term used to describe children who are low weight in relation to their age (low weight-for-age) when compared to the WHO standard population. As a child can have a low weight-for-age because they are short, thin or a bit of both this is a composite indicator for stunting and wasting. It has gone out of fashion with the separation of stunting and wasting programming but is still widely used for monitoring growth and remains a useful indicator for easily detecting linear and/or ponderal growth faltering.

3.2 Mortality risks and measures

The increased risks of death and disease associated individually with wasting and stunting have been widely investigated and documented (Collins 2007, Black, Allen et al. 2008, McDonald, Olofin et al. 2013). Both wasting and stunting are associated with increased risk of mortality with even mild deficits being associated with higher risk of dying and increasing progressively with the degree of the deficit. This means that any child experiencing a degree of wasting or stunting in any context is at heightened risk of dying. Wasting conveys double the risk of mortality conveyed by stunting and being both stunted and wasted an even higher risk (see Box 3). The biological mechanisms behind this pattern of increased mortality are discussed in section 5.

'Children with multiple deficits are at a heightened risk of mortality and may benefit most from nutrition and other child survival interventions'. (McDonald, Olofin et al. 2013),

The higher mortality risks related to wasting compared to stunting illustrated in box 3 are well known. However the significantly higher mortality risk of severe stunting compared to moderate wasting is notable. It does not appear to have been a particular focus of attention globally to date.

The above finding on greatly heightened mortality risk with multiple anthropometric deficits is particularly interesting in light of the available evidence on low MUAC. MUAC is widely used for the identification of children to receive treatment for acute malnutrition and has been shown to be the anthropometric measure most closely predictive of mortality in children under 5 years of age (Myatt, Khara et al. 2006) and associated with wasting (see Box 4).

Muscle arm indices, derived from MUAC and triceps skinfold thickness have also been found to be related to height-for-age (Frisancho and Garn

Box 3 Mortality risks multiply when both wasting and stunting are experienced concurrently

In 2008 The Lancet 'maternal and child nutrition' series authors estimated that a moderately wasted child was 3 times, and a severely wasted child 9.4 times more likely to die than the non-wasted child. They also estimated that a moderately stunted child was 1.6 times, and the severely stunted child 4.1 times more likely to die than the non-stunted child.

This mortality analysis has been recently updated and elaborated using a pooled analysis of 10 prospective studies (>53,000 children) from Africa, Asia and Latin America (Olofin, McDonald et al. 2013). This analysis using hazard ratios in comparison to a reference of ≥-1 z score of standard, found similar results:

Severely wasted - 11.6 times more likely to die (9.8-13.8)*
Moderately wasted - 3.4 times more likely to die (2.9-4.0)

Severely stunted - 5.5 times more likely to die (4.6-6.5)
Moderately stunted - 2.3 times more likely to die (1.9-2.7)

This analysis went on to investigate the hazard ratio associated with multiple anthropometric deficits finding that the child who is both stunted and wasted (even moderately) has the highest hazard of death, see below. Even higher than for severe wasting individually (McDonald, Olofin et al. 2013).

Wasted and stunted – 12.3 times more likely to die (7.7-19.6)

*95% Confidence interval

Box 4 Mortality risks and MUAC

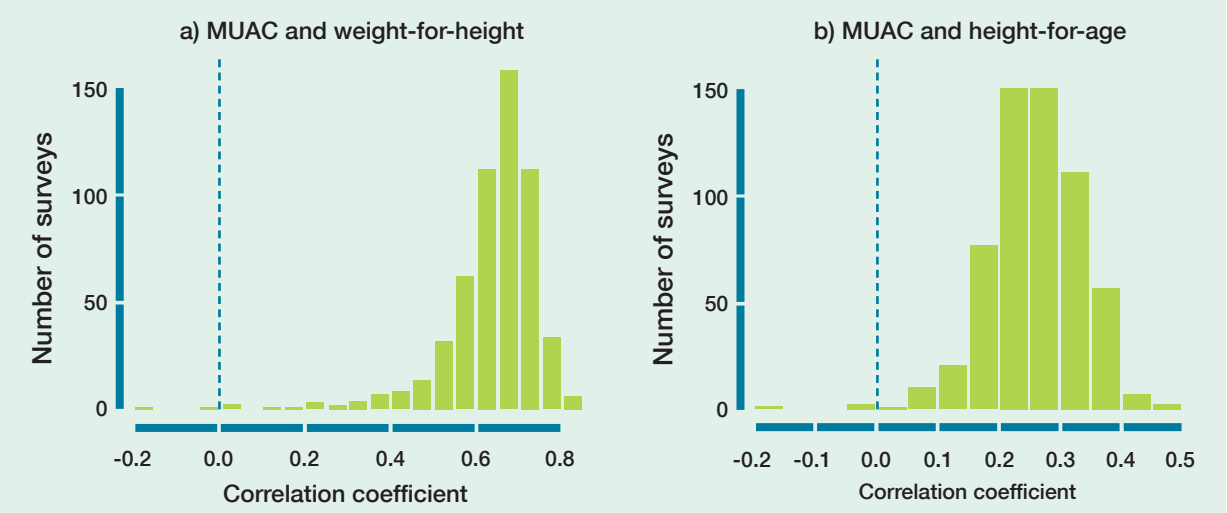
Prior to Waterlow's work on definitions, growth failure, along with body disproportion, had been identified as characteristic of what was then termed protein calorie malnutrition (PCM) in particular for the severe syndromes of Marasmus and Kwashiorkor. In 1969 Jelliffe and Jelliffe extensively reviewed the clinical, anthropometric, morphological and metabolic evidence for changes in muscle and fat mass during PCM (Jelliffe and Jelliffe 1969). They concluded that MUAC was a potentially useful, simple field measure for the assessment of PCM based on its ability to give composite information simultaneously on three important effects of PCM, namely; deficit in the muscle protein reservoirs, availability of energy stores in the form of subcutaneous fat, and growth failure. Subsequent research on the use of MUAC has focussed on its close relationship to mortality risk, which has been linked to it preferentially identifying younger children at greater risk of death and on its appropriateness as admission criteria for nutritional treatment programmes. Investigations have found that the relationship between MUAC and weight-for-height changes in different populations due probably to the influence of body shape (in particular the ratio of sitting height to standing height) on weight-for-height measures. (Myatt, Duffield et al. 2009). There are also some indications that MUAC may identify both wasted and stunted children (see Box 5).

Box 5 Results of analysis of the correlation of MUAC with weight-for-height and height-for-age z-scores.

Analysis was conducted on 560 nutrition survey datasets from a range of contexts and countries in Africa and Asia. Unsurprisingly the strongest correlation found was between MUAC and weight-for-height. However there was also a significant correlation between MUAC and height-for-age. See below Correlation and Relative Risk analysis (results weighted by survey sample size).

Pearsons correlation coefficients:

- In 557 (99.46%) of the 560 surveys MUAC was significantly correlated with weight-for-height at the individual level. Average strength of the correlation was r=0.6371 (0.6279 - 0.6469). See plot a.
- In 552 (98.57%) of the 560 surveys MUAC was significantly correlated with height-for-age at the individual level. Average strength of the correlation was r=0.2628 (0.2572 - 0.2689). See plot b.



Note: The dashed vertical line marks the position r = 0 (i.e. no correlation between the two measures

Relative risks of being wasted and stunted by MUAC category*

- MUAC category was significantly related to risk of being low weight-for-height (chi-squared p<0.05) in 554 (98.93%) of surveys
- MUAC category was significantly related to risk of being low height-for age (chi-squared p<0.05) in 493 (88.67%) of surveys

Compared to a child with MUAC≥125mm, a child with moderately low MUAC* was found to be:

- 8.79 (8.23 - 9.34) times more likely to be wasted
- 1.72 (1.62 - 1.91) times more likely to be stunted

A child with severely low MUAC* was found to be:

- 18.91 (17.27 - 20.67) times more likely to be wasted
- 2.23 (2.07 - 2.46) times more likely to be stunted

* Moderately low MUAC (115mm≤ MUAC <125mm), severely low MUAC (<115mm)
Note: 95% Confidence intervals given for estimates

source: Myatt, M. personal communication

1971), (Friedman, Phillips-Howard et al. 2005), (Tanner, Leonard et al. 2014). A relationship between MUAC and stunting has also been previously reported (Briend and Zimicki 1986, Guesdon, Aissa et al. 2013). This suggests that low MUAC children may be wasted and stunted and that MUAC could be of particular use in identifying those children who are suffering from degrees of wasting and stunting simultaneously. Given the above finding on heightened mortality risk for wasting and stunting combined, if MUAC was indeed identifying children suffering from both wasting and stunting this may partly explain the strong relationship found between low MUAC and mortality risk. Given that MUAC is already used for the identification of children for admission into treatment programmes we wanted to investigate whether this was also providing an opportunity to identify stunted children. The additional analysis by Myatt was therefore conducted and seems to support the hypothesis that MUAC tends to select both wasted children and stunted children (see Box 5). However, further research into this association will be needed.

3.3 Effects on morbidity and development

The literature also indicates that wasting and stunting share other important health implications. Wasting leads to reduced immune function and in some cases mucosal damage lowering resistance to colonization and invasion by pathogens. This both increases the risk and worsens the course of infectious disease particularly respiratory infection, malaria, intestinal infection, and diarrhoeal disease (Katona and Katona-Apte 2008). The term "malnutrition–infection complex" has been coined to describe the cyclical pattern that links infection, anorexia, complex metabolic adjustments (Schaible and Kaufmann 2007), malabsorption, as well as behavioural changes affecting feeding practices and in combination leading to malnutrition in the context of limited nutritional reserves (Tomkins and Watson 1989). The metabolic and physiological pathways involved are discussed in more detail in section 5. Stunting has also been found to be associated with heightened risk of death from infectious disease (particularly diarrhoea, pneumonia and measles) (Black, Allen et al. 2008). In general the relationship between all manifestations of undernutrition and infection is highlighted as an important mechanism linking them to mortality risk, although the precise nature of the immune defects in each manifestation of undernutrition has not yet been well characterised.

"Undernutrition can be deemed the cause of death in a synergistic association with infectious diseases; if the undernutrition did not exist, the deaths would not have occurred" (Black, Victora et al. 2013).

Stunting is also linked to poor school performance and in some studies to deficits in early motor development (Grantham-McGregor, Cheung et al. 2007). A recent study indicates that wasting may also lead to deficits in psychomotor and mental development (McDonald, Manji et al. 2013).

3.4 Shared risk factors

In a recent review (Piwoz, Sundberg et al. 2012) adequate nutrition, including micronutrients, immune health, a healthy gut and a healthy mother, were all identified as the prerequisites for healthy (linear) growth; although not stated, the same 'ingredients' are also necessary for maintaining healthy ponderal growth. A great deal has been researched and written on the causes of stunting and has been

summarised in the 2008 and 2013 Lancet series (Bhutta, Ahmed et al. 2008, Black, Victora et al. 2013). Fewer studies have investigated the factors that drive wasting (Fernandez, Himes et al. 2002, SCUK 2007, ACF 2011, ACF 2012, Ratnayake, Tesfai et al. 2013). A broad conceptual framework depicting these causal factors was developed back in 1990 by UNICEF (referred to as the UNICEF conceptual framework) and has been widely used and adapted internationally. It was recently further elaborated to include actions to address the causes outlined in the Lancet 2013 maternal and child nutrition series (Black, Victora et al. 2013). These frameworks deal with undernutrition as a whole, combining wasting and stunting and broadly cover the factors identified in the research literature associated with these manifestations of undernutrition. However, they do not delineate the overlaps and separations in causality between the two manifestations of undernutrition. See Table 1 for a compilation of the immediate[3] 'causal' factors identified for wasting and stunting in the literature.

Table 1 Immediate 'causal' factors suggested in literature for wasting and stunting[4]

	Wasting*	Stunting*
Associated factors	Maternal stature (Ozaltin, Hill et al. 2010	Maternal stature (Ozaltin, Hill et al. 2010) Maternal weight gain during pregnancy (WHO 1997)
	Infectious disease (Olofin, McDonald et al. 2013)	Infectious disease (Olofin, McDonald et al. 2013)
	Dietary inadequacy (Arimond and Ruel 2004)	Dietary inadequacy (Arimond and Ruel 2004)
		Zinc inadequacy (Imdad and Bhutta 2011)
	Diarrhoea (Richard, Black et al. 2013)	Diarrhoea (Checkley, Buckley et al. 2008) though not replicated by Richard et al in 2013 (Richard, Black et al. 2013)
	Inappropriate complementary feeding	Inappropriate complementary feeding (Bhutta, Das et al. 2013)
		Environmental Enteric Dysfunction (EED) (Keusch, Rosenberg et al. 2013)
	Intrauterine growth restriction[5] (Christian, Lee et al. 2013)	Intrauterine growth restriction (Black, Victora et al. 2013)

*including in-utero – inferred from measurements taken at birth

Notes:

- This table does not depict the strength of association found between these factors and wasting or stunting, simply where evidence exists for an association.
- For sub-optimal breastfeeding sufficient evidence was not found by Lancet review authors (Bhutta, Ahmed et al. 2008) for a link to linear or ponderal growth, or of promotion of breastfeeding positively impacting linear growth (Black, Victora et al. 2013)

Cross sectional studies have been utilised for conducting regression analysis in order to identify common and distinct causes of wasting and stunting. In general these studies conclude that there are common causes of both conditions, although different strengths of causality have been identified e.g. stunting more strongly related to wealth in Guatemala and India than wasting (ibid), while in a global study, female literacy and higher energy availability were more closely related to stunting and immunisation more closely related to

[3] Relating to the 'immediate' causes of malnutrition defined in the UNICEF conceptual framework (inadequate dietary intake and disease)

[4] The lack of evidence should not be taken as proof that particular factors are not linked to wasting as in some cases the links have not been looked for.

[5] Identified by measuring whether child is small for gestational age (SGA) at birth

wasting (Frongillo, de Onis et al. 1997). However, the limitations with the use of cross sectional data should be noted.

A review conducted in 2012 concluded that the current literature fails to identify causal factors for wasting, which are not also related to stunting (Martorell and Young 2012) although, of course, the contribution of the different factors can vary widely between contexts. This is in contrast to a number of causal factors, in particular specific nutrients and environmental enteric dysfunction (EED)[6] which current knowledge suggests are related to stunting but which have not been linked to wasting (see table 1). Additionally, and as could be expected, all studies found multiple causal factors for both conditions, therefore the few factors found to be distinct should not be taken as evidence that wasting and stunting are not linked. It is notable, also, that the complex interactions between these 'causal' factors (e.g. between different nutrient deficiencies, EED, and infections) in causing either weight or growth deficits are not well represented by these frameworks and are, in general, little understood (Prentice, Moore et al. 2013).

There are some areas of separation however. In addition to the above causal factors, insufficient quantities of specific micronutrients in the diet, or increased losses leading to deficiency in the body, have been suggested as specifically related to stunting. As these nutrients often occur together in foods it has proven difficult to identify their individual effects however. These nutrients are the 'Type 2' nutrients described by Golden in 1995[7] (Golden 1995). A possible explanation for their role in stunting is that linear growth requires synthesis of cartilage and bone tissues, which contain, for example, more phosphorus, magnesium and sulphur than other lean tissues. Requirements for these nutrients are therefore raised during periods of growth, including during catch-up growth and their deficiency may lead to growth faltering. Animal source foods and dairy products (and their protein profile in particular) have also been identified in a number of studies as increasing the levels of hormones related to growth (in particular Insulin-like growth factor) in the body. Therefore their presence or absence in the diet may also effect levels of stunting (Michaelsen, Hoppe et al. 2009). Though the interactions are complex, evidence suggests that specific nutrients are particularly relevant in governing linear growth in infancy and early childhood.

3.5 Shared response to intervention

As noted above, for many years the nutrition community has, in theory, worked with the UNICEF conceptual framework which integrates the causal factors for wasting and stunting and guides policy and programming. However, this framework has not generally translated to integrated programmatic approaches for wasting and stunting prevention addressing the multiple causal factors and monitoring progress according to improvement in both indicators. This is the case even for programmes such as growth monitoring and promotion (GMP) which in theory target wasting and stunting by using weight-for-age (a composite wasting and stunting indicator) but which have universally not demonstrated impact on underweight levels and have been criticised for not addressing the multiple causal factors responsible for low or falling weight-for-age (Ashworth, Shrimpton et al. 2008).

More recently, examples of programmes addressing a number of causes of wasting have

[6] Environmental Enteric Dysfunction (EED), formerly known as Environmental or Tropical Enteropathy, is a condition of in flammation and increased permeability of the gut thought to be caused by faecal bacteria ingested in large quantities by young children living in conditions of poor sanitation and hygiene. Humphrey, J. H. (2009). "Child undernutrition, tropical enteropathy, toilets, and handwashing." Lancet 374(9694): 1032-1035.

[7] Type 2 nutrients: potassium, sodium, magnesium, zinc, phosphorus, protein (nitrogen, carbon, threonine, lysine, sulphur).

been published, indicating the improved impact for the prevention of seasonal spikes in wasting by delivering a package of interventions (e.g. cash, blanket food supplements, immunisation and malaria treatment) (Epicentre, MSF et al. 2013, Bahwere, Dolan et al. In press). The effects on stunting alongside wasting have been investigated in only a few operational research studies however, and results are mixed with some studies indicating that both wasting and stunting can be impacted with the same prevention interventions in both the short and long term (Isanaka, Roederer et al. 2010, Huybregts, Houngbé et al. 2012)) and others showing impact on wasting only (Grellety, Shepherd et al. 2012, Thakwalakwa, Ashorn et al. 2012, Bahwere, Dolan et al. In press). It has been suggested that inadequacies in the composition of the supplement (limiting in specific micronutrients required for linear growth) may be responsible (Golden 2007).

A number of stunting prevention programmes have also taken a multisectoral approach, though demonstrated impact on stunting itself is sparse and wasting prevention as an additional outcome of interest is rarely investigated. There are currently a number of studies underway aiming to investigate the impact of combined approaches on linear growth e.g. water, sanitation and hygiene (WASH) with nutritional supplements (Arnold, Null et al. 2013), nutrient supplements with malaria and diarrhoea treatment (Hess, Abbeddou et al. 2013) though impact on wasting levels is not included so far in the proposed analysis.

3.6 Evidence of the role of maternal nutrition and the intrauterine period

In 2008, the Lancet nutrition series systematically reviewed the evidence of the impact of undernutrition on infant and child mortality and long term health and developmental, as well as the effective interventions to address undernutrition. It concluded that the optimal 'window of opportunity' for focussing interventions was the period from pregnancy to 2yrs of age, subsequently termed the 'first 1000 days'. It is therefore equally important to look at the first 9 months (or 270+ days) of those 1000 days when considering the relationships between wasting and stunting.

The pre-natal and intergenerational influences on infant growth failure are little understood (Prentice, Moore et al. 2013) and may differ in their importance in determining the burden of growth failure across populations (de Onis, Dewey et al. 2013). However, it is now recognised that the onset of linear growth faltering in particular occurs much earlier than previously thought, most likely beginning in the foetal period and continuing until about 24 months of age (Victora, de Onis et al. 2010). Maternal stature and weight gain during pregnancy have recently been shown to be associated with both length and weight at birth (Black, Victora et al. 2013). Some research from Africa also indicates that incidence of low birth weight (LBW[8]), in particular small for gestational age (SGA[9]) births, follow decreases in maternal weight in parallel to seasonal hunger gaps (Rayco-Solon, Fulford et al. 2005).

Intrauterine growth retardation is also an important part of the childhood wasting and stunting picture. Associations between deficits in physical growth of the infant and birth weight and gestational age of the new-born were observed in the 1970s (Mata 1978). More recent evidence indicates that being SGA is predictive of later stunting (Black, Victora et al. 2013). A recent meta-analysis of 19 birth cohort studies found that the odds ratio of childhood (12–60 months) stunting associated with SGA was 2.4, and preterm birth 1.9 – increasing to 4.5 for both

[8] Defined as infants born at term (gestational age 37 weeks or more) but whose birth weight is <2.5kg at birth

[9] Weight below the 10th percentile for the gestational age

SGA and preterm births i.e. that children born small were likely to be stunted during childhood. A similar pattern was found for wasting indicating that a large proportion of both stunting and wasting (an estimated 20% of stunting and 30% of wasting) has its origins in the foetal period (Christian, Lee et al. 2013). This pattern was comparable across different populations and regions. These studies do not imply causality as both intrauterine growth restriction and later undernutrition are influenced by many similar environmental, care and social factors. A growing body of evidence is available which links maternal undernutrition (manifest in the quality of breast milk; levels of essential fatty acids and key micronutrients) to nutrient deficits in the child (FAO 2011, Allen 2012). However a direct link to wasting or stunting in the child has not yet been demonstrated.

A commentary on the Christian study (de Onis 2013) highlights the significance of the results and the importance of interventions to improve maternal nutrition for reducing foetal growth restriction and in turn childhood wasting and stunting. The same commentary calls for the development of standards which allow for the delineation of linear growth and ponderal growth deficits in foetal life and at birth. This highlights an issue with the use of SGA measures in studies investigating the links with later wasting and stunting and the need for more detailed measures of birth anthropometry in line with those used to measure childhood malnutrition (see Box 6).

It is likely, given the existing evidence, that actions to address the causal factors of SGA will have beneficial knock on effects for addressing wasting and stunting in populations (see table 2). Some current research is underway to investigate this by measuring the effects of prenatal supplementation during pregnancy on SGA and new-born stunting[10].

Little is known about the differences (if any) that exist between children who are born with height and weight deficits and those who acquire them later on in their development; in terms of their

[10] Dewey, K. G. Personal communication

Box 6 Small for Gestational Age

Small for Gestational Age (SGA) is defined as a child born with a weight below the 10th percentile for the gestational age and is commonly used as a measureable proxy for Intrauterine Growth Retardation (IUGR). It is a more specific measure than Low Birth Weight (LBW) which can include children born early or born small. The use of SGA controls for preterm birth and therefore allows children who are smaller than they should be according to a reference population to be identified. A number of reference populations exist and choice of reference has been shown to have a great effect on the levels identified (Katz, Wu et al. 2014).

SGA is reported to arise from a genetic predisposition to small size or due to factors such as low maternal height, malnutrition, and/or infection during pregnancy. SGA infants are at increased risk of mortality, a risk that worsens with the severity of the SGA and which has been shown to continue into childhood. Different patterns of SGA are found in Africa and Asia compared to other regions with more SGA found in term rather than preterm infants.

There is recognition in the literature that there are two types of SGA infants, those who are 'proportionally small' (stunted) and those who are disproportionally thin (wasted) (Katz, Lee et al. 2013). One hypotheses is that the timing of foetal growth restriction during pregnancy may influence which of these types of SGA results (Barker 1997) 'the timing hypothesis'. However there is data that contradicts this idea and suggests that linear growth may precede or be more sensitive to prenatal stress than the ponderal index (Neufeld, Pelletier et al. 1999). However most research on mortality risk and the implications of SGA continues to focus on the overall SGA index, therefore does not allow us to identify the implications of, and relationships between, wasting and stunting which occur in utero.

needs and their response to interventions. However, a large body of research focusses on the intrauterine and intergenerational effects of foetal development in a resource poor intrauterine environment i.e. acquiring the thrifty phenotype and the consequences of this later in life (Hales and Barker 2001). There is increasing recognition that under energy-constraint, and potentially more so under severe energy-stress, some organs or tissues are prioritized over others. (Hales and Barker 1992) hypothesized that the brain is spared from energy stress through the selective sacrifice of other tissues, which can reduce in size without immediate penalties for survival. Body components already shown to be sacrificed to protect the brain during early life include the liver, kidneys, pancreas, lean mass and leg length (Hales and Barker 1992, Latini, De Mitri et al. 2004, Pomeroy, Stock et al. 2012) however there is still poor understanding of how the processes of wasting and stunting contribute to these effects, which components are affected, when during development this occurs, and what the longer-term penalties may be.

In some of the literature, this intrauterine 'programming' is referred to as an adaptation to living in a resource poor environment i.e. a biological programming to efficiently scavenge as much as possible from available food (Edwards 2012). While this adaptation may have important short- term survival effects for the resource-deprived foetus, it has also been described as a 'time bomb' for later chronic disease in light of rapidly westernising diets and activity patterns. There may well be a connection between these 'thrifty' children and those born short as there is some indication that certain elements of limb growth may also be sacrificed under tough conditions to conserve more functional traits (Pomeroy, Stock et al. 2012). However the mixed results found in the literature for the relationship between adiposity and short stature, (Pomeroy, Stock et al. 2014) with different studies finding adiposity linked to short or tall stature alternately, and in some cases to rapid post natal growth, indicates that this is a complex process in which the child's environmental and population history is important (Wells and Cole 2011). There is even some indication that fathers phenotype may play a role in the birth weight and nutritional profile of their offspring (Wells 2014) though the associations with wasting and stunting have not been investigated.

The long term implications of intensively feeding high energy diets to children recovering from wasting who may also have been born short and potentially 'thrifty', or who have become stunted later in their development are not well understood. Various research is being, or has been, carried out on the short and long term effects of rapid weight gain in infancy and childhood on disease outcomes (Barker, Osmond et al. 2005, Adair, Fall et al. 2013) however little looks particularly at the wasted child. Furthermore any long term adverse effects for the wasted child are likely to continue to be outweighed by the short term benefits to child survival and development.

Table 2 Factors associated with SGA or LBW

Type of deficit	Associated factor
SGA	Low Maternal BMI pre-pregnancy & low gestational wt. gain (Kramer 2003, Black, Victora et al. 2013)
SGA	Maternal stature[11] (Black, Victora et al. 2013)
SGA	Zinc deficiency (Imdad and Bhutta 2011)
LBW	Vitamin A deficiency – maternal night blindness (Tielsch 2008)
LBW	Iron deficiency (Imdad and Bhutta 2012)
LBW	Iodine deficiency (Zimmermann 2007)

[11] Maternal stunting (height <145cm) puts infants at risk of both term and preterm SGA

WFP/Shezad Norrani, Bangladesh, 2009

4 Evidence of Associations

Inconsistent relationships between weight-for-height and height-for-age have been identified, depending on the type of data that has been considered (e.g. population or individual level, cross-sectional or longitudinal) (Richard, Black et al. 2012).

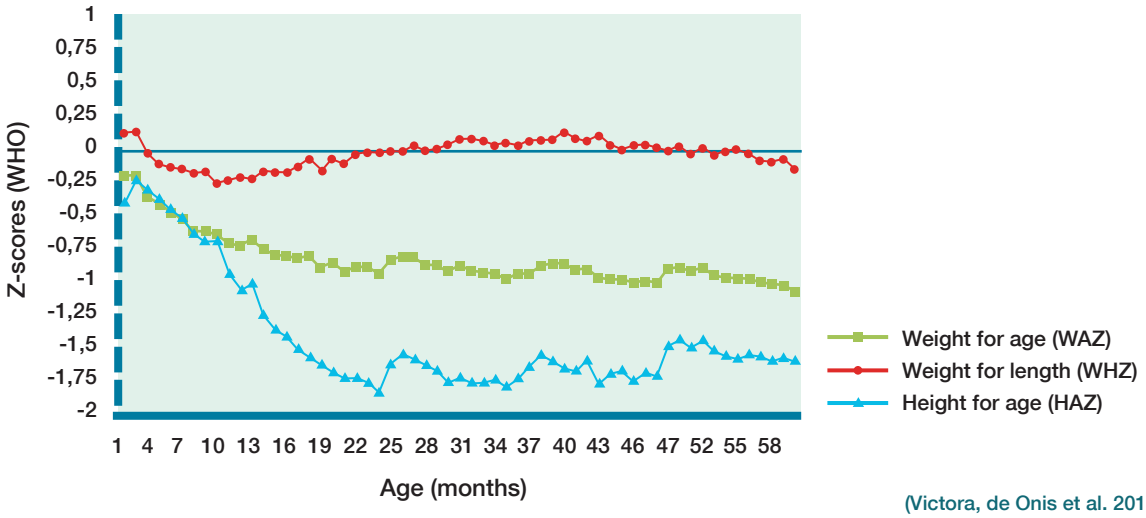
4.1 Evidence from cross sectional studies comparing patterns of wasting and stunting

Individual level cross-sectional studies have found little association between weight-for-height and height-for-age (Gorstein, Sullivan et al. 1994) and population level cross sectional studies have found variable results depending on context. Firstly, the patterns of wasting and stunting by age of child have been investigated, to look at convergence. Amalgamated data from 54 cross sectional national surveys demonstrates that height-for-age decreases throughout the first 2-3 years of life in many developing countries, whereas weight-for-height tends to falter during a more limited age window in the first year of life, after which it stabilizes (Shrimpton, Victora et al. 2001, Victora, de Onis et al. 2010) (see figure 1.). This has been used as evidence that different factors are responsible for wasting and stunting. However figure 1 is based on a composite of the cross-sectional studies which are in themselves problematic for a number of reasons (see annex 1 for more detail on the limitations of the evidence). This pattern does not represent the growth pattern of individual children which is heterogeneous within and across populations. More recent longitudinal data confirms the initial drop in height-for-age but illustrates a significant regain between 24 and 48 months (coinciding with more stabilised weight-for-height) and during puberty, indicating that perhaps these two manifestations of undernutrition are more closely connected than previously thought (Prentice, Ward et al. 2013).

The data in figure 1 was also analysed by country, for association between prevalence of wasting and stunting and variable results were found. Prevalence's of wasting and stunting were found to be positively associated in children 12-23 months of age in Asia and Eastern Mediterranean countries, but not in Latin America or Africa. Again, this has led to conclusions backed up by other

cross sectional studies using both worldwide and Africa specific data, that different underlying factors are at work (Frongillo, de Onis et al. 1997). However, it is recognised by some of the above authors and by Richards et al in their 2012 review of the evidence, that there are a number of critical limitations with the use of cross sectional data particularly for describing wasting trends, meaning these studies may misrepresent the relationships between these manifestations of undernutrition.

Figure 1 Change in indices of undernutrition with age



(Victora, de Onis et al. 2010)

4.2 Evidence from Longitudinal and Seasonal data

Longitudinal data, which follows children's growth (ideally) from birth looking at wasting, stunting, and the combination of the two, can add information by accounting for some of the above limiting factors. However, most studies looking at longitudinal data have been constrained by sample size limitations. To address this, a combined analysis from 8 cohort studies (1599 children) was carried out in 2012. These studies included measures taken every 3 months and the combined analysis indicates that the correlation between height for age and weight for height increases with age. Wasting in the first 6 months of life is not predictive of later height for age, but the prevalence of stunting at 18-24 months of age was correlated with a history of periods of wasting (variability in weight for height) (Richard, Black et al. 2012). Recent episodes of wasting also appeared to be associated with a lower height-for-age in this age group. Conversely, the study found that positive changes in weight-for-height during the first 17 months of life were associated with greater length-for- age at 18-24 months of age. These findings echo earlier studies, which linked variations in weight-for-height with linear growth (Walker, Grantham-McGregor et al. 1996).

This pattern of periods of wasting precluding changes in height-for-age is mirrored in several longitudinal studies exploring the relationship between acquisition of weight and height, in settings with seasonal variations in growth. It is well known that wasting and stunting levels vary seasonally, along with seasonal variations in disease, activity levels, food availability and even time for childcare. However these studies have observed that, at the population level, periods of lowest linear growth follow periods of lowest

weight acquisition i.e. that children grow in height only when their weight-for-height improves at the end of the hunger season (Brown, Black et al. 1982, Maleta, Virtanen et al. 2003). These findings suggest that there may be a lagged effect of weight on height growth, which can be illuminated by looking at additional longitudinal data at the individual level.

That linear growth on the individual level naturally occurs in bursts over time rather than as a continuum has been documented (Lampl, Veldhuis et al. 1992). The below studies suggest that changes in weight also play a role. Maleta et al. (Maleta, Virtanen et al. 2003), in a cohort of children followed from birth till 36 months of age, found that weight-for-height at the beginning of a given 3 month period was directly correlated to variation in their height during that period, although the relationship at the individual level was weak. In another individual level study, weight and height velocity in children in Nepal were compared. The study concluded that children with low weight-for-height at the beginning of the period had higher weight velocities and lower height velocities than children with normal weight-for-height at the beginning of the period (Costello 1989). The author suggests that children with low weight-for-height gained weight at the expense of height.

4.3 Evidence of wasting as a direct cause of stunting

A limited number of studies take this further to suggest that wasting may also be a direct cause of stunting. These studies examine the pattern of growth of children recovering from Severe Acute Malnutrition (SAM). The first study showed that, among SAM children who had linear catch-up growth, two thirds started to grow only after reaching at least a weight-for-height of 85% of the NCHS median (Walker and Golden 1988). In contrast, another study indicated that during SAM treatment, linear growth accelerated as weight-for-height increased, without a clear threshold above which growth resumed (Doherty, Sarkar et al. 2001). Both studies suggest that growth in height takes place only when the body has a minimum of energy reserves. A similar association between initial weight-for-height and growth in length in the following months, without a threshold effect, has also been reported in cohorts with a very low prevalence of wasting (Dewey, Hawck et al. 2005). These studies suggest that either the process of wasting, or of recovery from wasting may impact linear growth.

The recent Lancet nutrition series recognised the role of catch-up growth as central to the link between wasting and stunting. 'Severe infectious disease can lead to wasting (low weight-for-height), which may have longer-term consequences on linear growth, particularly if there is insufficient food availability to recover after a bout of infection' (Black, Victora et al. 2013). Factors facilitating rapid catch-up growth such as early health care seeking behaviour, effective treatment for illness and wasting and the availability of adequate diets for recuperation, are likely therefore to positively impact the cycle of infection → wasting → stunting. However, this relationship has yet to be fully described and requires the examination of both linear and ponderal growth velocities over time. A recent meta-analysis of 7 cohort studies[12] investigating diarrhoea burden and growth, found that diarrhoea during the 30 days prior to anthropometric measurement was consistently associated with lower weight at most ages, but found little short or long-term association with length (Richard, Black et al. 2013). A further analysis conducted on this data by the authors looking in more detail at catch-up indicates that indeed both linear and ponderal growth slowed during a current bout of diarrhoea and that catch-up could occur similarly in both weight and height if a diarrhoea free period

[12] 1,007 children with 597,638 child-days of diarrhoea surveillance and 15,629 anthropometric measurements

was then experienced (Richard, Black et al. 2014). The authors suggest that more research is needed to explore catch-up growth and potential confounders.

There are anecdotal programme reports of rapid linear growth occurring during treatment and follow-up for SAM once the child has reached a certain point in their recovery. One study on previously malnourished children also showed a significant degree of catch-up in linear growth when compared against unaffected siblings (Graham, Adrianzen et al. 1982). However, little has been published on this and a recent publication appears to contradict this indicating that height-for-age did not improve during severe acute malnutrition treatment and recovery (Kerac, Bunn et al. 2014, Kerac, Bunn et al. in press). Additional analysis conducted for this paper also indicates that linear growth catch-up is not occurring during wasting treatment in general, or on follow-up after discharge. Furthermore that height-for-age may deteriorate for the youngest age group (Box 7).

It has been suggested in a number of studies that children suffering with SAM are particularly deficient in essential fatty acids (Leichsenring, Sütterlin et al. 1995, Houssaïni, Foulon et al. 1999, Decsi and Koletzko 2000). Some studies also suggest that supplementing with lipid nutrient supplements containing essential fatty acids and/or milk protein may have a small positive effect on linear growth (Adu-Afarwuah, Lartey et al. 2007, Phuka, Maleta et al. 2008, Mangani, Maleta et al. 2013). However, gains in length found in these studies, though statistically significant, have been small, mostly in the severely stunted group, and the results not yet widely replicated. The most recent research[13], yet to be published, does suggest that RUTF may be lacking in some key nutrients required for development (such as these long chain essential fatty acids). There is also debate as to whether the formula optimally supports linear growth during and after wasting recovery. This could perhaps explain the differences in results found between the above studies and point towards potential longer term advantages in revisiting the RUTF formulation.

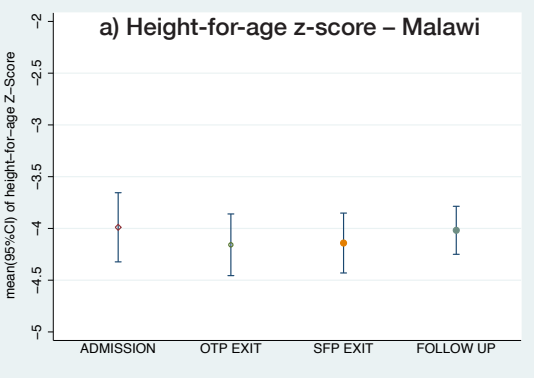
Evidence for a role of stunting as a direct cause of wasting, or alternatively as protective of wasting, was not found during the development of this paper. However, some additional analysis indicates that the majority of children admitted into programmes for the treatment of SAM are also stunted. This suggests that there may be a relationship between stunting and wasting though it may not be direct (see box 7). In addition, some evidence for an association between being born small and wasting during childhood is presented above in section 3.6.

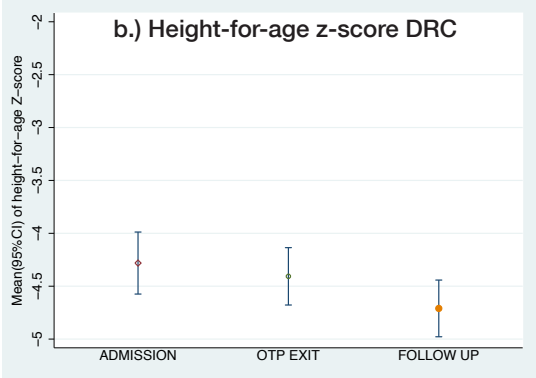
[13] http://clinicaltrials.gov/ct2/show/NCT01593969, http://clinicaltrials.gov/show/NCT02053857

C Wilkinson, DRC, 2007

Box 7 Linear growth during recovery from severe acute malnutrition

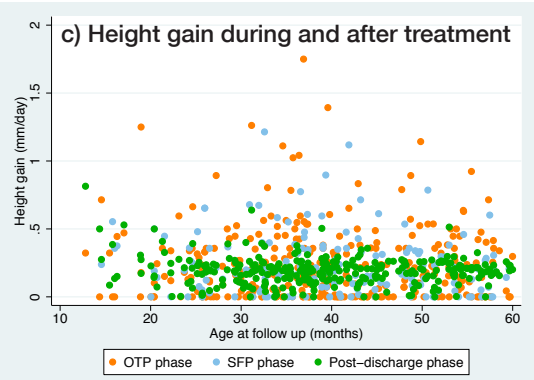
Mean height-for-age z-score at admission, discharge and at follow-up after discharge was investigated for 166 children treated in Dowa District, Malawi (see plot a.) and 89 children treated in DRC (see plot b.). Length of time to follow-up was 3-24 months for the Malawi data which was a retrospective cohort and at 6 months from discharge for the DRC data. In both cases defaulters were followed up to identify any deaths. Different admission criteria were being used for the two programmes*, however for the purposes of the analysis we selected cases of severe wasting (WHZ<-3) and oedema with wasting (WHZ<-2 and oedema) in order to investigate linear growth in children being treated for wasting.

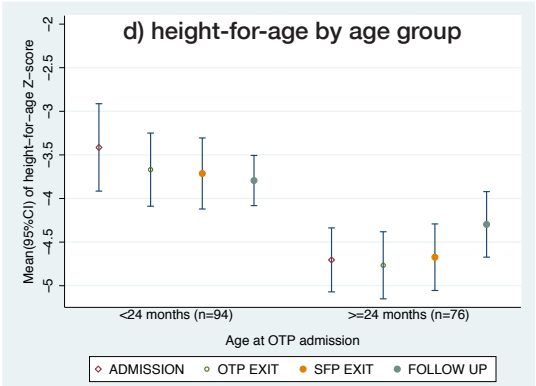




The above should be taken in the context of a demonstrated trend in catch-up in both weight-for-height and in weight-for-age during treatment and after follow-up in both contexts. The results indicate that when the sample of children is taken as a whole, height-for-age catch-up does not occur as a result of therapeutic treatment for severe acute malnutrition, and in the case of DRC that height-for-age may even continue to deteriorate during treatment. We ran the same analysis separately for 1. children with severe wasting and no oedema 2. children with severe wasting including those with severe wasting and oedema, and found the same patterns each time.

Additional analyses were conducted on the Malawi data. Actual height gain (mm) per day was investigated (see plot c.). This analysis indicates that although height-for-age is not in general being caught-up, linear growth is occurring in children, particularly during wasting treatment. Unfortunately with these datasets we are not able to see what the linear growth trajectory of the child was prior to admission to treatment for comparison. Analysis of height-for-age catch-up was also conducted with children divided into those <24months and ≥24 months of age at admission (see plot d.). This analysis indicates that a degree of catch-up may occur on follow-up in the older age group and conversely that for children <24months there is actually a trend of continued stunting both during and after treatment. This perhaps indicates that particular nutrient needs either during or after wasting treatment for the younger age group are not being met or that linear growth is not being prioritised biologically during wasting catch-up.





The other finding we can draw from Malawi and DRC datasets is that in both programmes, almost all children admited* were also stunted (height-for-age <-2 zscores).
81.2% of children in the Dowa dataset and 92.7% in DRC were stunted.

*admission criteria were based on weight-for-height % of the median using NCHS standards in Malawi and according to MUAC<115mm in DRC.

source: Bahwere, P. personal communication

Alima, Niger, 2010

5 Evidence of shared physiological mechanisms

In his early papers, Waterlow postulated that children with wasting had an altered body composition and that the association of wasting and stunting puts children in a high risk category for mortality (Waterlow 1972, Waterlow 1979). Forty years later, this question is still being debated. One explanation of this association with mortality is indeed that both wasting and stunting reflect changes in body composition, in particular a decrease of muscle mass, which, if severe, compromises the provision of fuel to vital organs, especially during periods of infection (Briend, Khara et al. 2014). Another explanation emphasises the role of body fat and in particular of hormones secreted by fat tissue.

Physiologically we know in that in adults when energy intake is insufficient to sustain metabolism, different adjustments occur to allow key organs to live from the body's nutritional reserves, mainly from fat and muscle. These adjustments follow rapid changes in the insulin and glucagon levels and also from both short term and long term regulation of key enzymes; putting the organism in an energy-sparing mode and shifting to fat as its main energy source. In the absence of infections, metabolism is mostly sustained by mobilising fat stores. The brain, which usually consumes large amounts of glucose, starts to use ketone bodies (also derived from fatty acid metabolism) after a few days of insufficient energy intake. Amino acids from muscle are needed to sustain protein metabolism when protein intake is insufficient (which usually goes hand in hand with deficient energy intakes), but in the absence of infections, protein catabolism is maintained at a minimum and the organism lives on fat body stores. Death occurs when this fat reserve is exhausted (Cahill 2006).

During infections associated with malnutrition, there is a double nutritional stress as food intake is usually reduced as a result of the anorexia which accompanies infection. Additionally, there is an increased demand for amino acids as part of the immune response for the accelerated synthesis of acute phase proteins in the liver and to produce glutathione (an antioxidant involved in the neutralisation of free radicals). This increased demand for amino-acids is met by mobilising them from muscles (Reeds, Fjeld et al. 1994). As a result, muscle mass is a major determinant of survival in malnourished adult patients with infections (Wolfe 2006).

Both muscle mass and fat mass hypothèses are challenged by the fact that changes in body composition in child wasting or stunting have hardly been measured since the 1970s. Limitations in the application of methods to measure muscle and fat mass in children is one reason as most methods require subjects to remain still.

The role of muscle loss in mortality risk, was first suggested in 1989 (Briend 1989) and is supported by epidemiological studies in contexts where the association between infection and malnutrition is a major cause of death (Briend, Garenne et al. 1989,

Van den Broeck, Eeckels et al. 1998). Two studies which did measure muscle-mass in children suffering from SAM also support the association between wasting and muscle mass loss. These studies found that muscle mass was drastically reduced in relation to body weight in these children compared to healthy controls (Reeds et al., 1978) (Nagabhushan and Narasinga Rao, 1978). There is also indirect evidence that muscle mass is reduced in stunting. As noted in section 3.2. muscle arm indices are related to height-for-age. Arm and leg length are also likely to be determinants of muscle mass and a reduced limb length may lead to a decreased muscle mass in the stunted child. Epidemiological studies show that leg length deficit predominates during stunting, as growth retardation usually occurs during the first two years of life, at an age where linear growth predominates in the lower part of the body (Bogin and Varela-Silva, 2010).

The presence of a low muscle mass in both wasting and stunting and the link between muscle mass and survival during infection, suggest that both wasting and stunting could increase the risk of death through decreased muscle mass. The greater decrease of muscle mass associated with wasting could explain the higher risk of death associated with severe wasting compared to stunting (Box 3) (Olofin et al., 2013) and the combined effect on muscle mass of having limbs that are both shorter and thinner could explain why the risk of death is considerably increased when wasting and stunting are both present in the same child (McDonald et al., 2013). It is notable that severe stunting confers a higher mortality risk than moderate wasting though the factors underpinning this are unclear. These results could also explain the strong association of low MUAC (a measure sensitive to changes in muscle mass) with mortality risk which has been illustrated in children (Myatt, Khara et al. 2006) in adults (Irena, Ross et al. 2013) and more recently also in infants (Mwangome, Fegan et al. 2012). However as MUAC is also a measure sensitive to changes in fat mass this could also support the below hypothesis. An effect of wasting and stunting on mortality through a reduced muscle mass also suggests that young infants and children should be especially vulnerable to malnutrition, a finding that is borne out by the results of nutrition surveys.

The evidence that linear growth is interrupted when a child is suffering from wasting may also be explained by the role of fat in regulating bone mass and linear growth. Recent advances suggest that fat and bones can both be regarded as endocrine organs secreting hormones and interacting with each other. In particular, fat tissues produce leptin which evidence suggests, has an influence on bone density and catch-up growth (Karsenty, 2006), (Gat-Yablonski et al., 2004). Leptin is a hormone made by fat tissue that acts on the brain to regulate food intake and body weight, as well as influencing immune function (Friedman and Halaas 1998). A study in moderately wasted children suggests that catch-up growth in length takes place only in children with an increase in leptin concentration (Büyükgebiz et al., 2004). These early findings need confirmation in children recovering from SAM and also in moderately wasted children but they suggest that low fat stores associated with wasting are likely to halt linear growth and may prevent linear catch-up growth if untreated. Low levels of the adipose tissue hormone leptin have also been found in recent research to be strongly associated with survival in children identified with severe acute malnutrition (Bartz, Mody et al. 2014). This suggests that fatty acid metabolism may play a central role in the adaptation to wasting and that fat mass may indeed play a more direct role in the mortality associated with wasting, and potentially stunting (though stunting was not the subject of the study).

In parallel to the continued discussions on the role of muscle and fat mass in the different manifestations of undernutrition, debates continue as to the composition and resulting functionality of tissue gained during rapid catch-up from a period of wasting. The interplay between these two debates may explain why studies of community-based approaches for SAM indicate that treating cases early on in the progression of disease return them to the baseline population mortality risk after treatment (Bahwere, Mtimuni et al. 2012). However some similar, studies conducted on cohorts of children admitted to inpatient care (usually presenting late in the progression of the disease with greater severity of wasting) are reporting raised mortality risk continuing after wasting recovery (Kerac, Bunn et al. 2014).

Lucia Zoro, Northern Nigeria, 2011

6 Conclusions based on the evidence

A number of conclusions were drawn by the TIG from the review of the evidence which informed this paper:

Conclusions

Burden

1. Both wasting and stunting often coexist in the same child though the extent to which this happens is largely unreported (despite the fact that the data required is available in all standard nutrition surveys). This condition may have particular causal pathways and effects which are not yet fully understood.
2. Seasonality has a marked impact on both wasting and stunting prevalence (the magnitude of the effect is, in general, greater for wasting).
3. Rates of gain in weight and height often take place at different times of year and seem to be related over time in a consistent way, with height faltering peaking 2-3 months after weight loss/ wasting levels have peaked.
4. Measuring the association between wasting and stunting at population level is challenged by the use of prevalence data. Wasting has a relatively shorter duration than stunting and is also highly variable seasonally. Therefore, the relatively large proportion of incident wasting cases occurring over time will be missed and, depending on the timing of the survey, seasonal peaks may also be missed. Combined, this may lead to underestimates of yearly burden of wasting compared to stunting, the burden of which is better captured by cross sectional surveys.

Shared risk factors

5. Wasting and stunting have many common risk factors as illustrated by the UNICEF conceptual framework and indicated by the literature.
6. There is good evidence that in-utero conditions and foetal growth contribute significantly to stunting at birth and during infancy; there is emerging evidence of contributions to wasting. Evidence suggests that height trajectory during childhood is related to initial height-for-age at birth (and by association foetal growth) and to some extent, to initial weight-for-height at birth.

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7. Infectious diseases in early childhood make an important contribution to both wasting and stunting. Diarrhoea, in particular, is associated with short-term weight loss. Evidence is less strong for the long-term effect of diarrhoea on linear growth.
8. There is evidence to suggest that inflammation and gut health may also play an important role in stunting (either via the effects of chronic inflammation, malabsorption and/or appetite effects) and there is a need to investigate effects on wasting also.
9. A diet adequate in the nutrients required for growth and development (and limited in anti-nutritive factors) is required for the prevention of both wasting and stunting. Additional specific nutrient requirements are associated with treatment (catch-up of ponderal and/or linear growth). In the majority of countries where wasting and stunting are common a diet complete in these nutrients is not available to a large proportion of the population[14].
10. How the causal pathways for wasting and stunting develop over time separately and in combination is poorly understood. Collection and analysis of longitudinal data tracking children's status over time is required to better inform the design of services aiming to intervene in these causal pathways.

Shared effects

11. Both wasting and stunting are associated with increased mortality. Where they coexist the risk multiples.
12. There is evidence of a decrease in muscle mass in wasted children and indirect evidence of it in stunted children
13. Stunting is associated with child mental (cognitive) and psychomotor development. Evidence for wasting being associated with mental (cognitive) and psychomotor development is less strong.

Direct relationships

14. Evidence suggests that wasting adversely affects linear growth in that episodes of wasting in the previous 3 months (approximately) have an impact on attained length-for-age. Therefore, early identification and treatment of wasting may play a role in the prevention of stunting in particular contexts.
15. During wasting there is a point at which linear growth slows and potentially stops. Though we do not know exactly when this occurs, it is thought that linear growth may be regulated by body fat levels.
16. Evidence that wasting treatment and recovery benefits linear growth of individual children is mixed. However there are indications that optimising the RUTF formula to include specific nutrients required for linear growth and development could have positive effects.

Programmatic approaches

17. There is some encouraging operational research to suggest that both wasting and stunting may be reduced with similar preventative food based approaches. However, thus far the effects illustrated by these programmes on linear growth in particular are small.

[14] Chastre, C., A. Duffield, H. Kindness, S. LeJeune and A. Taylor (2009). The minimum cost of a healthy diet: Findings from piloting a new methodology in four study locations.

Seema Arora, Ethiopia, 2008

7 Programme and Policy implications and Actions

This briefing paper confirms the assertion, also made elsewhere, that there are compelling reasons to bring wasting and stunting policy, programming and resourcing more closely together (Bergeron and Castleman 2012, Menon and Stoltzfus 2012) at the global and national level, due to their evident overlapping pathways and, critically, because of the links between ponderal and linear growth. The authors and TIG members believe that the evidence as it stands provides sufficient justification to elaborate the following implications and call for actions. It is also clear from the review and TIG discussions that there are various issues with, and gaps in the evidence for the relationship between wasting and stunting which are also outlined below. If these gaps can be filled, the case could be further strengthened for more integrated and holistic policy and programming at a practical level, ensuring that interventions are optimally designed in terms of targets, timing and content.

The group also recognises that though there remain a number of questions and research gaps in terms of optimal programme approaches for preventing both stunting and wasting, and for treating stunting, this should not be a reason for inaction. We have effective interventions to treat wasting and a number of effective direct nutrition interventions have been identified in the 2008 and 2013 Lancet maternal and child undernutrition series. The implementation of these interventions at scale should continue to be prioritised alongside the further actions suggested below.

7.1 Bridging divides at programme and policy level

Evidence does not support the current degree of separation of wasting and stunting into acute and chronic conditions or humanitarian and development contexts as both conditions occur over a number of months in an individual child and are found in a variety of contexts. The prevailing separation in policy, guidance and resourcing for wasting and stunting limits both the sustained recovery of the wasted child (by creating a disconnect between their treatment and ongoing rehabilitation), and the prevention of further episodes of wasting, with potential implications for linear growth.

Given that wasting and stunting share many common risk factors and given the indications that wasting can impact on stunting, clearer policy

directives and funding support are needed to encourage and facilitate practical links, for more integrated programming. Though it is recognised that in the acute emergency context treating wasting remains a major priority, the heightened mortality risk associated with combined stunting and wasting indicates that there is a need to ensure programmes are targeted to reach this group (see section 7.4). In addition the mortality risk associated with severe stunting in particular warrants attention wherever this is prevalent.

It is also recognised that, though initial emergency response funding is by nature short term, the majority of emergency assistance for nutrition is in situations characterised as protracted or as a chronic emergency. In these situations, there are compelling reasons to be implementing more joined up stunting and wasting programming. This will require donors and institutions with mandates and responsibilities for wasting and stunting to examine optimal financing, policy and programmatic links between wasting and stunting prevention and treatment. Furthermore, operations research and standard programme monitoring and evaluation systems need to better capture the impact of current efforts to reduce both wasting and stunting simultaneously so that more is understood about optimal approaches to address childhood undernutrition through integrated programming.

Action – Agencies with mandates and responsibilities for wasting and stunting to examine their policy and programmes to find ways to optimise convergence between wasting and stunting approaches beyond the acute emergency phase.

Action – Donors to re-examine their financing arrangements so that wasting and stunting can be simultaneously addressed in the contexts where they are present (i.e. both relief and development contexts) in a more coherent way including through funding of appropriate operations research.

Action – Academic institutions, agencies and NGOs to prioritise research to fill the gaps in knowledge and practice for coherent and effective wasting and stunting prevention and treatment programming.

Action – Dissemination to national government bodies and research institutions of this paper in order to share the evidence and debates and trigger appropriate national level actions.

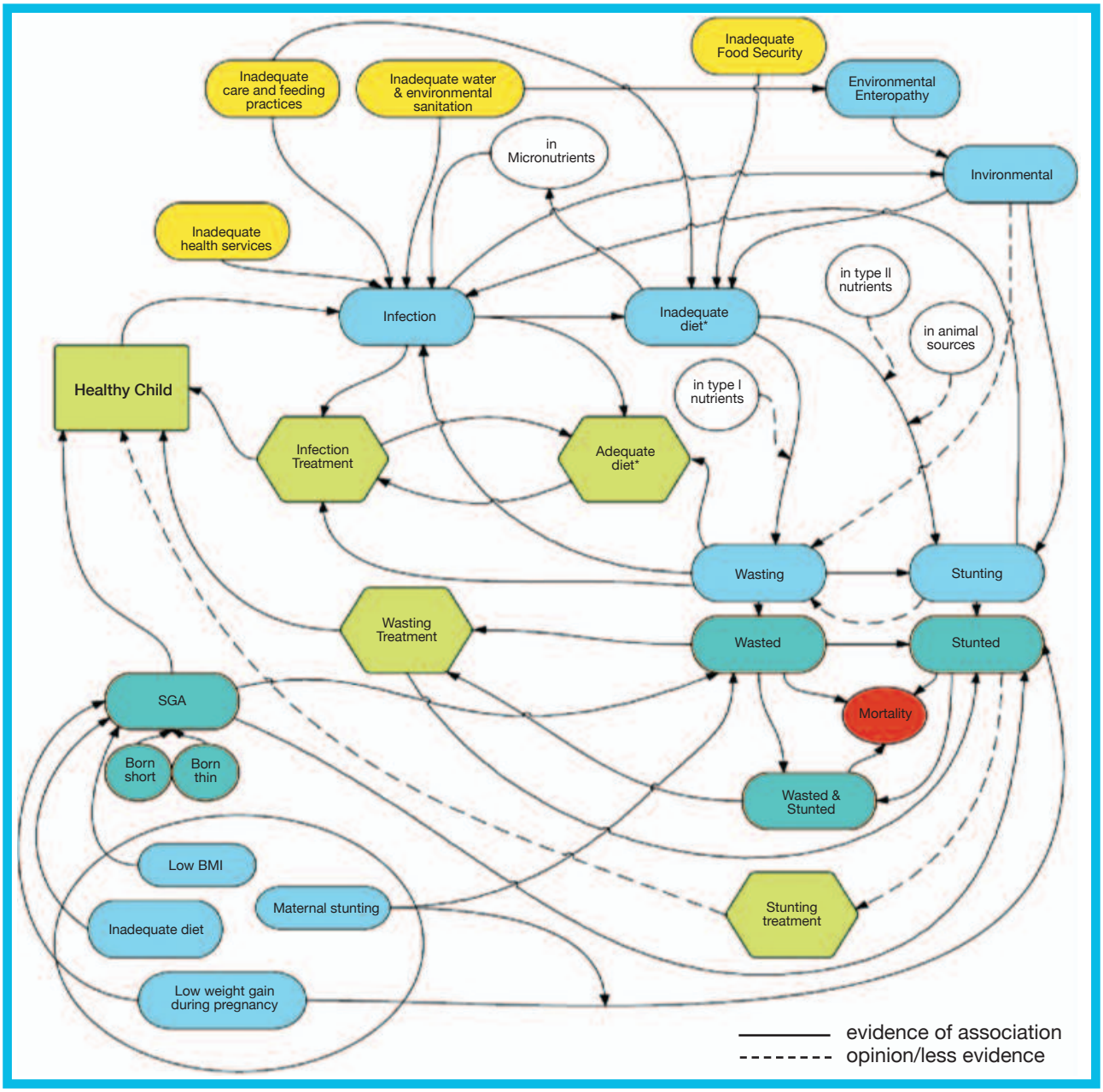
7.2 A joint framework for wasting and stunting policy, programming and research

The need to bring together programming and research for the prevention of wasting and stunting is borne out by the body of evidence presented above. It is clear that the interrelationships between risk factors for wasting and stunting are complex and therefore nutrition specific and sensitive services tackling the risk factors common to wasting and stunting need to be linked, rather than each relationship dealt with separately. In fact, the complexity of the associations between these factors means that it may actually be inappropriate to separate them. For example, the poorest among the community are more likely to be stunted, AND they are more likely to suffer from infections and poor diet which are also the main risk factors for wasting.

Action – Use of a joint wasting and stunting framework for linked services

By mapping the factors and associations involved in a child's pathway to wasting and/or stunting and attempting to depict the complex cyclical relationships, we have started to develop a framework which could be used as a basis for more coherent policy, programming and research (see Figure 2). The aim is to provide a framework which can be used to assess the primary causal factors in a given context and for the planning, and

Figure 2 Pathways to infant and child wasting and stunting



design of support which coherently addresses both these manifestations of undernutrition simultaneously. There are a number of limitations to this current version some of which are in common with existing frameworks. In particular it doesn't represent the strength of the associations it depicts and it doesn't depict the possible mechanisms for the direct association between wasting and stunting. It also doesn't depict how these manifestations of undernutrition develop and interact with each other over time. We present this therefore as the start to a process of developing a more useful framework and hope it's limitations can be addressed in further versions as evidence grows.

Research needs

- **Operations research demonstrating practical and effective ways to combine treatment and prevention for wasting and stunting.**
- **Further investigation of effective approaches for stunting reduction including optimal formulation of any supplements used to support linear growth.**
- **Investigate whether interventions outside of the 1000 days, e.g. pre-school, school age and adolescence, lead to catch-up in height and in other developmental markers.**

7.3 Maternal health and nutrition support

Given the evidence that weight and length at birth determine childhood linear growth (and potentially ponderal growth), programmes targeting the in-utero environment e.g. via effective evidence-based maternal health and nutritional support which have been documented[15,16], can be seen as important stunting (and potentially wasting) prevention interventions. Although there has been increased global attention on this area, progress remains very slow. These interventions need to span the preconception, pregnancy, intrapartum and postnatal periods.

Action – prioritise implementation of effective evidence based interventions for maternal health and nutrition

A number of interventions have been shown to be effective for supporting maternal nutrition. Their implementation at scale should be prioritised and, where possible, the effects on infant nutritional status at birth measured. These interventions include:

- Maternal balanced energy protein supplementation
- Maternal iron/folate/multiple micronutrient supplementation
- Maternal calcium supplementation (in at risk populations)
- Reducing maternal disease risk (malaria), insecticide treated nets and preventative treatment
- Optimising age at first pregnancy and inter-pregnancy intervals – through reproductive health initiatives
- Access to appropriate antenatal and obstetric care.

Research needs

- **Further investigation of the role of pre-pregnancy nutritional status (and the effect of pre-pregnancy supplementation) in determining risk of being born stunted and/or wasted.**
- **Further investigation of foetal growth and/or status at birth as a predictor of wasting and stunting in childhood. Including more detailed measures of nutritional status at birth in order to differentiate deficits in ponderal and linear growth.**
- **Operational research into effective packages of interventions for both maternal nutrition and new-born outcomes**
- **Understand how to effectively and appropriately deliver pre-pregnancy nutrition support particularly for adolescent girls.**

7.4 Early action for addressing the burden of undernutrition

There is clear evidence of predictable seasonal patterns of both wasting and stunting. There is also some indication that these peaks are related to each other and that action in one area may have a positive effect on the other, particularly through early interventions to prevent incident wasting. In order to maximise the effectiveness of programmes aimed at preventing increased incidence of wasting and stunting during these periods, there is a need to design programme

[15] Khara, T. N. and E. Mates (2013). Maternal Nutrition in Emergencies: summary of the state of play and key gaps: a technical review, DG ECHO, Lassi, Z. S., A. Majeed, S. Rashid, M. Y. Yakoob and Z. A. Bhutta (2013). "The interconnections between maternal and newborn health-evidence and implications for policy." J Matern Fetal Neonatal Med 26 Suppl 1: 3-53

[16] Lassi, Z. S., A. Majeed, S. Rashid, M. Y. Yakoob and Z. A. Bhutta (2013). "The interconnections between maternal and newborn health--evidence and implications for policy." J Matern Fetal Neonatal Med 26 Suppl 1: 3-53.

interventions that are put in place in advance to mitigate seasonal peaks in undernutrition and their effects.

Similarly the use of international standards to identify children below a particular cut-off may not be appropriate for early prevention approaches as these children have already experienced a significant period of wasting and/or stunting. The evidence suggests that for prevention, it may be more appropriate to deliver interventions to all children (where possible during seasonal peaks) or based on weight loss and/or slowing of linear growth thus picking up children before they reach a given cut-off when they are potentially easier and more cost effective to treat and before their risk of mortality is greatly raised.

Action – Support from governments and donors to address population level seasonal peaks in both wasting and stunting

In view of the seasonal patterns of both wasting and stunting, there is a need ensure that policies, financing and programmes are geared to facilitate early preventative interventions aimed at mitigating seasonal peaks in wasting and stunting.

Action – Exploration of prevention approaches to address wasting and stunting early on an individual basis

Investigation of approaches which catch wasting and stunting early on an individual level when they may be the easiest to address.

Research needs

- **Understanding and estimation of incidence of wasting over time in different contexts.**
- **Further operational research into timely approaches to mitigate seasonal peaks in undernutrition (both wasting and stunting).**
- **Investigate the potential for nutrition support triggered by a drop in weight or height for prevention of both wasting and stunting. The weight-for-age index could be an appropriate means to identify these drops (perhaps linked to existing growth monitoring programmes) and trigger nutritional inputs aimed at supporting the child to convalesce before growth deficits are incurred.**

7.5 Treatment for reduced mortality and improved linear growth outcomes

We have an effective proven life-saving model for treating wasting which is increasingly being integrated into national health systems[17]. Children identified in a timely fashion at community level can be treated with simple protocols at decentralised health facilities[18] and their mortality risk brought back in line with that of the non-wasted child[19] However, the current low level of global coverage for the treatment of wasting in children is adding to the burden of mortality in the under-five population and, given the evidence presented, is also likely to be limiting the optimal linear growth of millions of untreated children. Furthermore, despite severe stunting carrying a large risk of mortality, there are as yet no proven treatment approaches to tackle it.

Action – inclusion of wasting treatment as a component of stunting prevention

Given the evidence of effectiveness and

[17] WHO, WFP, UNSCN and UNICEF (2007). Community-based management of severe acute malnutrition: a joint statement, WHO.

[18] Collins, S., N. Dent, P. Binns, P. Bahwere, K. Sadler and A. Hallam (2006). "Management of severe acute malnutrition in children." Lancet 368(9551): 1992-2000.

[19] Bahwere, P., A. Mtimuni, K. H. Sadler, T. Banda and S. Collins (2012). "Long term mortality after community and facility based treatment of severe acute malnutrition: Analysis of data from Bangladesh, Kenya, Malawi and Niger." Journal of Public Health and Epidemiology 4(8): 215-225.

implications both for mortality and for child growth (ponderal and linear), treatment of wasting should be scaled-up in all contexts where wasting exists as an integral part to both mortality reduction and stunting reduction programming.

Action – Scale-up of treatment for high risk low MUAC children.

The evidence presented also indicates that children who are both wasted and stunted, and those in the younger age group, should be prioritised for treatment aimed at mitigating mortality risk. The additional analysis described above in Box 5 suggests that the use of MUAC for admissions may adequately discern the wasted and stunted young child at most risk of dying.

Research needs

- **The need for more longitudinal studies to further illustrate the process of wasting and stunting in individuals, including the level of wasting at which linear growth slows down or speeds up.**
- **Revisit the formulations of RUTF to fulfil all nutrient requirements and promote optimal ponderal growth and support linear growth during and after SAM recovery.**
- **Further investigation of the extent to which MUAC preferentially identifies children who are both wasted and stunted (in particular severely stunted) for treatment in different contexts**
- **Implications of rapid weight gain (as during wasting treatment) on body composition and function in the short and long term.**

7.6 Understanding of the physiological and body composition changes during wasting and stunting

It is clear from this review that there are fundamental gaps in our knowledge of what happens physiologically during wasting and stunting, in particular when both processes are underway concurrently in the same child. Our understanding of the changes in body composition both during wasting and stunting and during recovery is particularly limited and is essential for optimising approaches aimed at promoting recovery and catch-up of ponderal and linear growth in the short and longer term.

Action – Research to fill key knowledge gaps related to body composition

The community working in obesity research and programming are far ahead in terms of their understanding of the physiological processes and the use of different body composition measures to investigate changes occurring during the progression and treatment of the condition. There is therefore a lot that could be learnt from making links with those working in this area.

Research needs

- **Further elaboration of physiological changes during wasting and stunting and when both are underway concurrently.**
- **Need for more detail in measures of wasting and stunting to allow us to see the physiological/ functional outcomes of the conditions and of 'recovery' in children (e.g. use of knee-heel length, standing:sitting height ratio, muscle mass measures).**
- **Evidence for body composition in stunted and wasted children, in particular muscle and fat mass.**
- **Understand whether the active process of stunting (slowing of linear growth) or wasting (loss of weight) carries greater risks for a child compared to the end point of being stunted or wasted in relation to the growth reference.**
- **The role of gut health/inflammation in wasting as well as stunting.**
- **Early life undernutrition may have a long-term impact on adult health – the relative contributions of wasting, stunting and the combination of both, need to be further explored.**

Annex 1
Limitations of the evidence

Standards: Studies conducted prior to 2006 when the WHO growth standards for infant and young children we released, use NCHS reference for the identification of stunted and wasted children. Therefore, the associations found or not found between wasting and stunting may not be comparable with studies using the WHO standards. In addition, there is some indication that the weight-for-height index is affected by body shape (specifically sitting-to-standing height ratio), therefore particularly in 'long legged' populations (such as pastoralists) it may overestimate 'wasting' as a result (Myatt, Duffield et al. 2009).

Classification v. process: Studies tend to categorise children as stunted and/or wasted and then look at the associated factors. This has a number of limitations.

- *Stunting v. stunted:* a child defined as stunted will, depending on where they were previously growing on the height for age curve, have already gone through a period of stunting before reaching the 'stunted' classification. Another child may have been born already in the 'stunted' category. The factors leading to stunting in these two children are likely to vary and the role of wasting in each of them may also be different.
- *Wasting v. wasted:* Similarly, depending on their previous weight-for-height, the period and magnitude of weight loss which leads to a child being classified as 'wasted' will vary. If studies only look for the relationship between being wasted and stunted they may miss associations between periods of wasting (or weight loss) and slowing or halting of linear growth i.e. stunting.
- *Shifted distributions:* In developing countries the entire distribution of child heights can be shifted downwards compared to the WHO standard. In this case it is apparent that actually the majority of children may be growing beneath their full potential, not just those below the <-2SD cut-off.

Cross sectional data: Much of the evidence for the associations between wasting and stunting, particularly at population level uses cross sectional data. This is problematic however, for a number of reasons:

- *Status v. process:* Cross sectional data only represents a child's current anthropometric status, not what they went through in terms of height gain velocity or weight loss to get to that point. As noted above, the strength of associations identified between wasting and stunting may be influenced by this.
- *Prevalence v. incidence:* Evidence suggests (as noted above) that wasting is more acute and reversible than stunting, therefore the use of prevalence rather than incidence of bouts of wasting over time is more likely to be misleading.
- *Seasonality:* Evidence of seasonal and divergent patterns in both wasting and stunting prevalence throughout the year, mean that the timing of cross sectional surveys (which may be done at a time of low or high wasting prevalence) can lead to a distorted understanding of the levels of both wasting and stunting in a population. Incidence and/or longitudinal data, with repeated measure over time, would be needed for a representative picture.
- Separation: Some studies treat wasting and stunting as separate phenomena rather than potentially overlapping processes, which are often occurring at the same time in the same child and are influenced by a multitude of f actors. This separation fails to recognise the possibility that a child who is stunted but not wasted, may have been exposed and be responding to a different combination of causal pathways, to one who is stunted and also currently wasted.

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