MQSUN+ REPORT

The Aetiology of Wasting

16 February 2018

About MQSUN+

MQSUN+ aims to provide the Department for International Development (DFID) with technical services to improve the quality of nutrition-specific and nutrition-sensitive programmes. The project is resourced by a consortium of five leading non-state organisations working on nutrition. The consortium is led by PATH.

The group is committed to:

- Expanding the evidence base on the causes of undernutrition
- Enhancing skills and capacity to support scaling up of nutrition-specific and nutrition-sensitive programmes
- Providing the best guidance available to support programme design, implementation, monitoring and evaluation
- Increasing innovation in nutrition programmes
- Knowledge-sharing to ensure lessons are learnt across DFID and beyond.

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About this publication

This report was produced by the Emergency Nutrition Network (ENN), through the MQSUN+ programme. Drawing on the work of the ENN coordinated Wasting and Stunting (WaSt) and Management of At-risk Mothers and Infants (MAMI) technical groups, this report summarises the state of the thinking on the aetiology of wasting. It is not, however, based on a systematic review of the published literature.

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Abbreviations

BMI	body mass index
DFID	Department for International Development
ENN	Emergency Nutrition Network
MQSUN+	Maximising the Quality of Scaling Up Nutrition Plus
MUAC	mid-upper arm circumference
SD	standard deviation
UNICEF	United Nations Children's Fund
WFA	weight-for-age
WHO	World Health Organization
WHZ	weight-for-height z-score

Executive Summary

Although wasting is commonly considered an acute condition because it can be relatively rapid in onset and resolution compared to other manifestations of undernutrition, the immediate or underlying factors that drive wasting are long-standing in nature.

In considering wasting, we must look beyond the standard World Health Organization (WHO) definition to additional measures that identify nutritional vulnerability and risk of death.

In order to better understand wasting aetiology, we need to consider its dynamic nature (incidence), seasonal patterns and its relationship with previous wasting and other deficits, in particular stunting.

Our knowledge of the physiology of wasting is still limited, although evidence suggests that associated metabolic disturbances continue beyond the episode of wasting, leading to increased vulnerability to repeated periods of wasting and subsequent stunting. We therefore need to prevent and catch wasting (faltering/loss of weight) early to both maximise survival and prevent longer-term deleterious effects impairing the child's ability to thrive.

Analysis of risk factors for wasting in different contexts concludes that there are multiple risk factors at play, that the combination changes over time and with the age of the child and that these factors interact with each other. Therefore, although there are some usual suspects, good context-specific causal analysis that maps pathways to wasting over time is required to inform the design of appropriate packages of interventions to prevent wasting effectively.

It is clear that risk of wasting originates from the early stages of a child's development (including in utero) and that these early experiences continue to influence wasting and the associated risk of death / poor development throughout childhood. This highlights the need to act to address these early determinants (through support to adolescents and women) to support optimal foetal development and infant feeding to reduce the burden of childhood wasting and the associated risks.

A number of key research questions arise in relation to wasting aetiology specifically. These include the following: Why are boys consistently more at risk of wasting than girls? What mechanisms lead one child down the pathway to wasting compared to another child born into the same impoverished conditions? How and to what extent does in utero experience amplify risk of wasting in response to external factors during infancy and childhood?

The growing evidence base demonstrating the association between wasting and stunting, the overlap of risk factors and the multiplicative effect of dual deficits on mortality risk points to the need for joint strategies for identification of risk and for prevention. It is time to reconceptualise how we deal with different forms of malnutrition, to forge a joined-up approach centred on degrees of vulnerability to death and impaired development. A new framework would aim to prevent periods of nutritional vulnerability, including during pregnancy and the first six months of life, from leading to progressively more at-risk children, both in the short- and long-term.

1. Introduction

The Department for International Development (DFID) has commissioned, through the Maximising the Quality of Scaling Up Nutrition Plus (MQSUN+) programme, a multiphase scope of work on '*Adopting a Strategic, Evidence-based Approach to Wasting Prevention*'. The Emergency Nutrition Network (ENN) has taken on this work on behalf of MQSUN+. The first phase is to compile a summary of the current state of thinking on wasting prevention. As such, ENN has prepared this report, which describes current knowledge/thinking on the aetiology (causality) and physiology of wasting, to lay the foundation for the work. The subsequent piece in this phase will be a summary of the evidence of what works to prevent wasting and the key actors involved in this area.

2. Background

Only 29 out of 193 countries are on course to achieve the World Health Assembly 2025 target of maintaining levels of wasting below 5.0 per cent (Development-Initiatives 2017). There are an estimated 52 million wasted children in the world at any point in time, representing 7.7 per cent of all children under five years of age (United Nations Children's Fund [UNICEF], World Health Organization [WHO], and Bank 2017). This burden figure is likely significantly higher if corrected for incidence, as is the standard practice in estimating caseloads for programmes. Even when underestimated, these levels are significant and notably not confined to areas of humanitarian crisis. In South Asia, for example, where 15.4 per cent of children under five years of age are wasted, this constitutes an ongoing, critical public health emergency according to WHO (ibid). These global estimates are also problematic for the estimation of burden of wasting specifically in infants under six months of age due to the exclusion of the smallest infants (less than 45 cm long). Burden of wasting in infants under six months of age has been elsewhere estimated to total 8.5 million (Kerac et al. 2011).

Wasting leads to weakened immunity, susceptibility to long-term developmental delays and an increased risk of death, especially in its most severe form or when combined with stunting (McDonald et al. 2013). Different estimates find that severely wasted children 6 to 59 months of age are 9 to 12 times more likely to die than are their healthy counterparts (Black et al. 2008; Olofin et al. 2013). On a population level it has been calculated that wasting is a cause of death for 12.6 per cent of children under five years of age (Black et al. 2013), though, as indicated above, this is an estimate based on prevalence rather than incidence figures.

Where previously the global community had tended to focused on wasting in relation to mortality risk and in the context of humanitarian crisis, there is increasing recognition that its impact is broader. There is emerging evidence from a number of analyses that wasting is a 'harbinger of stunting', (Richard et al. 2012; Schoenbuchner et al. 2018; H. Stobaugh et al. 2018 in press) indicating that progress on wasting may also affect progress towards World Health Assembly stunting targets.

There are many identified gaps in our understanding of the aetiology of wasting.[i] A recent article by Trehan and Bassat looks back at the last two decades and notes remarkable progress in the

[i] https://www.nowastedlives.org/researchagenda

treatment of severe wasting, in contrast to the neglected study of the fundamental risk factors, mechanism and pathophysiologic changes contributing to the condition's development. This knowledge gap, it is argued, critically hampers our ability to prevent wasting (Trehan and Bassat 2018).

3. Scope and Definition

This report explores what we know about the physiology of wasting and the causes, predispositions and pathways that lead to the condition (its aetiology). We focus on the period of conception to five years of age, exploring the evolution of wasting over time, its relationship with stunting, its presentation in boys and girls and the importance of context in wasting aetiology.

At the outset, it is important to note that the definition of 'wasted' in Box 1, whilst standard, is limited for the purposes of this note. Firstly, in order to explore aetiology, it is important to investigate the process of wasting, not just the state of being wasted (i.e., what factors lead a child to go through a period of weight loss in relation to his/her height, which may lead to a diagnosis of being 'wasted'). Secondly, it is also important to consider what can cause a child to become progressively more wasted, with increasingly dire consequences, is also important to consider.

Wasting is commonly considered an acute condition, simply because compared to other manifestations of undernutrition it can be relatively rapid in onset and resolution. Hence the term 'acute malnutrition' (divided into moderate and severe) is commonly used to describe children who are wasted. However, the term 'acute malnutrition' also includes children suffering from the other relatively rapid onset form of undernutrition, kwashiorkor (characterised by nutritional oedema), as well as children with a low mid-upper arm circumference (MUAC) characterised by a loss of muscle and fat tissue (see Box 1).

In the potential confusion of different definitions, it is important to note that malnutrition in general, and wasting in particular, is a functional problem—specifically, 'a lack of uptake or intake of nutrition leading to altered body composition [...] and diminished physical and mental function' (Cederholm et al. 2015), for which anthropometric measures are only proxies. For this reason, although they are outside of the standard WHO definition of 'wasted', included in this note is consideration of the other recognised ways of identifying a relatively acute period of undernutrition (acute malnutrition) associated with heightened risk of death. These are Kwashiorkor (see Box 2) and low MUAC (WHO and UNICEF 2009).

We also include some consideration of low weight-for-age (WFA) due to strong evidence for its relationship with mortality in infants and children and because it partly reflects wasting on an individual level (Myatt et al. 2017; Pelletier, Frongillo, and Habicht 1993). In infants under six months of age, WFA and MUAC have been identified as the best measures for targeting those with the highest risk of subsequent mortality (M. Mwangome et al. 2017).

Box 1. Definitions (children 0–59 months)

Wasted
Weight-for-height <–2 SD of the WHO Child Growth Standards median
And for severely wasted <–3 SD (WHO)

Acute Malnutrition (including severe)
Weight-for-height <–2 SD of the WHO Child Growth Standards median
MUAC<125 mm
Nutritional oedema (Kwashiorkor)

Severe Acute Malnutrition
Weight-for-height <–3 SD of the WHO Child Growth Standards median
MUAC<115 mm (for infants a smaller cut-off has been suggested)
Nutritional oedema (Kwashiorkor)

Note: SD=standard deviation.

The Gender Equality Act of 2014 requires meaningful, proportional consideration of gender issues in all DFID investments. This report does this by considering how risk of acute malnutrition can differ by gender (Section 5).

4. The Physiology of the Wasted Child

Our understanding of the physiological mechanisms that accompany wasting comes mainly from literature on long-term starvation and chronic illness (Bhutta et al. 2017).

Starvation

We know that, in the short-term, in response to several days of fasting, the body depletes its fat stores and then breaks down proteins in order to use them to maintain essential metabolic processes. The release of hormones regulates this process but can also lead to reduction of appetite and breakdown of skeletal muscle (muscle wasting).

Infection and metabolic disturbance

For many years we have recognised that the relationship between infection and undernutrition is cyclical (Jones and Berkley 2014). Children with severe wasting are highly susceptible to life-threatening infections as a consequence of immune dysfunction. A recent review takes this further, proposing that immune dysfunction is both a cause and a consequence of malnutrition, contributing directly to the mortality and morbidity associated with undernutrition in general and wasting in particular (Bourke, Berkley, and Prendergast 2016). There are a number of mechanisms for this. Firstly, during wasting the skin, respiratory and intestinal mucosa can become impaired and therefore vulnerable to attack by pathogens. Infection can also compromise the integrity of the gut,

leading to malabsorption of nutrients. In addition, immune response to pathogens/bacteria may be reduced or a chronic inflammatory response activated. Infections, in turn, suppress appetite and further deplete nutrient stores (Bhutta et al. 2017).

Studies looking at relapse in children treated for severe wasting or low MUAC find that those who are more severely malnourished on admission for treatment (i.e., those with the greatest metabolic disturbance) are most likely to relapse (H. Stobaugh 2017 in draft). One possible explanation for this is that treatment does not adequately correct the metabolic disturbances / biological mechanisms involved, leaving children with a deficient immune defence. Quality of protein may also impact relapse rates as ready-to-use foods containing milk have been associated with lower relapse rates following consumption by children treated for moderate wasting than in those treated who had no animal-sourced protein consumption (Chang et al. 2013; H. C. Stobaugh et al. 2017; H. C. Stobaugh et al. 2016). It may also be that changes in the gut bacteria that accompany wasting do not recover during treatment, affecting the child's ability to absorb nutrients even when they are no longer wasted (Kerr et al. 2015; Keusch et al. 2013; Subramanian et al. 2014).

Recent analysis from The Gambia found that infants who were wasted in the first lean or hungry season of their lives had a 3.2 times higher risk of being wasted in their second similar season, even if they had recovered during the intervening dry season (Schoenbuchner et al. 2018). This is important because, like the above, it indicates that a wasted child is more vulnerable to subsequent wasting. It is possible that some of the above unresolved metabolic disturbances are at play here.

An alternative explanation for heightened vulnerability to wasting following a first episode is simply that the same environmental and/or external conditions that initially caused the wasting remain, or even that an earlier risk factor, perhaps during foetal development (see Section 5), leaves a child more vulnerable to becoming wasted in response to seasonal stresses. Though concrete evidence is still lacking on the role of the above metabolic factors versus or alongside persistent environmental/external factors in the progression of wasting and relapse, their potential involvement underlines the importance of catching children early in the process of wasting before these metabolic disturbances occur.

Knowledge of the physiology of wasting in infants under six months of age is especially lacking as they are often inadequately represented in research and programmes addressing wasting. We do know that there is a higher mortality found in this group, compared to older children, during treatment for severe wasting (Grijalva-Eternod et al. 2017), but the question of whether this is linked to physiological consequences of their small size at birth or issues with late presentation and inappropriate treatment has not been sufficiently examined. It is clear, however, that we need to consider the mechanisms and consequences of small size at birth (i.e., low birth weight, premature or small for gestational age), susceptibility to illness and the role of suboptimal breastfeeding in understanding the progression of wasting in this group.

5. Determinants and Pathways to Children Becoming Wasted

As noted in a recent state-of-the-art summary on severe malnutrition in children, when it comes to exploring the aetiology of wasting, we need to recognise 'the long-standing nature of the combined

infectious and environmental insults that can occur in such cases' (Bhutta et al. 2017). In other words, although the condition may be relatively acute, the immediate or underlying factors that drive wasting are not necessarily so.

Analysis of risk factors

Wasting, characterised by loss of muscle and fat tissue, is understood, on a simple level, to be caused by inadequate protein and energy intake resulting from food insecurity, poor diet and disease (Bhutta et al. 2017). However, individual country-level studies and reviews (Akombi et al. 2017; Bhutta et al. 2017) conclude that there are multiple risk factors for wasting in a given context and that the combination of these factors change over time and with the age of the child. Factors found to be significant in one context may not be in another; and in contexts of population displacement, conflict and food shortage, for example, there may be heightened impact of the same risk factor that was in place pre-crisis. Various studies and systematic reviews have explored the different risk factors for wasting, though it is worth noting here that a larger body of study focuses only on risk factors for stunting without consideration of wasting. Table 1 lists common risk factors for wasting identified in reviews across a number of contexts.[ii]

Table 1. Risk factors associated with becoming wasted (moderate or severe) in children.

Category	Risk Factor (reference)
Maternal	Maternal stature (Ozaltin, Hill, & Subramanian, 2010)
	Low maternal body mass index (BMI), or thinness (Victora et al., 2015)
	Intrauterine growth restriction[iii] (Christian et al., 2013)
	Mothers education level (Victora et al., 2015) and level of empowerment[iv] (Kerac, Frison, Connell, Page, & McGrath, 2018 submitted)
Child Diet and Disease	Infectious disease (Olofin et al., 2013)
	Diarrhoea (Richard et al., 2013)
	Delayed start of breastfeeding & pre-lacteal feeds[v] (Kerac et al., 2018 submitted)
Environmental/ Cultural/Social	Seasonality (Brown, Black, & Becker, 1982; Kinyoki et al., 2016; Schoenbuchner et al., 2018)
	Household wealth (Akombi et al., 2017; Martorell & Young, 2012)
	Gender (Akombi et al., 2017; Khara, T, Mwangome, Ngari, & Dolan, 2017)

Unsurprisingly, given the conclusions on risk factors above, a number of additional factors have been identified inconsistently in individual studies; these include water sanitation and hygiene practices (Raihan et al., 2017) aflatoxin exposure (McMillan et al., 2018) and dietary diversity (Amugsi, Mittelmark, & Larty, 2014).

[ii] Factors identified in individual context studies have not been mentioned here. They are numerous and a specific review of the literature would be required to document all of them.
[iii] Identified by measuring whether the child is small for gestational age at birth.
[iv] In infants under six months of age.
[v] In infants under six months of age.

A limitation to interpretation of the significance of different risk factors is that the majority of studies do not deal with the complex interactions between risk factors and do not recognise that several can have a cyclical relationship with wasting (i.e., as both a cause and result of wasting). It is these interactions that make the aetiology of wasting so complex. Although depicted as linear in the commonly-used UNICEF conceptual framework on undernutrition, different determinants of wasting—such as disease, diet, feeding practices and access to health care—do not act in isolation. For example, a bout of diarrhoea may lead to a child losing weight and becoming wasted as the body loses nutrients and appetite becomes poor. However, weight loss may not lead to wasting if a number of preconditions are met: the issue is identified early (knowledge), appropriate treatment is sought and received (health service access and quality), other positive feeding and caring practices are not stopped during the illness (e.g., breastfeeding due to beliefs about disease), appropriate foods are available to sustain the child and support recovery and children have sufficient time to recover before succumbing to a new bout of diarrhoea. The absence of one or more of these preconditions may lead to the child becoming wasted (i.e., meeting any one of them in isolation will likely be insufficient to protect the child from wasting). This complex web of factors makes it difficult to impact levels of wasting through single interventions.

Box 2. What do we know about the aetiology of Kwashiorkor

Recent analysis of the prevalence and importance of Kwashiorkor (nutritional oedema) concludes that it is likely far more common than surveys suggest, representing more than one-third of admissions to therapeutic programmes in a significant number of countries. Kwashiorkor is most common in Africa, often occurring alongside wasting or low MUAC (though this is variable according to context). It is common among younger children from 6 to 29 months of age (Alvarez, Dent, Browne, Myatt, & Briend, 2016) but rarely found in infants under 6 months of age. Children with Kwashiorkor have high mortality, particularly when it occurs alongside low MUAC, and have in the past been notoriously difficult to treat. Although its management has spectacularly improved since its first documentation in 1933, the aetiology of the condition remains an enigma. Specific micronutrient deficiencies have been suggested, as has insufficient protein intake or low intake of specific amino acids, guided by the response of the condition to a milk-based treatment. A possible role for kidney dysfunction, aflatoxin ingestion, oxidative stress in response to infection, abnormalities in the gut microbiota or a combination of these has also been suggested, with variable evidence (Briend 2014). However, there is still no agreement, and calls for more hypothesis testing remain relevant (Manary, Heikens, Golden, 2009). Ongoing initiatives are under way to fill this evidence gap (MSF 2017).

Origins

From a combined analysis of 19 studies measuring children at birth and tracking their progress throughout childhood, we know that across different populations, about 30 per cent of wasting has its origins in the foetal period (i.e., that wasting during childhood is strongly associated with foetal growth restriction in the womb) (Christian et al. 2013). Although the mechanism is not clear, maternal nutrition or epigenetic effects (changes in gene expression that occur during foetal growth) are suggested.

The study of infants who are wasted at birth is complicated by the fact that traditionally we measure whether a child is low in birth weight or small for his or her gestational age, neither of which differentiates between whether the infant is stunted or wasted. A large multi-country project specifically identified infants wasted at birth and found that a low educational level of the mother (less than 8 years of schooling) was associated with a 40 per cent greater risk of her infant being

wasted than that of mothers with higher educational levels (12 years of schooling or more). However, as noted above, there are many potential confounding factors in the relationship between mothers' education and infant wasting. The newborns of short mothers (height <150 cm) were 1.9 times more likely to be wasted compared with those who were taller (≥170 cm), and low maternal BMI (<18.5) was associated with an approximately 2-fold increase in risk of both stunting and wasting compared with a BMI of 25 or more (Victora et al., 2015). What is clear is that there are important determinants of wasting at play prior to birth.

Persistent wasting

A recent review of contexts where wasting levels have remained high despite numerous interventions (so-called persistent wasting) highlights the limited understanding of the pathways to wasting and, therefore, the optimal points at which to intervene. The review concludes that increased support for context-specific causal analysis is required as part of the programme cycle, in addition to longitudinal analysis which takes into account seasonal patterns in nutritional status, in order to produce a more reliable understanding of the cause-and-effect pathways and to allow appropriate packages of interventions to be designed (Young & Marshak, 2018).

Wasting and seasonality

Peaks in wasting levels at certain times of year are commonly documented (Brown et al., 1982; Egata, Berhane, & Worku, 2013; Kinyoki et al., 2016). These often coincide with periods of heightened food insecurity or disease, but there is not a consistent pattern between countries (i.e., not always in the lean or hungry season) (Young & Marshak, 2018). This probably reflects seasonal patterns in the different types of determinants, their interactions with each other and with underlying vulnerabilities.

In an analysis of longitudinal data from The Gambia (Schoenbuchner et al., 2018), infants born at the start of the hungry season were found not to experience the same gains in weight during the first three months of life as their peers born in other months. This indicates that it is not only nutritional status at birth but also the season of birth, which may predetermine a child's experience of wasting throughout childhood. The reasons for this pattern may lie in infant feeding practices or maternal nutrition, or in the sorts of epigenetic effects mentioned above.

The finding (detailed in Section 4) that a child who experiences one period of wasting is more vulnerable to subsequent periods of wasting, particularly during seasonal peaks each year, is also important irrespective of the mechanism for this, as it indicates that prior wasting is an important indicator in determining current risk.

Wasting and gender

A number of recent multi-country analyses have highlighted the higher levels of wasting and of concurrent wasting and stunting in boys compared to girls (Khara et al., 2017; M Myatt et al., 2017; Schoenbuchner et al., 2018). This is contrary to the assumption often made by development professionals that girls are more vulnerable to malnutrition, fuelled by a perception that boys get

preferential care/priority in general, and perhaps by studies illustrating preferential infant feeding practices for boys (Fledderjohann et al. 2014). The reasons for these higher levels of wasting in boys are unknown but a similar pattern has been found for stunting across multiple countries (Wamani, Astrøm, Peterson, Tumwine, & Tylleskär, 2007). Theories include sex-specific gender differences in stress response, established in utero, or the existence of cultural practices that apply specifically to boys and may inadvertently undermine their nutrition. There is also an ongoing debate amongst international technical nutrition groups regarding the possibility that the construction of the WHO growth standards has in some way created this disparity. Overall, there is currently a lack of clarity as to why this vulnerability exists.

6. A Cautionary Note: Complexities related to the assessment of wasting

Population level

Estimating the proportion of wasted children in a population is based on whether they fall significantly below the WHO's Child Growth Standards[vi] weight for their height at the time of measurement. However, the acute and dynamic nature of the condition means that the number of children experiencing a period of being wasted within a year is not well captured with this method. Country-specific estimates of incidence suggest that as many as 13 times the number of children who are wasted at one point in time (prevalence) may experience a period of being wasted within a year (incidence) (Bulti et al., 2017). Furthermore, as noted above, since weight-for-height z-score (WHZ) cannot be calculated in infants less than 45 cm in length, this excludes the youngest children from prevalence or incidence analysis. These various challenges limit the usefulness of population-based surveys to explore the relationship between incidence of wasting and different risk factors as many infants and children who are wasted will not be included. We also know that levels of wasting are not uniform across geographies and sociocultural strata and that levels tend to surge at particular times of year (Altare, Delbiso, & Guha-Sapir, 2016). This means that extrapolations either within or between populations should be made with caution.

Individual level

As noted above, a child is defined as being wasted if he or she falls significantly below the standard WHO growth reference cut-off point. Further division is made into severely or moderately wasted depending on standard deviation cut-offs. On an individual level, this wrongly suggests that something fundamentally different happens to a child at that cut-off point, whereas in general functional outcomes deteriorate progressively as undernutrition worsens (Pelletier et al., 1993). Secondly, we are not able to differentiate between the ways in which a child may reach that cut-off

[vi] Standards are based on healthy, mostly breastfed children living under conditions likely to favour achievement of their full genetic growth potential. They are based on measurements taken from privileged populations in Brazil, Ghana, India, Norway, Oman and the USA to reduce the impact of environmental variation.

point. There is a common assumption that to get to the 'state' of being wasted, the child has gone through an acute period of weight loss. However, there is evidence on the effect of body type on the weight-for-height wasting measure, suggesting that in certain 'long-limbed' pastoralist populations (e.g., Ethiopia, Somalia, South Sudan), a child with a normal and healthy weight may fall into the 'wasted' definition without the associated mortality risk (Myatt, Duffield, Seal, & Pasteur, 2009). The magnitude of this effect has not been quantified but adds to the complexity of interpreting measures in certain subpopulations.

At the other end of the spectrum, the focus on the state of being wasted rather than on the process of wasting leads us to be unconcerned about a child who may start with an above-average weight for his or her height but who then experiences a dramatic weight loss which does not yet fall below the stated cut-off. These children are also at risk. However, the move away from periodic monitoring of growth due to implementation issues and lack of demonstrated effectiveness means we seldom have sufficient regularity of measurements to identify children experiencing weight loss and to intervene before they become wasted.

A case definition for wasting amongst infants under six months of age is not yet clearly established, although this has been identified as a top research priority (Angood et al. 2015). A number of questions exist: whether the same WHZ thresholds used for older children are appropriate for infants; what measures could work for the smallest children; and whether anthropometric measurements themselves are reliable in early infancy (M. K. Mwangome & Berkley, 2014). Evidence suggests that the length measurement in particular is most often missed in this age group (Grijalva-Eternod et al., 2017). This continued lack of agreement is a barrier to examination of aetiological mechanisms of wasting in this age group.

7. Towards a Broader Understanding of Nutrition Vulnerability

A review of the literature on risk factors for both stunting and wasting conducted in 2012 concluded that there are no risk factors for wasting that are not also risk factors for stunting (Martorell & Young, 2012) . An overlapping pattern of intrauterine and maternal risk factors was found for children born wasted and those born stunted (Victora et al., 2015). This does not mean that by preventing stunting, wasting will automatically also be prevented, or vice versa. As noted above, the combination of factors, and their interaction in a given context, may differ. However, it does mean that it is likely that approaches that aim to prevent wasting and stunting could benefit from looking for common determinants.

Research also indicates that there is a direct relationship between wasting and stunting—in particular, that periods of being wasted, or of fluctuating weight, increase the odds of a child becoming stunted within the next three months (Richard et al., 2012; Schoenbuchner et al., 2018). A similar relationship has been described in infants under 6 six months of age in a study in Bangladesh. In this context, infants who were severely wasted (WHZ<–3) at birth were significantly more stunted, and at severely stunted levels, at six months of age than their non-severely wasted controls (Islam et al., 2018 submitted). These findings concur with recent research indicating that linear growth slows during periods of severe wasting and speeds up again after recovery (Isanaka, 2018; H. Stobaugh et al., 2018 in press).

Being wasted and stunted concurrently leads to a multiplicative increase in mortality risk (McDonald et al., 2013; Myatt et al., 2017). For these children, having both deficits in some way amplifies the risk of death to levels that are comparable to that of the most severe form of wasting. This evidence concurs with the common finding that measures reflecting both wasting and stunting in infants and children (i.e., MUAC and WFA) are most closely related to risk of death (A. Briend & Zimicki, 1986; M. Mwangome et al., 2017; Pelletier et al., 1993). The mechanisms for this heightened mortality risk are not clear, but one proposed theory is that effects of dual deficits on muscle mass may play a role given that a combination of shortness and thinness has a multiplicative effect on loss of muscle (A. Briend, Khara, & Dolan, 2015). Irrespective of the mechanism, however, the evidence suggests that the heightened risk from being both stunted and wasted needs to be considered to identify children most vulnerable to dying as a result of nutritional deficits.

8. Conclusions and Implications

Programme

- The aetiology of wasting is complex and there are numerous, interdependent and context-specific causal and associated factors at play. This means that more attention must be given to robust context-specific analysis of causes to ensure programmes are designed to address the main determining factors along the causal pathway to wasting. Current methodologies for causal analysis are not yet strong enough to do this and will need to evolve.
- Wasting has its origins at the very early stages of a child's development (including in utero), and early life factors continue to influence a child's experience of wasting and associated risk of death / poor development through childhood. This highlights the need to act to address these early determinants (through support to adolescents and women) to promote optimal foetal development and infant feeding to reduce both the burden of childhood wasting and the associated risks. Early actions to reduce wasting in the infant under six months of age also have the potential to reduce the burden of wasting in older children.
- The implications of the progression to being wasted and increasingly more wasted can be long lasting and include a heightened risk of concurrent stunting, repeated periods of wasting and impacts on body composition and metabolism, including immunosuppression. Therefore, we need to prevent and catch wasting (faltering/loss of weight) early, both to maximise survival and to prevent longer-term deleterious effects that impair the child's ability to thrive. There may be opportunities to do this through the entry point of existing monitoring of growth using WFA (which is still widespread in health facilities, even at the community level, despite poor demonstration of effectiveness), facilitating the identification of children most at risk and/or who are deteriorating and who need to be referred for appropriate action/services.
- Seasonal patterns in risk factors play an important role in the aetiology of wasting, both prenatally and during childhood. More work is needed on the development and piloting of comprehensive seasonal approaches which coherently focus on mothers, infants and children and monitor seasonal effects on the incidence of wasting.

- The growing evidence that concurrent wasting and stunting heightens mortality risk implies that current programmes that aim to address wasting need to broaden their scope to consider the interaction with stunting to identify those children at greatest risk and prevent their death.

Research

- The differential experience of wasting amongst boys and girls offers a good example of why gender is such a critical consideration and has been highlighted as a priority area for further investigation.
- Though evidence suggests a link between in utero, infant and childhood experience of wasting (and indeed stunting) there is work to be done in understanding how the in utero experience interacts with social/environmental stresses to amplify the risk of becoming wasted, and repeatedly so.
- As recognised in the introduction, there are still many unanswered questions around the aetiology of wasting. The question remains why some infants and children born into and/or living in the same impoverished conditions, exposed to the same pathogens and environmental toxins, and exposed to the same poor diets and feeding practices become wasted, while others manage to avoid this fate or become stunted instead. To prevent wasting, we must better answer that question. Questions of wasting aetiology and how it differs by age and geography have already been highlighted in a recent research prioritisation initiative.[vii] In the coming months, under this project, work will be undertaken to build on this and prioritise the major research questions to be answered relevant to the prevention of wasting, including these elements of aetiology that remain enigmatic.

Policy

- The growing evidence base demonstrating the association between wasting and stunting, the overlap of risk factors and the multiplicative effect of dual deficits on mortality risk points to the need for joint strategies for identification of risk and for prevention.
- Finally, and a key conclusion, it is time to reconceptualise how we deal with different forms of malnutrition, to forge a more joined-up approach centred on degrees of vulnerability to death and impaired development. The current focus on wasting treatment and stunting prevention is unhelpful in this respect. Rather, we need to stop periods of nutritional vulnerability, including during pregnancy and the first six months of life, from leading to progressively more at-risk children both in the short- and long-term. For example, we can do this by addressing the drivers of nutrition vulnerability by reaching adolescent girls and women, as well as infants and young children, to prevent weight loss from turning into wasting and wasting into more severe wasting and/or stunting and to prevent a lethal combination of both driving more childhood deaths.

[vii] http://www.ennonline.net/newsroom/nowastedliveschnriacutemalnutrition

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