



Practice of Epidemiology

Estimates of the Duration of Untreated Acute Malnutrition in Children From Niger

Sheila Isanaka*, Rebecca F. Grais, André Briend, and Francesco Checchi

* Correspondence to Sheila Isanaka, Department of Nutrition, Harvard School of Public Health, 665 Huntington Avenue, Boston, MA 02115 (e-mail: sisanaka@hsph.harvard.edu).

Initially submitted September 14, 2010; accepted for publication November 16, 2010.

Expected incidence of acute malnutrition is the most appropriate measure for projecting the needs of a nutritional treatment program over time in terms of staffing, food, and other treatments, but direct estimation of incidence is rarely feasible at the onset of an intervention. While incidence may be approximated as prevalence/average duration, ethical constraints preclude measurement of the duration of acute malnutrition in the absence of treatment. The authors used a compartmental model to estimate the duration of untreated moderate acute malnutrition (MAM) and severe acute malnutrition (SAM) in children aged 6–60 months. The model was informed by data from a community-based cohort of children in Niger followed from August 2006 to March 2007. Maximum likelihood estimates for the duration of untreated MAM, defined by weight-for-height z score and middle upper arm circumference, were 75–81 days and 101–116 days, respectively. The duration of untreated SAM, defined by weight-for-height z score, was 45 days. The duration of untreated MAM appears to have been shorter among children aged 6–35 months compared with those aged 36–60 months. Such estimates of the duration, and thus incidence, of untreated malnutrition can be used to improve projections of program needs and estimates of the global burden of acute malnutrition.

child; incidence; malnutrition; Niger; prevalence

Abbreviations: CI, confidence interval; MAM, moderate acute malnutrition; MUAC, middle upper arm circumference; SAM, severe acute malnutrition; WHZ, weight-for-height z score.

Acute malnutrition, which is highly prevalent among young children in developing countries, can have devastating short- and long-term consequences; it is currently estimated that 15% of all child deaths worldwide are attributed to acute malnutrition (1). The diagnosis of acute malnutrition is based on anthropometric and clinical assessment, and its prevalence in children aged 6–59 months can be used to benchmark the severity of the nutritional situation in settings where a suspected nutritional crisis is ongoing (2, 3).

Measures of prevalence are often available through rapid cross-sectional surveys and are useful for guiding decision-making on the need for intervention. However, they do not allow for adequate projection of program needs in terms of staffing, capacity of nutritional centers, quantity of food, and other treatments required, since they measure only a single point in time. Such projections are critical for cost-efficient

planning but are often based on guesswork, leading to potential shortages or wastage of resources. The projection of program needs based on measures of expected incidence would be more appropriate and could improve the ability of program managers to deliver adequate resources over time.

Direct estimation of incidence entails following a cohort of children over time, but such studies are rarely feasible at the onset of a nutritional intervention. When incidence cannot be directly observed, it may be approximated using the simple mathematical relation between incidence, prevalence, and average duration of an episode, where incidence is approximately equal to prevalence/average duration (4, 5). While this approximation is subject to important assumptions, it provides a potentially simple method for combining an estimate of prevalence from a cross-sectional survey with an additional estimate of average duration to project the

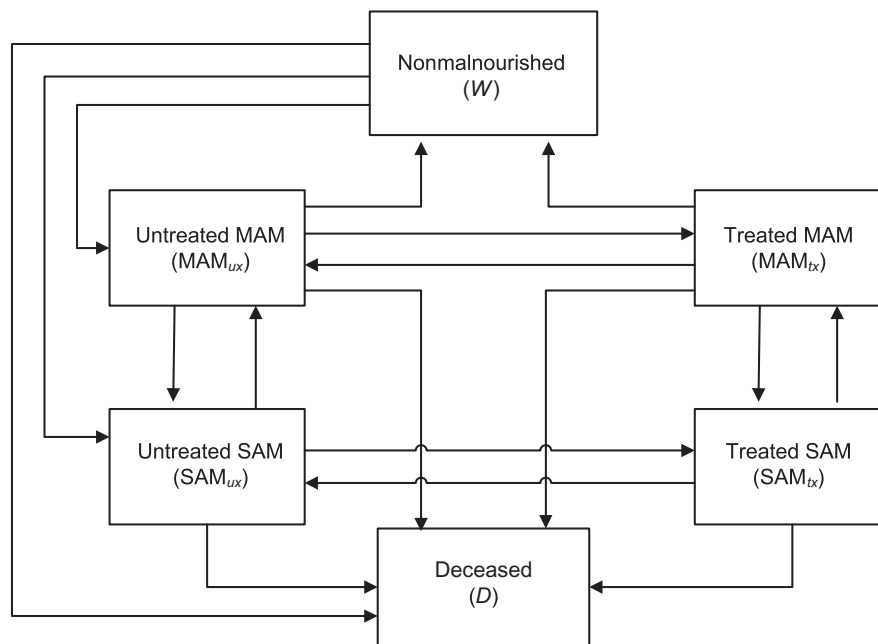


Figure 1. Compartmental model structure for the progression of acute malnutrition in children aged 6–60 months. The arrows illustrate the flow into and out of various compartments, the basis of which is the assumed natural history of acute malnutrition. Additional flows into and out of compartments due to migration are omitted for clarity. MAM, moderate acute malnutrition; SAM, severe acute malnutrition.

expected incidence over a given time horizon and thereby provide a starting estimate of a program's initial needs.

Because the prevalence estimate in the prevalence-incidence approximation refers to a time prior to implementation of the program, the average duration of *untreated* acute malnutrition is in fact the parameter of interest. Today, ethical constraints preclude direct estimation of the duration of acute malnutrition in the absence of treatment, and to our knowledge, only 1 such estimate has been described in the published literature using historical data (6). Therefore, in this paper, we use a mathematical model informed by data from a community-based cohort study in Niger to estimate the duration of untreated moderate acute malnutrition (MAM) and severe acute malnutrition (SAM), as a necessary step to project expected incidence.

MATERIALS AND METHODS

Compartmental model structure

A framework for the progression of acute malnutrition is shown in Figure 1. Although the progression of acute malnutrition is biologically complex and difficult to illustrate in detail, the model shown should be taken to generally represent the temporal dynamics of 6 distinct health states or compartments: nonmalnourished or “well” (W); moderate acute malnutrition without treatment (MAM_{ux}); moderate acute malnutrition with treatment (MAM_{tx}); severe acute malnutrition without treatment (SAM_{ux}); severe acute malnutrition with treatment (SAM_{tx}); and deceased (D). The total population is open, allowing for in- and outmigration,

and $N = W + MAM_{ux} + MAM_{tx} + SAM_{ux} + SAM_{tx} + D$. Residence in the 5 uppermost compartments may be determined by weight-for-height z score (WHZ) according to the 2006 World Health Organization growth standards (nonmalnourished: $WHZ \geq -2$; MAM: $-3 \leq WHZ < -2$; SAM: $WHZ < -3$) (3, 7) or, alternatively, by middle upper arm circumference (MUAC) (nonmalnourished: $MUAC \geq 125$ mm; MAM: $115 \text{ mm} \leq MUAC < 125$ mm; SAM: $MUAC < 115$ mm) (2, 8). The arrows in Figure 1 illustrate the direction of transition into and out of each compartment, the basis of which is the assumed natural history of acute malnutrition. The rate of each transition controls the movement of children into and out of each compartment.

To estimate the average duration or amount of time spent in the MAM_{ux} and SAM_{ux} compartments, we may simplify the model by focusing only on the compartments of interest and consolidating the rates of transition into and out of these compartments. The resulting reduced model of MAM_{ux} duration includes the 2 compartments MAM_{ux} and MAM_{tx} (Figure 2). The resulting model for estimation of average time spent in SAM_{ux} is conceptually identical to that for MAM_{ux} , including the same 2 corresponding compartments: SAM_{ux} and SAM_{tx} .

As Figure 2 shows, the reduced model features a collective rate of entry into either MAM compartment—that is, the incidence of new MAM cases per unit of time (λ). Of the MAM cases, a proportion c are treated (MAM_{tx}) and a proportion $1 - c$ are untreated (MAM_{ux}), such that c represents the coverage of treatment. Untreated children (MAM_{ux}) must eventually exit the compartment through natural progression to SAM, spontaneous recovery, or death; these 3

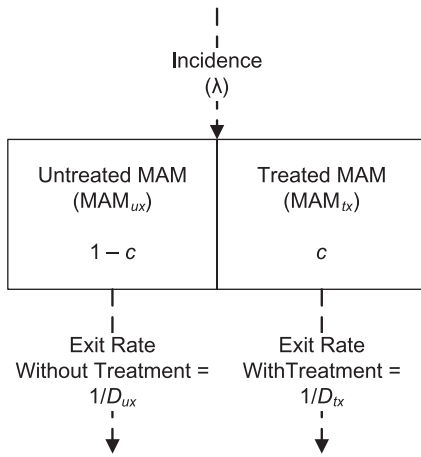


Figure 2. Reduced compartmental model structure for estimation of the duration of untreated moderate acute malnutrition (MAM) in children aged 6–60 months. Directions and rates of progression into and out of each state are expressed by the arrows. Details are provided in Table 1.

possible events are combined into a single exit rate. Assuming an exponential distribution of untreated MAM residence times (i.e., a time-independent exit rate due to natural progression), the rate of exit is the reciprocal of the mean duration of stay within the compartment. Therefore, the collective rate of exit due to natural progression to SAM, spontaneous recovery, or death is represented as $1/D_{ux}$, where D_{ux} is the mean duration of untreated MAM. Similarly, children who receive treatment (MAM_{tx}) must eventually exit the compartment through recovery, progression to SAM despite treatment, or death while under treatment; and, as above, the collective rate of exit is $1/D_{tx}$, where D_{tx} is the mean duration of MAM under treatment.

The same framework applies to the reduced model for SAM_{ux} , although, in the case of SAM, exit from either compartment can be due to recovery, improvement to MAM, or death (a mathematically irrelevant difference) and D_{ux} is the mean amount of time spent with untreated SAM before exit due to recovery, improvement to MAM, or death.

We can write the model shown in Figure 2 as a differential equation specifying the rate of change in the sum of the 2 MAM compartments, for a given small time unit:

$$\begin{aligned} \frac{d(MAM_{ux} + MAM_{tx})}{dt} \\ = \lambda - MAM_{ux} \left(\frac{1}{D_{ux}} \right) - MAM_{tx} \left(\frac{1}{D_{tx}} \right). \end{aligned} \quad (1)$$

MAM cases are added due to incidence and are depleted due to exit from either the untreated compartment or the treated compartment. Using the relation between the number of children treated and the treatment coverage (c), such that $MAM_{tx} = c(MAM_{ux} + MAM_{tx})$ and $MAM_{ux} = (1 - c)(MAM_{ux} + MAM_{tx})$, after substitution we can rewrite equation 1 as

$$\begin{aligned} \frac{d(MAM_{ux} + MAM_{tx})}{dt} \\ = \lambda - \left(MAM_{ux} + MAM_{tx} \right) \left[\left(1 - c \right) \frac{1}{D_{ux}} + c \frac{1}{D_{tx}} \right]. \end{aligned} \quad (2)$$

Equation 2 may be used to predict the prevalence of MAM ($MAM_{ux} + MAM_{tx}/N$) over time. The equation for SAM is conceptually identical.

Model parameterization

The data sources and values for model parameters are provided in Table 1 and Table 2, respectively. The number of incident cases (λ), the total number of children under follow-up (N ; e.g., the denominator in the prevalence calculation), and the observed numbers of MAM and SAM cases were taken from a previously described community cohort in Niger (9). In brief, children aged 6–60 months in 12 study villages in Maradi, Niger, were followed from August 2006 to March 2007. Field teams of trained nutritional assistants and research nurses took anthropometric measurements (weight, height, presence of bipedal pitting edema, and MUAC) on a monthly basis. Any child found to have MAM or SAM between August and December of 2006 or found to have SAM in 2007 was referred to the nutritional program, but reliable data on actual treatment coverage were not collected in the community cohort. Nonmalnourished children in 6 randomly selected villages received short-term preventive supplementation with ready-to-use-therapeutic food, while children in the 6 remaining villages received no preventive supplementation. We utilized all available follow-up data for children in the 6 study villages that did not receive the intervention ($n = 1,862$ children; 13,182 follow-up visits between August 2006 and March 2007). Of the 8 monthly data points, the first was used to set starting conditions for the model (i.e., $MAM_{ux} + MAM_{tx}$ and $SAM_{ux} + SAM_{tx}$ at $t = 0$), while the remaining 7 provided observed prevalence data points for maximum likelihood estimation (see below).

The mean duration of MAM or SAM treatment (D_{tx}) was estimated from a Médecins Sans Frontières malnutrition treatment program implemented in Maradi during 2006 ($n = 68,101$) (10). This program had a much wider catchment population than the 6 villages included in the community cohort; thus, the estimates of treatment duration are not necessarily representative of children in the cohort villages. Children were eligible for admission to the program if they were 60–110 cm tall and fulfilled at least 1 of the following criteria: presence of bipedal pitting edema, MUAC < 110 mm, or weight-for-height less than 80% of the US National Center for Health Statistics reference median (11). The Médecins Sans Frontières program used an integrated home- and facility-based approach, whereby children with sufficient appetite and no serious complications were offered home-based treatment with the provision of ready-to-use-therapeutic food. Children were discharged from the program when they reached a weight-for-height greater than

Table 1. Parameters of a Reduced Compartmental Model for Estimation of the Duration of Untreated Moderate Acute Malnutrition in Children Aged 6–60 Months, Maradi, Niger, 2006–2007

Notation	Parameter	Units	Source Data/Notes
N	Total no. of children in cohort	No.	Community cohort
MAM_{ux}	Untreated MAM cases	No.	Model prediction
MAM_{tx}	Treated MAM cases	No.	Model prediction
$MAM_{ux} + MAM_{tx}$	Total MAM cases	No.	Observed data from community cohort, compared with model prediction
λ	Rate of incidence into MAM	Cases/day	Community cohort Includes entry into MAM compartment from all other compartments (including incidence from the well state or partial recovery from the SAM state). Computed separately for each month as the number of new MAM cases observed over the given month, divided by 30.4 days.
D_{ux}	Mean duration of untreated malnutrition	Days	Estimated from model as the mean amount of time spent with untreated malnutrition before exit due to any cause. Candidate values are allowed to range from 7 days to 300 days.
D_{tx}	Mean duration of treated malnutrition	Days	Estimated from the Médecins Sans Frontières nutritional program database as the mean difference in days between program admission and discharge among all nondefaulting children admitted with MAM (WHZ < -2 according to the WHO growth standards or MUAC < 125 mm) or SAM (WHZ < -3 according to the WHO growth standards or MUAC < 115 mm) in 2006. Program discharge for all children occurred at weight-for-height $\geq 80\%$ of the NCHS reference median after 2 consecutive weighings before November 5, 2006, or at weight-for-height $\geq 85\%$ of the NCHS reference median upon 1 weighing on or after November 5, 2006.
C	Treatment coverage (proportion of MAM cases admitted to the treatment program)	%	Estimated from the model in the first estimation approach. Candidate values were allowed to range from 0% to 99% but were held at 0% during the last 3 months of the time series for MAM because of interruption of MAM referral and treatment during this period. Random values were drawn from a uniform distribution in the second estimation approach. This is the “effective” coverage, that is, the proportion of children who enter the program and do not default from it.
T	Time	Days	

Abbreviations: MAM, moderate acute malnutrition; NCHS, National Center for Health Statistics; SAM, severe acute malnutrition; WHO, World Health Organization; WHZ, weight-for-height z score.

or equal to 80% of the National Center for Health Statistics reference median after 2 consecutive weighings before November 5, 2006. On or after November 5, 2006, children were discharged when they reached a weight-for-height greater than or equal to 85% of the National Center for Health Statistics reference median at a single weighing. The duration of treated MAM or SAM was calculated as the mean difference in days between program admission and discharge among nondefaulting children admitted with MAM (WHZ < -2 according to the World Health Organization growth standards or MUAC < 125 mm) or SAM (WHZ < -3 according to the World Health Organization growth standards or MUAC < 115 mm), respectively.

Lastly, D_{ux} and c are unknown and were the subject of estimation (see below).

Estimation of the duration of untreated MAM and SAM

The model was implemented with daily time increments to approximate continuous time, but predictions were evaluated against observed prevalence data at the 7 monthly data time points. We applied 2 alternative maximum likelihood

estimation approaches. In the first approach, which was fully deterministic, we jointly estimated D_{ux} and c by evaluating the fit of each possible combination of their respective values. For each possible combination of D_{ux} and c , the log binomial likelihood of each monthly prevalence prediction, given the observed prevalence, was computed and summed over the 7 data points. The set of (D_{ux} , c) values yielding the maximum likelihood was adopted as the best estimate. The confidence interval was provided by the 2.5th and 97.5th percentiles of the joint likelihood profiles, as shown by Bolker (12).

In the second approach, we evaluated the fit of each candidate D_{ux} value in 1,000 model runs, with c being allowed to assume a random value at each time step in each run. A maximum binomial likelihood estimate and profile 95% confidence interval were then computed, after summing likelihoods of all model runs for each possible value of D_{ux} .

For simplicity, we assumed that the rate of exit from either compartment was time-independent (i.e., that a child was equally likely to recover, deteriorate, or die at any point in his or her MAM or SAM episode) and that the durations of untreated MAM and SAM were constant throughout the

Table 2. Values for Parameters^a in a Reduced Compartmental Model for Estimation of the Duration of Untreated Moderate and Severe Acute Malnutrition in Children Aged 6–60 Months, Maradi, Niger, 2006–2007

	Total (N)	WHZ-Based Definition		MUAC-Based Definition	
		MAM	SAM	MAM	SAM
No. of children observed					
August 2006	1,689	119	20	59	9
September 2006	1,660	116	27	63	10
October 2006	1,664	205	46	81	12
November 2006	1,618	121	12	56	7
December 2006	1,627	69	4	36	9
January 2007	1,635	70	12	44	7
February 2007	1,646	86	17	60	15
March 2007	1,643	113	19	60	11
Duration of treatment, days		32.55	35.51	34.46	38.38

Abbreviations: MAM, moderate acute malnutrition; MUAC, middle upper arm circumference; SAM, severe acute malnutrition; WHZ, weight-for-height z score.

^a Total number of children under follow-up (N) and total number of MAM ($MAM_{ux} + MAM_{tx}$) and SAM ($SAM_{ux} + SAM_{tx}$) cases over time as observed in the community cohort in Maradi, Niger. Data on treatment coverage were not collected from this cohort; thus, values shown do not account for actual treatment status. Duration of treatment (D_{tx}) was estimated from the 2006 Médecins Sans Frontières malnutrition treatment program in Maradi as the mean difference in days between program admission and discharge among nondefaulting children admitted with MAM or SAM.

7-month model evaluation period. The model implicitly assumes the same average duration estimate for first and repeated episodes of malnutrition.

Estimation was attempted for both MAM and SAM using the WHZ- and MUAC-based definitions of acute malnutri-

tion and stratification by age group (6–35 months, 36–60 months), where sample size allowed. The analysis was performed using SAS, version 9.1 (SAS Institute Inc., Cary, North Carolina) and R (13). The institutional review board of the Harvard School of Public Health found that this re-analysis of existing data met the criteria for exemption, and additional review was not required.

RESULTS

Maximum likelihood estimates for the duration of untreated MAM and SAM and treatment coverage are provided in Table 3. In the first estimation approach jointly estimating untreated duration and treatment coverage, maximum likelihood estimates of the duration of untreated MAM defined by WHZ and treatment coverage were 75 days and 39%, respectively. Corresponding estimates for untreated MAM defined by MUAC were somewhat higher for duration (101 days) and lower for coverage (29%). The second estimation approach produced point estimates for the duration of untreated MAM, defined by either WHZ or MUAC, that were similar to those obtained with the first approach. The number of MAM cases predicted by applying the above estimates was closely aligned with the number observed in the community cohort during most months, suggesting an acceptably good fit (Figure 3, parts A and B).

The model did not converge to a single solution set for the untreated duration of SAM (defined by WHZ or MUAC) and treatment coverage using the first estimation approach. The duration of untreated SAM defined by WHZ was found to be 45 days using the second approach (Table 3), with a reasonable fit of the predicted data to the observed data in most months (Figure 3, part C).

Finally, we examined untreated duration of MAM among children aged 6–35 months and 36–60 months. The first estimation approach yielded an estimated duration of untreated MAM (defined by WHZ) of 70 days (95%

Table 3. Maximum Likelihood Estimates of the Duration of Untreated Moderate and Severe Acute Malnutrition^a and Treatment Coverage in Children Aged 6–60 Months, Maradi, Niger, 2006–2007

	Estimation Approach 1				Estimation Approach 2 (Duration, days)	
	Duration, days		Coverage, %		MLE	95% CI
	MLE	95% CI	MLE	95% CI		
MAM						
$-3 \leq \text{WHZ} < -2$	75	61, 104	39	12, 53	81	69, 93
$115 \text{ mm} \leq \text{MUAC} < 125 \text{ mm}$	101	75, 196	29	4, 50	116	94, 171
SAM						
$\text{WHZ} < -3$	N/A ^b		N/A		45	31, 68
$\text{MUAC} < 115 \text{ mm}$	N/A		N/A		N/A	

Abbreviations: CI, confidence interval; MAM, moderate acute malnutrition; MLE, maximum likelihood estimate; MUAC, middle upper arm circumference; N/A, not applicable; SAM, severe acute malnutrition; WHZ, weight-for-height z score.

^a Duration of untreated MAM is the mean amount of time spent with untreated MAM before exit due to recovery, progression to SAM, or death. Duration of untreated SAM is the mean amount of time spent with untreated SAM before exit due to recovery, improvement to MAM, or death.

^b Model did not converge to a single solution.

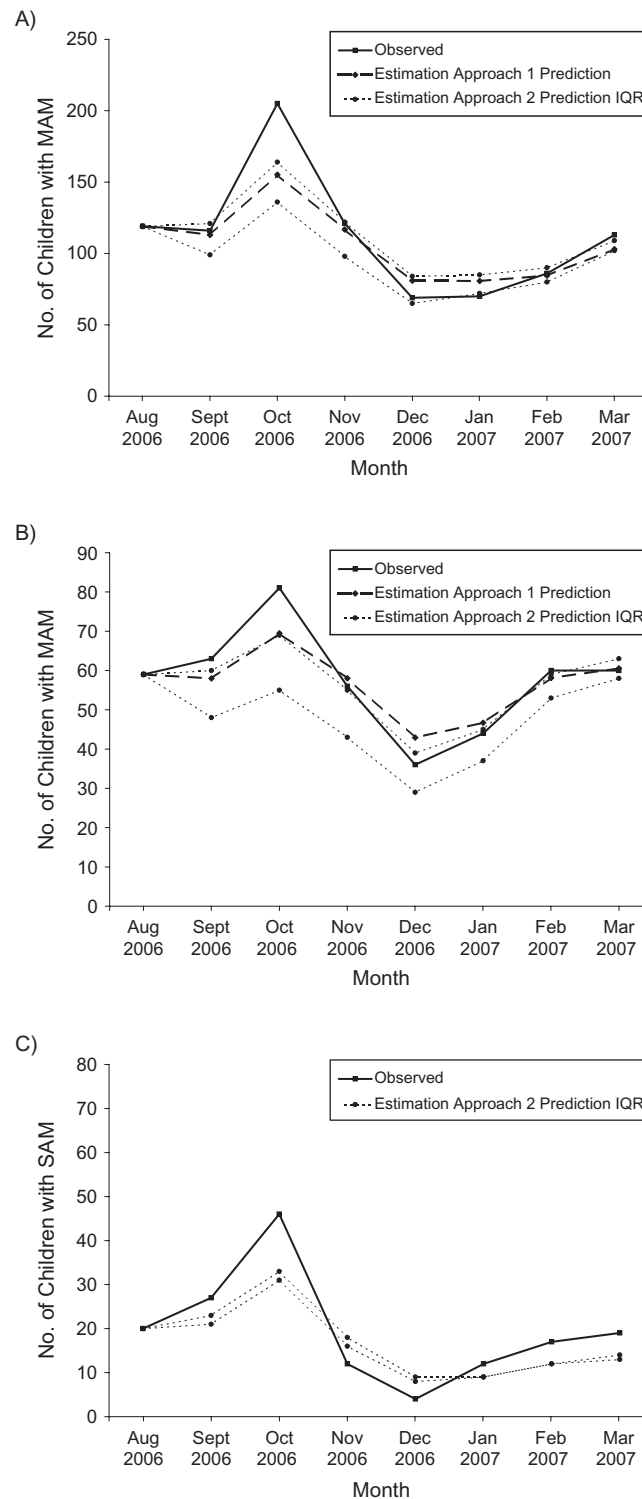


Figure 3. Observed burden of moderate acute malnutrition (MAM) and severe acute malnutrition (SAM) versus predicted burden in children aged 6–60 months, Maradi, Niger, 2006–2007. A) Observed number of children with MAM ($-3 \leq$ weight-for-height z score < -2) versus predicted number of children with MAM using the maximum likelihood estimates (MLEs) from the first estimation approach ($D_{ux} = 75$ days and $c = 0.39$) and the predicted interquartile range (IQR) of the number of children with MAM from 1,000 runs using the MLE from the second estimation approach ($D_{ux} = 81$ days). B) Observed number of children with MAM ($115 \text{ mm} \leq$ middle upper arm circumference $< 125 \text{ mm}$) versus predicted number of children with MAM using the MLEs from the first estimation approach ($D_{ux} = 101$ days and $c = 0.29$) and the predicted IQR of the number of children with MAM from 1,000 runs using the MLE from the second estimation approach ($D_{ux} = 116$ days). C) Observed number of children with SAM (weight-for-height z score < -3) versus the predicted IQR of the number of children with SAM from 1,000 runs using the MLE from the second estimation approach ($D_{ux} = 45$ days).

confidence interval (CI): 53, 100) and treatment coverage of 46% (95% CI: 10, 64) among children aged 6–35 months. The corresponding maximum likelihood estimate of untreated duration using the second estimation approach was similar (67 days, 95% CI: 57, 80). Among children aged 36–60 months, the first estimation approach did not produce a single solution set; however, the 4 most likely solutions were consistent and suggested an estimated duration of untreated MAM (defined by WHZ) ranging from 97 days to 100 days (95% CI: 68, 237) and treatment coverage ranging from 27% to 29% (95% CI: 1, 51). Using the second estimation approach, the estimated duration of untreated MAM among children aged 36–60 months was 116 days (95% CI: 90, 196). Using the MUAC-based definition of MAM, the first estimation approach yielded 2 similar solution sets among children aged 6–35 months, suggesting an estimated duration of 129–130 days (95% CI: 87, 257) and treatment coverage of 37% (95% CI: 7, 51), whereas the second estimation approach yielded an estimated duration of untreated MAM of 140 days (95% CI: 110, 215). Neither estimation approach converged to a single solution set with the MUAC-based definition of MAM among children aged 36–60 months.

DISCUSSION

In this paper, we provide estimates for the duration of untreated MAM, defined by WHZ and MUAC, of 75–81 days and 101–116 days, respectively, and for the duration of untreated SAM defined by a WHZ of 45 days. Estimating the duration and thus the incidence of untreated malnutrition is an essential aspect of projecting program needs. The methods and results presented here represent a novel attempt to develop these estimates.

There are now interventions that have been proven effective for the treatment of acute malnutrition, but these interventions require the delivery of adequate resources over time to achieve their full effect. Compared with the use of prevalence estimates alone, local estimates of duration and incidence projections can help program managers avoid potential shortage or wastage of resources in the early stages of an intervention and improve the overall cost-efficiency of essential nutrition programs. For instance, in a population of 100,000 children, a MAM prevalence of 15% obtained through a rapid cross-sectional survey might suggest that 15,000 children would initially be enrolled in a planned supplementary feeding program (assuming 100% treatment coverage). This prevalence-based calculation, however, reflects only the number of children expected to enroll at the onset of the program and does not provide information on how many children might be expected to enroll over a given time horizon. Alternatively, combining estimates of prevalence and untreated duration of MAM in the same scenario (e.g., 15% (MAM prevalence)/75 days (average duration of untreated MAM) in a population of 100,000), an incidence-based calculation would suggest 200 children per day or 1,400 children per week to be enrolled in the early stages of the treatment program. The latter calculation is likely to be more informative for projecting initial program needs

until direct measures of incidence can be prospectively observed and calculated from program data.

Information on the duration and incidence of acute malnutrition may also be used to improve available estimates of the mortality and global burden of disease associated with MAM and SAM. Current estimates of the number of deaths attributable to acute malnutrition use the relative risk of mortality and the prevalence of acute malnutrition in order to calculate the proportional reduction in mortality that would be seen if acute malnutrition were removed from the population—that is, the population attributable fraction (1). This method implicitly assumes that all episodes of acute malnutrition have an average duration of 1 year or that there is no mortality associated with acute malnutrition once all of the children with initial cases have recovered or died; this method does not account for deaths among additional incident cases that occur during this assumed period of 1 year. Our results indicate that the duration of an untreated episode of MAM and SAM is far shorter than 1 year, suggesting that current global projections of MAM- and SAM-associated mortality based on prevalence data may be underestimates. These burden estimates would also benefit from accounting for the expected incidence.

To our knowledge, there is little other published work on estimation of the incidence and untreated duration of acute malnutrition. Garenne et al. (6) reported the duration of SAM to be approximately 7–8 months in 2 historic cohorts of children aged less than 5 years in Senegal and the Democratic Republic of Congo. Differences between these previous estimates and our model-based estimates may be due to assumptions or simplifications of the modeling approach, differences in the study settings (with the previously published estimates derived from data originating in the 1980s and early 1990s), or the long intervals between anthropometric assessment in the historic cohorts. The anthropometric status of children was assessed every 3 months in the Democratic Republic of Congo and every 6 months in Senegal—intervals that may have allowed for shorter episodes of acute malnutrition to be missed and the observed duration of episodes to be overestimated.

We present 2 maximum likelihood approaches for estimation of the untreated duration of acute malnutrition: a fully deterministic approach to jointly estimate both untreated duration and treatment coverage and a second approach to estimate untreated duration while allowing coverage to randomly vary. To our knowledge, no other mathematical model for estimating the untreated duration of acute malnutrition has been described. Both approaches presented here produce similar results, though we suggest that the joint estimation procedure of the first may be preferred by program managers given the additional information provided on treatment coverage. However, this approach does require a relatively greater number of events to implement than the second approach. As a result, when data are limited and do not support the use of the first approach, the second approach may be used to provide an acceptable alternative estimate of untreated duration. Overall, both approaches provide a reasonable fit to the observed data over most months in the study period. Model predictions for the month of October 2007, the end of the hunger

season in this setting, do differ notably from the observed values. These differences are probably due to inconsistency between a simplifying assumption of the model and reality.

We emphasize the need for caution in generalization of the estimates provided here. The duration of untreated episodes of acute malnutrition will probably vary geographically and temporally depending on a number of contextual factors, such as the severity and type of malnutrition (kwashiorkor vs. marasmus), the prevalence of infectious illness, access to health services, and the age structure of the population. As a result, a single estimate of average duration is not likely to apply to all settings.

There are limitations to the model presented. As with all models, we intentionally made a number of simplifying assumptions. We assumed that the transition rates in this simple model were constant and thus independent of time and season. In reality, a child's likelihood of recovery, deterioration, or death may in fact vary within an episode of MAM or SAM, and the risks of these events may similarly vary across seasons because of changing food availability and accessibility. While there is little published evidence to inform a more appropriate assumption about time and seasonal dependence in progression rates, the reasonable fit of our model overall suggests that introducing such dependencies would not have altered our findings substantially, though it might have improved the prediction for October 2007. The model allowed for migration into and out of the cohort. While we do not expect migration of nonmalnourished children to have influenced estimation of the untreated duration of MAM or SAM (Figure 2), the outmigration of children with MAM or SAM before reaching an outcome (recovery, deterioration, or death) may have resulted in underestimation of the duration parameters of interest. However, outmigration of cases before they reached an outcome was infrequent (data not shown). We were unable to fully explore the dependence of our estimates on child age owing to a limited sample size. Our findings suggest that malnutrition episodes last longer in older children, but future work using data from other settings should include age stratification to further address this issue. Finally, our estimates for the duration of untreated SAM should be considered less robust than those for untreated MAM, owing to the small number of severe events in this setting. Although we were only able to obtain a solution for the duration of untreated SAM using the second estimation approach, we do not expect that the second approach introduced significant bias compared with the first, as both produced similar results for the duration of untreated MAM (75 days vs. 81 days).

The high mortality and disease burden of acute malnutrition calls for implementation of effective interventions at scale, but the timely and cost-efficient execution of such programs will depend on the appropriate application of available epidemiologic tools. Estimating the duration, and thus incidence, of untreated malnutrition remains an essential aspect of projecting program needs. We recommend that the utility of the model developed here be further evaluated through its application to data from other settings. The estimation and dissemination of additional estimates will help to confirm the generalizability of the model and

our initial estimates of the untreated duration of acute malnutrition.

ACKNOWLEDGMENTS

Author affiliations: Departments of Epidemiology and Nutrition, Harvard School of Public Health, Boston, Massachusetts (Sheila Isanaka); Harvard Humanitarian Initiative, Harvard University, Cambridge, Massachusetts (Sheila Isanaka, Rebecca F. Grais); Epicentre, Paris, France (Rebecca F. Grais, Francesco Checchi); Department of International Health, University of Tampere Medical School, Tampere, Finland (André Briend); and Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom (Francesco Checchi).

This work was supported by the Department of Nutrition for Health and Development, World Health Organization (S. I.) and by Médecins Sans Frontières (R. F. G.).

The authors thank the Ministry of Health of Niger and the Regional Public Health Office of Maradi. They also thank the teams of Epicentre and Médecins Sans Frontières staff for their work and dedication in the collection of the data used in this analysis.

Conflict of interest: none declared.

REFERENCES

1. Black RE, Allen LH, Bhutta ZA, et al. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet*. 2008;371(9608):243–260.
2. Médecins Sans Frontières. *Nutrition Guidelines*. Paris, France: Médecins Sans Frontières; 1995.
3. World Health Organization. *The Management of Nutrition in Major Emergencies*. Geneva, Switzerland: World Health Organization; 2000.
4. MacMahon B, Pugh TF. *Epidemiology Principles and Methods*. Boston, MA: Little, Brown & Company; 1970.
5. Miettinen O. Estimability and estimation in case-referent studies. *Am J Epidemiol*. 1976;103(2):226–235.
6. Garenne M, Willie D, Maire B, et al. Incidence and duration of severe wasting in two African populations. *Public Health Nutr*. 2009;12(11):1974–1982.
7. World Health Organization. *The WHO Child Growth Standards*. Geneva, Switzerland: World Health Organization; 2010. (<http://www.who.int/childgrowth/standards/en>). (Accessed August 4, 2010).
8. World Health Organization and United Nations Children's Fund. *WHO Child Growth Standards and the Identification of Severe Acute Malnutrition in Infants and Children*. Geneva, Switzerland: World Health Organization; 2009.
9. Isanaka S, Nombela N, Djibo A, et al. Effect of preventive supplementation with ready-to-use therapeutic food on the nutritional status, mortality, and morbidity of children aged 6 to 60 months in Niger: a cluster randomized trial. *JAMA*. 2009;301(3):277–285.
10. Defourmy I, Minetti A, Harczy G, et al. A large-scale distribution of milk-based fortified spreads: evidence for a new approach in regions with high burden of acute malnutrition. *PloS One*. 2009;4(5):e5455. (doi: 10.1371/journal.pone.0005455).

11. Hamill PV, Drizid TA, Johnson CL, et al. *NCHS Growth Curves for Children Birth–18 Years*. (Vital and health statistics, series 11, no. 165). Hyattsville, MD: National Center for Health Statistics; 1977. (DHEW publication no. (PHS) 78-1650).
12. Bolker BM. *Ecological Models and Data in R*. Princeton, NJ: Princeton University Press; 2008.
13. R Development Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2010.