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A review of methods to detect cases of severely malnourished infants less than 6 months for their admission into therapeutic care

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Photos
Martha Mwangome/KEMRI-Wellcome, Kenya.

Background

It is estimated that worldwide 8.5 million infants under the age of 6 months (<6m) are wasted[1]. However it is only in recent years that acute malnutrition in infants <6m has been recognised as an issue requiring recommendations in international guidelines[2]. The 2013 World Health Organisation (WHO) guidelines on the management of severe acute malnutrition (SAM) now make separate and specific recommendations for infants <6m. However these recommendations are based on "very low quality" evidence[2]. With growing appreciation that malnutrition in infants <6m is a neglected public health issue[3] and recognising the huge paucity of current evidence, a systematic prioritisation of research questions was conducted in 2015[4]. Sixty-four experts scored 60 research questions and concluded that, as well the development of community-based treatment options, defining SAM in this age group was the top priority question.

The WHO guidelines currently recommend using weight-for-length (W/L) z-scores to diagnose SAM in infants <6m; however, this recommendation emerged from conventions of diagnosis in older children, rather than on scientific evidence. Since the publication of these guidelines in 2013, a small but growing number of robust studies have been published on diagnostic criteria, as well as additions to the existing body of grey literature. In striving to answer this basic and most urgent question regarding case definition, this report aims to review recent evidence in order to evaluate possible methods for detecting acute malnutrition in infants. The format closely follows that of a 2006 publication which reviewed methods for detecting SAM in children 6-59 months[5].

Objective

To review methods to detect cases of SAM in infants < 6 months in either community or healthcare settings.

Method

Guided by an existing review of methods for detecting SAM in children 6-59 months[5], we reviewed clinical and anthropometric methods for detecting SAM in infants <6m and assessed their ability to reflect both mortality risk and nutritional status.

Myatt et al.[5] based their framework for assessing SAM indicators on a general framework developed by Sacket and Holland for assessing the appropriateness of case-detection methods in different contexts using a scoring system within a set of seven properties: simplicity; acceptability; cost; precision (aka reliability); accuracy; sensitivity; specificity; and predictive value[6]. Following exploration of other case-detection frameworks[7,8], Myatt et al. identified three further properties that

are important for SAM case defining, namely objectivity; quantitativeness; and independence of age[5]. We therefore used these 11 properties in our review in order to assess each of the SAM indicators for infants <6m.

Indicators of SAM in infants <6m were selected based on those discussed in the 2012 systematic literature review for admission and discharge criteria for this age group[9]. A literature search of PUBMED, using the same search terms (see footnote[‡]), was conducted in order to identify any further indicators of SAM and evaluations of indicators that have been published since the 2012 review was conducted. Personal communications with authors of research in this field also took place in order to identify new or *in press* publications for inclusion.

Results

The 2012 literature review of SAM admission criteria noted that studies and national guidelines were using W/L for infants <6m as used for SAM in older children but differed in that there was no mid-upper arm circumference (MUAC)-based definition in this age group[9]. Although not included in the WHO guidelines for infants <6m, the WHO MUAC-for-age z-score reference data does begin at 3 months of age. The literature also highlights other possible infant indicators including weight-for-age (W/A), length-for-age (L/A), MUAC, MUAC-for-age

(MUAC/A) and clinical indicators, either for the infant or for risk factors in the mother such as the infant being too weak to suckle effectively or the mother not having enough milk or having other breastfeeding issues (aka "maternal milk insufficiency" (MMI))[9].

This report reviews each of the above selected indicators against each of the properties outlined by Myatt et al[5], drawing on data from the literature where available. The results are discussed below and summarised in **Table 2**.

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‡ Search terms: "protein energy malnutrition", "protein caloric malnutrition", "severe malnutrition", "marasmus", "kwashiorkor", "mortality" and "after recovery", "post-discharge" or "long term"

Simplicity

It is usually recommended that clinical assessments should only be performed by examiners who have been carefully and practically trained[8]. For assessment of undernutrition specifically, Myatt et al. highlight three studies which used clinical assessment to identify malnutrition in children 0-59 months, with variable results[5,10-12]. These, however, relied on anthropometry-trained health professionals. Two types of clinical assessments for identifying SAM in infants <6m months have been recommended in some national guidelines: 1) infant too weak to suckle 2) MMI[9]. There is some literature on assessing infant suckling suggesting that it is a process that requires patience and training[3]. Regarding MMI, this is less well described, and tends to rely on mother's reporting rather than a formal clinical assessment. A new tool (the 'C-MAMI tool') aimed at identifying and assessing infant malnutrition is currently being piloted and includes both anthropometric and clinical assessments in its protocol (http://files. ennonline. net/attachments/2435/C-MAMI-Tool-Web-FINAL-Nov-2015.pdf). A recent qualitative evaluation of this tool found that the clinical assessment sections of the tool were preferred by basic health staff for their greater simplicity compared to calculating anthropometric z-scores[13]. Although many of the clinical assessments in this tool are used to identify effective treatment pathways following diagnosis of malnutrition, there are some useful, simple signs of disease and breastfeeding problems listed which can be used for initial triage. Formal assessment of the effectiveness of this tool will be useful.

Many of the anthropometric assessments used for detecting SAM require assessment of age to compare with a reference population. Age is often not as simple in older children, described as Myatt et al., as difficult and often inaccurate, even in healthcare settings[5]. However, age in infants <6m is usually more reliable, given that the range of possibilities is much smaller and the issue of maternal recall bias is diminished. No formal studies were found assessing the simplicity or accuracy of age assessments in infants <6m.

The issue of preterm birth, where birthday may not be an accurate reflection of age, is relevant for this age group. There are concerns that preterm or low birth weight infants are more likely to be identified as malnourished and could lead to intervention whilst they are actually growing normally. However a recent study in Kenya found an elevated risk of mortality associated with anthropometry among preterm and low-birth weight infants, suggesting that they should be equally included in nutrition interventions[14]. The recent INTERGROWTH-21 project[15] which generated W/A and L/A growth standards for newborn and preterm infants, may be useful in clinical settings although are unlikely to be simple enough for all contexts.

Measuring length can be more challenging in infants <6m than older children due to their natural reflex to bend their legs. Length boards require that the infant lie flat on the board with their head against one plate while another plate is pressed against their feet. Any pointing of toes or bending of knees will affect the accuracy of this measure. One recent study which measured weight, length and MUAC in 1226 infants in Kenya[16] conducted an informal qualitative study to review the experiences of the field team conducting the measurements[17]. Their result suggested that mothers found the processes of measuring length quite distressing and some feared that the standard practice of "applying gentle pressure to the knees to keep them straight" would hurt and/or distress their infant. Health workers with no or little experience of measuring infants also reported that they found the process of handling the infants difficult. The article recommends training and practice in order to overcome this. Low confidence among staff at measuring infants in general, but especially infant length, was also noted in an earlier survey of international field staff[18].

Weight is a routine and more acceptable measure for all infants across many parts of the world, often recorded at each visit to a health centre, including immunisation visits. For example Integrated Management of Childhood Illness (IMIC) suggest

using weight to assess nutritional status in children as scales are likely to be available in most settings but length boards are not[10]. In Kenya, health workers reported that the only issue for taking weight was the removing of all clothes which the caregivers found concerning as it would expose the infants to cold and unhygienic equipment[17]. It was suggested that these issues could be overcome by initiating rapport with the caregiver and using clean sanitized equipment.

Besides raw values of weight and length, most anthropometric measures require conversion to z-scores or comparing a value to a reference cut-off before it can be used to identify malnutrition. A variety of studies have highlighted the added complexity for healthcare staff in calculating z-scores or using look-up tables[13,18,19]. Both W/A

z-scores and W/L z-scores have been highlighted as complex and error-prone,[20] however the additional complication of different length and height tables may make W/L the most complex of the indicators.

One anthropometric indicator which is used without z-scores is MUAC. For older children, MUAC is widely thought to be one of the simplest anthropometric measures, and the measure most strongly associated with mortality risk[21]. Although not currently used as a routine measure for infants, those who have used MUAC on infants <6m have not reported any issues in doing so[17]. As with older children, MUAC has the benefit of requiring only very simple equipment and minimal training and qualifications, making it ideal for community-based assessments.

Acceptability

Clinical assessment of both mother and infant, if the infant is breastfeeding, is likely to be an intimate process. Although a review of 15 breastfeeding assessment tools, none of which were developed specifically for identifying SAM in infants, was unable to formally assess acceptability of each tool, it does suggest that presence of a male health worker, and/or insufficient privacy from other staff and patients, would likely reduced the acceptability of these clinical assessment tools[3]. Those assessments which rely on questions alone rather than observations or examinations are likely to be the most acceptable to carers.

As discussed by Mwangome et al., carers and infants can become distressed during both length and weight measurements[17]. Infants often begin

crying during these measures as they are separated from their mother; and mothers and operators can have some anxieties relating to these methods, although they are not necessarily altogether "unacceptable". Additionally, the portability of some equipment, particularly height boards which can be heavy and bulky, may reduce the acceptability of length assessments in the eyes of community health workers. Acceptability of MUAC for infants <6m has not been formally reviewed, however studies that have applied MUAC have reported that it is more acceptable to carers and operators than height and weight as the infant can remain dressed, remain in their carer's arms, the mother can take the measurement[22], and MUAC tapes are highly portable.

Cost

Clinical assessments, in most disorders, require relatively highly trained personnel, which is costly[5]. The MAMI review of breastfeeding assessment tools found that 8/15 tools would not be

appropriate for a community-setting due to the personnel, equipment and time requirements[3]. There were some tools, such as the "Breastfeeding Assessment Score" (BAS) and UNICEF b-r-e-a-s-t

observational checklist which may be simple enough for use by community health workers, although some training would still be required. The recently developed 'C-MAMI tool' has specifically simplified the clinical assessment so that it requires less training and is therefore more cost effective, although it has yet to be formally evaluated (http://files.ennonline.net/attachments/2435/C-MAMI-Tool-Web-FINAL-Nov-2015.pdf).

A 2006 survey of 41 humanitarian relief workers found that balance beam scales were most commonly used in clinical settings and hanging spring scales in community settings[23]. Hanging spring scales cost £60-100, require replacing every 2-4 years with heavy use and lack the precision required for this age group. It is not clear whether this level of cost is acceptable across all settings, however as many rural clinics and community programmes routinely measure infant weight, resources could be saved by over-lap of equipment needs. Length, on the other hand, is not as routinely measured and therefore might pose too costly for some decentralised programmes relying on community health workers or volunteers, as is the case for older SAM programmes[10,24]. MUAC is likely to be the least costly assessment method as the equipment required is cheap (£0.30 (www.talcuk.org)) and training required is relatively minimal[24].

Objectivity and Quantitativeness

Clinical assessment is generally considered to be subjective, difficult to standardize and difficult to express quantitatively[5,8,12]. There are some objective indicators within clinical assessment which might be useful in triaging "at risk" infants, such as presence of infant structural abnormalities including cleft palate, outlined in the 'C-MAMI tool'. More nuanced assessment of infant feeding and maternal health is often subjective but can be useful, and indeed may be critical, in prescribing possible interventions for SAM rather than just detecting it. In contrast, anthropometric indicators are generally objective and quantitative, although not completely free of operator bias. It is important to note the distinction between frontline community screening for SAM which needs to be simple, low-cost and objective, and secondary level assessments after the problem has been identified, which would need to be more tailored, less simple and less objective.

Independence of Age

Myatt et al., outline that an indicator can be independent of age if either it is not influenced by age, or if its predictive power (specifically mortality) is not influenced by age[5]. Adjusting for age is one way of overcoming age dependence. However, as mentioned above, age assessments are sensitive to random errors, although this is less of an issue in infants <6m than in older children as errors in age assessment increase with age[25]. In early studies that promoted the use of MUAC as a tool for identifying mortality risk, MUAC was found to be relatively independent of age in older children (aged 1-5 years) but less so in infants <1 year of age[26].

However, a recent study in Kenya focussing on MUAC in infants <6m found that a single MUAC threshold of <11cm performed similarly to MUAC-adjusted-for-age (MUAC/A) in predicting mortality[14]. This was not to say that MUAC was independent of age, and as in older children, a single cut-off biases admission of younger infants who are more at risk of mortality, its predictive value is as good as MUAC/A and a single cut-off comes with many practical benefits. This same study also found that W/L, W/A and L/A were associated with age in infant <6m[14].

Precision and Accuracy

Accuracy refers to the closeness of a measure to a gold standard or known value. Precision refers to the closeness of measurements when repeated. Both accuracy and precision of age has been highlighted as questionable by some studies among older children[8,12], although this has not been formally assessed for determining malnutrition in infants <6m.

It can be argued that weight is usually inaccurate in many cases, as conventional hanging scales with 100g graduation units are not precise enough for calculating W/A in infants <6m[5,18], exemplified in Figure 1. However, the difference in mortality-related sensitivity, specificity and predictive value of hanging scales vs specialist infant scales for SAM in infants has not been formally assessed. A survey of relief workers found that, although not as portable as hanging scales, balance beam scales were considered accurate enough for field use[23]. Infant digital bench scales, although the most precise, were not commonly used in any settings. It must also be noted that the accuracy of weight can also be greatly influenced by clothing; in an audit of routine immunisation measurements in 375 infants in Malawi, clothes accounted on average for 9% of the infant's body weight (456g), highlighting the importance of removing all clothing before measurement[27].

Velzeboer et al., found that health workers made fewer mistakes using MUAC than W/A and W/H when assessing older children[24]; this is likely to be similar for infants. A recent audit of infants <6m admitted to a tertiary hospital in Malawi found that staff significantly under-diagnosed the proportion of infant malnutrition using W/L criteria; when W/L z-score was calculated post-hoc from raw recorded values, prevalence of wasting was 22.6% whereas at the time of measurement, ward staff only identified 3.1% as wasted, even following training[19]. The authors suggest that the true accuracy could be even poorer than presented as very short infants (<45cm) did not have a W/L calculation due to the lack of reference data.

Precision or reliability of weight and length, when measured under controlled research conditions, are thought to be generally high in children 0-2 years[28]. However, the reliability of z-score calculations was much lower than that of raw anthropometric values, especially in children <2 years[29]. For infants <6m specifically, a study in Kenya found that length was less reliable than weight and MUAC (intra-class correlation coefficient (ICC) measured by health professionals was 0.82 for length, 0.88 for MUAC and 0.99 for weight)[16]. For z-score calculations, W/L scored least reliable (ICC 0.60) followed by L/A (ICC 0.73) and then W/A (ICC 0.98). In addition, accuracy of W/L cannot be assessed in a significant proportion of this age group since, as noted earlier, there are no reference values for W/L in infants <45cm. A study comparing infant anthropometry data with older children found that infants <6m had significantly more missing data and more indices flagged as outliers than older children, largely due to lack of reference data for infants <45cm[30].
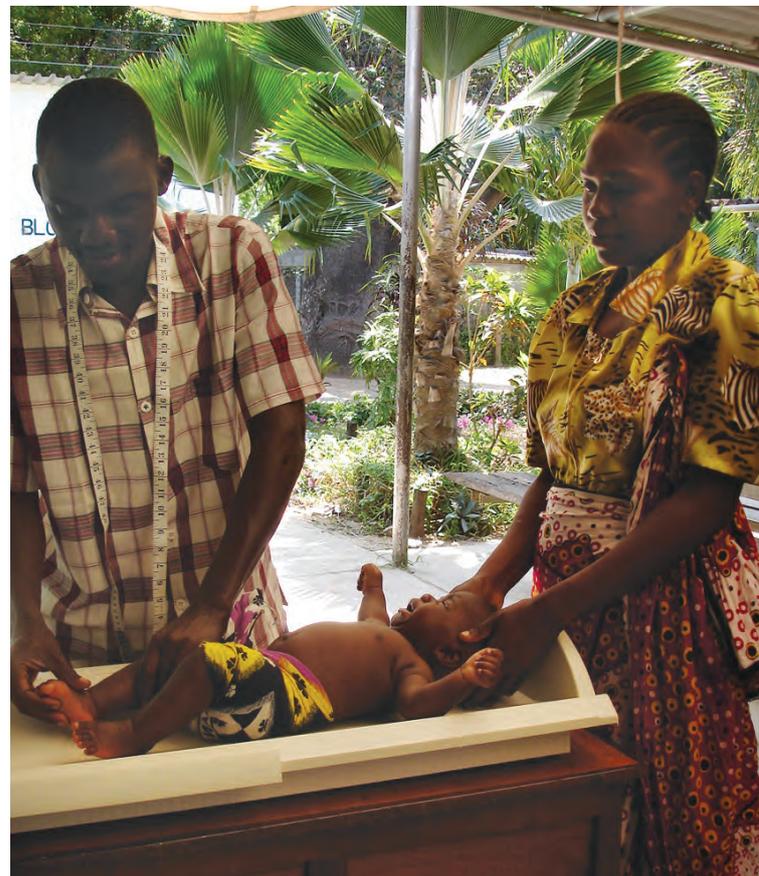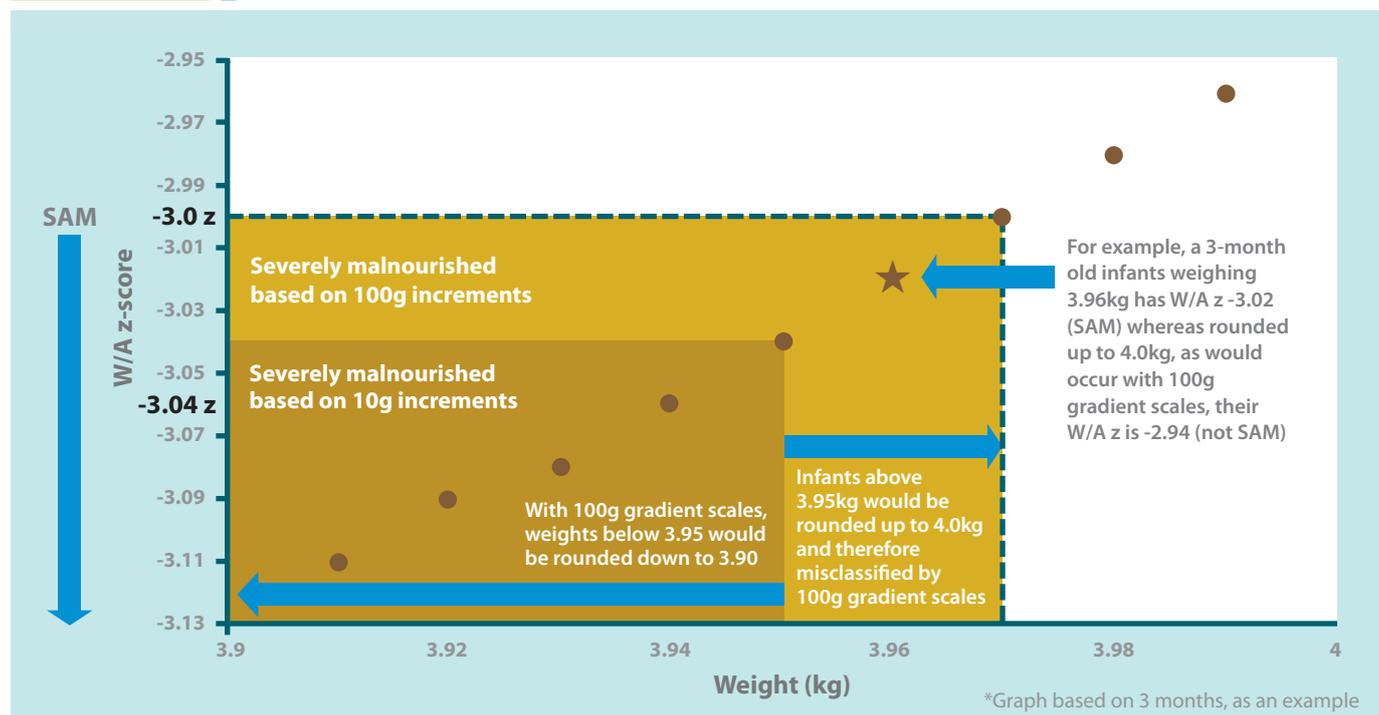
Figure 1 Weight-for-Age Z-score calculations for 100g gradient scales vs 10g gradient scales for a 3 month old infant

SAM

Severely malnourished based on 100g increments

Severely malnourished based on 10g increments

With 100g gradient scales, weights below 3.95 would be rounded down to 3.90

Infants above 3.95kg would be rounded up to 4.0kg and therefore misclassified by 100g gradient scales

For example, a 3-month old infants weighing 3.96kg has W/A z -3.02 (SAM) whereas rounded up to 4.0kg, as would occur with 100g gradient scales, their W/A z is -2.94 (not SAM)

*Graph based on 3 months, as an example

Note: W/A <-3 z-scores classifies an infant as "severely underweight" and could be used to classify SAM. This graph only shows weights 3.9kg to 4.0kg for a 3 month old infant, as an example.

Sensitivity, specificity and predictive value

In older children (12-59 months), a basic clinical assessment (described as "signs of visible severe wasting") had a sensitivity of 47% and specificity of 93% for predicting inpatient mortality[31,32], however, we did not find a study that had formally assessed this in infants <6 months. A review of existing breastfeeding assessment tools found that none would be sensitive enough for outpatient care nor specific enough for inpatient care in their current formats[3]. An audit of hospitalised infants in Malawi found that 72% of malnourished infants (identified by staff using W/L) were reportedly exclusively breastfed and most (63%) mothers reported confidence in breastfeeding[19], suggesting that these indicators alone may have low sensitivity for infant SAM or the method of assessment was inaccurate. Reported recent weight loss was high (>70%) among lower W/L infants, suggesting that clinical indicators for infants might have better sensitivity than breastfeeding indicators. However, a survey of infants attending routine immunisation

clinics in Malawi found that mothers who reported breastfeeding problems had infants who were 6.4 times more likely to be malnourished than those indicating no breastfeeding problems, suggesting high specificity[27]. In addition, a study in Bangladesh found that reported dissatisfaction with breastfeeding was significantly higher among mothers of SAM infants (22%) than non-SAM infants (10%)[33]. Further studies on the sensitivity, specificity and predictive abilities of clinical indicators for infant SAM are required, particularly identification of standardised breastfeed indicators which correctly capture mothers' concerns as these are likely to be sensitive and predictive.

A study in Kenya found that a MUAC cut-off of <11cm identified 24% of hospitalised infants at risk of inpatient mortality with a sensitivity of 70% and specificity of 68%[14]. For W/A, <-3 z-scores was less sensitive (55%) but more specific (80%) than MUAC. In the Malawian hospital audit, W/L z-score

was found to be 43.5% sensitive and 69.5% specific during standard practice; this improved to 62.3% sensitivity and 95.6% specificity following the introduction on a specialist feeding nurse[19].

In terms of predictive value, the study in Kenya found MUAC and W/A to be strongest at predicting mortality compared to W/L and L/A in an inpatient setting (see **Figure 2**)[14]; a similar result was found in The Gambia for infants in the community[34]. W/A was also found to have better predictive value than W/L and L/A in studies in Ghana, Peru and India[35]. It has been suggested that W/L is less predictive of mortality than other measures, due to its greater inaccuracy and unreliability, and due to its more indirect relationship with muscle and fat mass, unlike MUAC[34]. With regard to MUAC cut-off values, a trial of co-trimoxazole use as part of treatment of SAM in infants <6m found that those with a MUAC <11cm had a high incidence death rate (31 per 100 child-years) suggesting that the cut-off should not be any less than 11cm[37].

| **Figure 2** | Area under the receiver operating curve (ROC) (95% CI) for inpatient mortality associated with MUAC (blue), W/A z-score (brown) and W/L z-score (yellow) |

Mwangome et al., 2017[14]
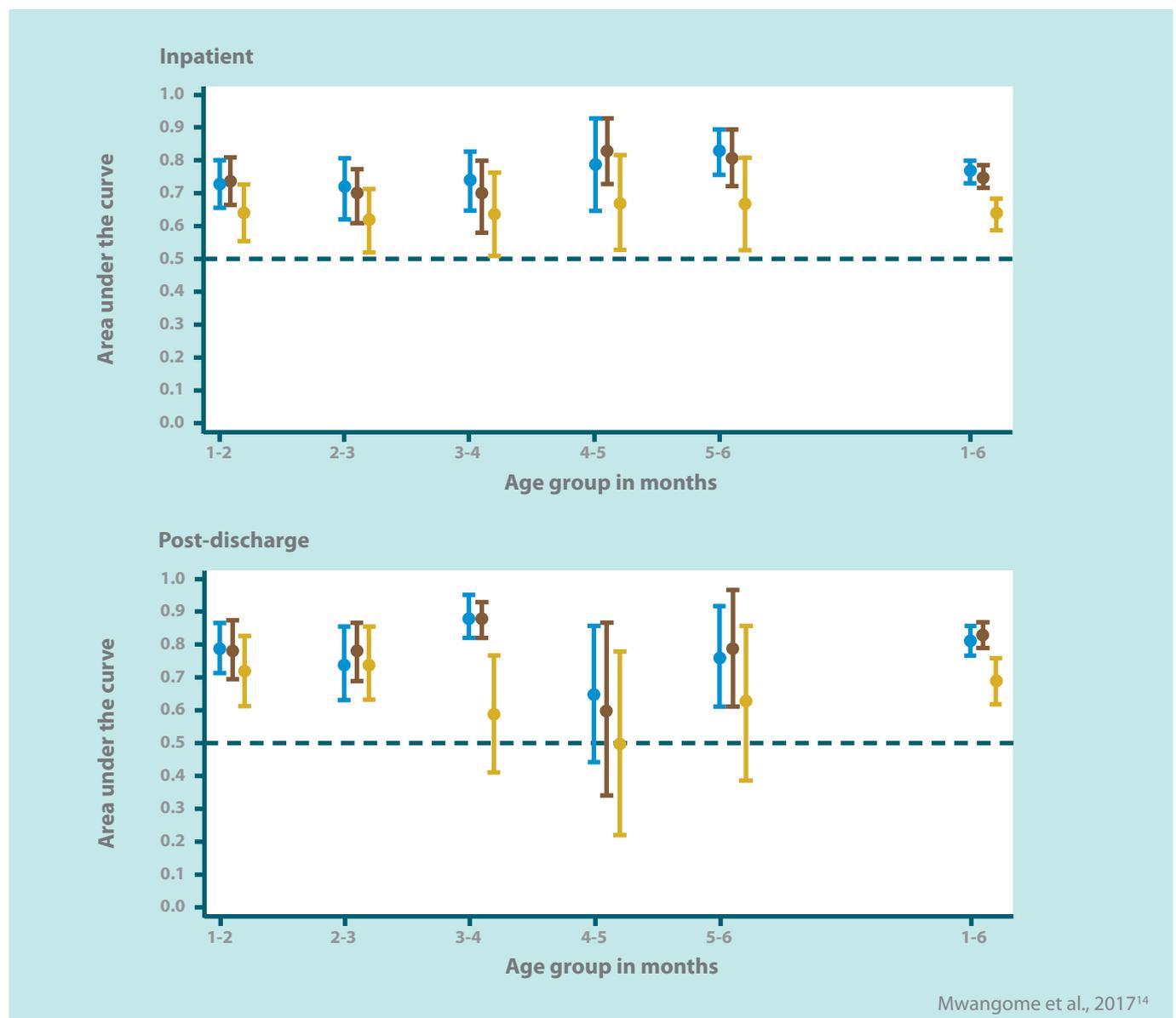
Note: greater area under the receiver operating curve indicates greater association with mortality outcome. MUAC and W/A z-score have consistently better predictive ability than W/L z-score across the 1-6 month age group. The dotted line at 0.5 indicates the level of ROC that is of no predictive value.

Using the recent Kenya data, Mwangome et al. have also explored predictive value of identifying SAM in infants using 'MUAC only', 'MUAC or W/A' or 'MUAC and W/A' using inpatient mortality rates, as has been done for older children[36]. They found no significant difference in predictive value (expressed as ROC) when using a combination of MUAC and/or W/A compared to using MUAC alone (Table 1)[14]. However, W/A did identify additional cases not identified by low MUAC (157 additional cases) and these additional infants did have a high case fatality (5% compared to 2.7% for infants with MUAC>11cm)[14].

Table 1	Differences in predictive value of using MUAC alone for diagnosis compared to a combination of MUAC and/or W/A z-score[37]					
Criteria	**Number of cases**	**Number of death**	**Sensitivity**	**Specificity**	**Receiver operating characteristic (ROC)**	**P value***
MUAC<11cm (Ref)	682 (23.7%)	80 (11.7%)	64.3	70.4	0.68 (0.63 to 0.72)	
MUAC<11cm or W/A Z<-3	839 (29%)	88 (11%)	62.9	72.6	0.68 (0.64 to 0.72)	0.89
MUAC<11cm and W/A Z<-3	473 (16.4%)	69 (15%)	49.3	85.3	0.67 (0.63 to 0.71)	0.76

 Note: MUAC= mid-upper arm circumference; W/A Z = weight-for-age z-score
*Compared to MUAC <11cm

Kwashiorkor in Infants

Assessment of kwashiorkor as an indicator of SAM is also required for infants <6m, as is the case for older children. The standard assessment for this is observation of bilateral pitting on the feet. Using this method of identification, an audit of infants admitted to hospital in Malawi found that 3.6% of those identified as malnourished were diagnosed with kwashiorkor[19]. This is much higher than in a community setting where only 0.6% of infants measured at a routine immunisation clinic were diagnosed with kwashiorkor. This, in turn, is much lower than community levels of kwashiorkor in older children (6-59 months) which is thought to be around 1.8% in the community in Malawi[38]. Despite relatively low prevalence, checking for kwashiorkor should be included as an additional indicator of SAM in infants <6m as it is simple, acceptable, low cost, largely objective and independent of age.

Conclusions and proposed indicators

Using the 11 properties reviewed in this report, W/A, MUAC and MUAC/A are rated the best indicators of acute malnutrition and associated mortality in infants <6m, based on current evidence (see Table 2). A fixed MUAC cut off rates particularly highly as it does not depend on age, which can add inaccuracy. Even if age is ascertained accurately among this age group, MUAC/A compared to MUAC with a single cut-off of <11cm does not appear to add to sensitivity, specificity or predictive value. W/A suffers from the potential inaccuracy of cost-effective scales, however the over-lap of weight measurements with a variety of other routine health checks makes W/A attractive as a diagnostic criterion in many settings. W/L, the current recommended indicator, scored poorly in this review, largely due to the inaccuracy, difficulties associated with measuring length and poorer predictive value for mortality.

With the view to move in line with the success of community-based management of acute malnutrition in children 6-59 months, we propose the use of MUAC and W/A, alongside simple clinical indicators and identification of kwashiorkor, as the standard indicators for acute malnutrition in infants <6m. We also recommend that infants born small or preterm should have the same anthropometric criteria for receiving interventions due to their heightened risk of mortality.

Priorities for future research include a formal evaluation of the 'C-MAMI tool' in order to assess its validity, particularly as a community-based application, which is currently lacking. As W/A and MUAC have already been validated in multiple research settings, the next step should be to assess their use at scale in the community for infants <6m, taking into account use of different weighing scales and (for W/A) accuracy of age calculations.

Table 2	Capability of common indicators of infant SAM against properties for assessing appropriateness of case-detection methods in community settings						

Properties	Indicator						
	Clinical* (infant)	Clinical* (mother)	W/A	L/A	W/L	MUAC	MUAC/A
Simplicity	No	No	No	No	No	Yes	No
Acceptability	No	No	Yes	Yes	Yes	Yes	Yes
Cost	No	No	No	No	No	Yes	Yes
Objectivity	No	No	Yes	Yes	Yes	Yes	Yes
Quantitativeness	No	No	Yes	Yes	Yes	Yes	Yes
Independence of age	Yes	Yes	No	No	No	Yes	No
Precision (reliability)	Unknown	Unknown	Yes	No	No	Yes	Yes
Accuracy	Unknown	Unknown	No‡	No	No	Yes	No
Sensitivity	No	No	Yes	No	No	Yes	Yes
Specificity	No	No	Yes	No	No	Yes	Yes
Predictive value	Unknown	Unknown	Yes	No	No	Yes	Yes

*clinical (infant) includes "too weak to suckle" or "recent weight loss"; clinical (mother) includes maternal milk insufficiency (MMI). W/A= weight-for-age; L/A = length-for-age; L/W = length-for-weight; MUAC= mid-upper arm circumference; MUAC/A =mid-upper arm circumference for age.
‡ based on commonly-used hanging sales.

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