A Mathematical Model to Estimate The Incidence of Child Wasting In Yemen

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A Mathematical Model to Estimate the Incidence of Child Wasting In Yemen

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Abstract

Introduction:

The ongoing civil war in Yemen has severely restricted imports of food and fuel, disrupted livelihoods and displaced millions, worsening already high pre-war levels of food insecurity. Paired with frequent outbreaks of disease and a collapsed health system, this has brought rates of wasting in children under five to the country's highest recorded levels, which continue to increase as the crisis worsens and aid becomes increasingly limited. In their planning of services to treat and prevent wasting in children, humanitarian agencies rely on a standard calculation to estimate the expected number of cases for the coming year, where incidence is estimated from prevalence and the average duration of an episode of wasting. The average duration of an episode of moderate and severe wasting is currently estimated at 7.5 months – a globally-used value derived from historical cohort studies. Given that incidence varies considerably by context – where food production and availability, treatment coverage and disease rates all vary – a single estimate cannot be applied to all contexts, and especially not a highly unstable crisis setting such as Yemen. While recent studies have aimed to derive context-specific incidence estimates in several countries, little has been done to estimate the incidence of both moderate and severe wasting in Yemen.

Methods:

In order to provide context-specific estimates of the average duration of an episode, and resultingly, incidence correction factors for moderate and severe wasting, we have developed a Markov model. Model inputs were estimated using a combination of treatment admission and outcome records compiled by the Yemen Nutrition Cluster, 2018 and 2019 SMART surveys, and other estimates from the literature. The model derived estimates for the governorate of Lahj, Yemen; it was initialized using August 2018 SMART survey prevalence data and run until October 2019 – the date of the subsequent SMART survey. Using a process of repeated model calibration, the incidence correction factors for severe wasting and moderate wasting were found, validating the resulting prevalence against the recorded value from the 2019 SMART survey.

Results:

The average durations of an episode of moderate and severe wasting were estimated at 4.86 months, for an incidence correction factor *k* of 2.59, and 3.86 months, for an incidence correction factor *k* of 3.11, respectively. It was found that the annual caseload of moderate wasting was 36% higher and the annual caseload of severe wasting 58% higher than the originally-assumed values, estimated with $k = 1.6$.

Conclusion:

The model-derived incidence rates, consistent with findings from other contexts that a global incidence correction factor cannot be sufficient, allow for improved, context-specific estimates of the burden of wasting in Yemen. In crisis settings such as Yemen where funding and resources are extremely limited, the model's outputs holistically capture the burden of wasting in a way that may guide effective decision-making and may help ensure that limited resources are allocated most effectively.

Keywords: Yemen, acute malnutrition, wasting, mathematical modeling, incidence correction factor, child health

53 **Introduction:**

54 Food security crises are closely linked to armed conflict [1]. As a result of both the widespread
55 destruction and devastation that violent conflict brings as well as many of the indirect effects of war
56 which disrupt the daily lives of civilians, conflict creates many of the conditions that drive hunger. War
57 frequently disrupts the food supply - with starvation used as a tactic of war and warring parties
58 deliberately restricting the distribution of food and critical supplies or through the destruction of farms
59 and livestock. In contexts where health services are also extremely limited and much of the health
60 infrastructure destroyed, conflict-affected areas often see high rates of untreated disease, which
61 worsens the risk of undernutrition. Young children are particularly vulnerable to wasting, a rapid
62 deterioration in nutritional status over a short period of time, and often suffer severe and irreversible
63 consequences as a result [2].

64 In Yemen, where the country's current hunger crisis is largely the result of warring parties' deliberate
65 efforts to restrict food, and the war has crippled the economy and disrupted livelihoods, the role of
66 conflict in creating the conditions that drive wasting among children is strikingly clear. The ongoing civil
67 war in Yemen has resulted in what has been called the worst humanitarian crisis in recent history. The
68 latest IPC analysis for Yemen revealed that 13.5 million people (45% of the analyzed population) were
69 facing high levels of acute food insecurity – in IPC Phase 3 or above [3]. Child wasting rates in Yemen are
70 among the highest in the world and continue to increase as the crisis worsens and aid becomes
71 increasingly limited [4]. In some areas of Yemen, it is estimated that more than one in four children
72 suffer from wasting [5]. Untreated wasting can permanently impair a child's cognitive and physical
73 development and places them at an increased risk of morbidity and mortality; a wasted child is highly
74 vulnerable to severe and recurrent infections [2]. Nutritional interventions to address child wasting are
75 implemented according to the Community-Based Management of Acute Malnutrition (CMAM) Model, the
76 globally endorsed standard for management of acute malnutrition, also known as wasting. The CMAM
77 model aims to reduce mortality and morbidity from wasting by providing early case-finding and

effective treatment and by strengthening the local community's capacity to prevent, identify and manage wasting.

Since the conflict in Yemen began in 2015, humanitarian agencies have scaled up efforts to both prevent, identify and treat cases of Global Acute Malnutrition – Moderate Acute Malnutrition (MAM), also known as moderate wasting, and Severe Acute Malnutrition (SAM), also known as severe wasting– in children under five. (Though the terms wasting and acute malnutrition are often used interchangeably, acute malnutrition is the umbrella term under which wasting falls. Acute malnutrition is defined by the presence of wasting and/or bilateral pitting nutritional oedema [6]. However, the terms moderate and severe wasting will be used throughout this paper to refer to the broader category of acute malnutrition. This is in accordance with the recent shift within the public health and nutrition community towards a generalized use of the term wasting to refer to acute malnutrition as defined by Weight-for-height Z-Score (WHZ), mid-upper arm circumference (MUAC) and/or oedema.)

For planning purposes, humanitarian agencies use prevalence estimates and historical program data to estimate the expected number of cases of moderate and severe wasting as well as expected treatment coverage for the coming year. Knowing the rate of incidence, defined as the number of new cases of wasting which develop over a specified period of time, is critical in anticipating the needs of a program and effectively planning treatment services and resource allocation. However, given that it is difficult to directly observe and measure rates of incidence, estimates of annual wasting caseloads are found using a standard relationship between incidence, prevalence and the average duration of an episode of wasting as described by Equation 1. Estimates of the prevalence of wasting are available through cross-sectional SMART surveys conducted annually in Yemen, and the average duration of an untreated episode of moderate and severe wasting has been estimated at 7.5 months (for $k = 1.6$). This approach for incidence estimation has been proposed for use in the CMAM model to estimate under-five wasting caseloads across all contexts [7].

102 **Equation 1.** $Incidence = prevalence \times \frac{12}{duration\ of\ episode}$

103 Or, expressed in terms of the incidence correction factor k:

104 $$Incidence = prevalence \times k$$

105 The value currently taken as the average duration of an untreated episode of moderate and severe
106 wasting (7.5 months) was found from two cohort studies conducted in the Democratic Republic of
107 Congo and Senegal in the 1980s and, in the absence of other estimates, is currently used globally [8]. It is
108 difficult to directly observe and estimate the duration of an episode of wasting and so revised, context-
109 specific estimates of the duration of an episode remain limited. (Ethical constraints prevent the
110 possibility of directly measuring the duration of an untreated episode given that this would require
111 following a cohort of wasted children while denying them treatment.) The assertion that a single,
112 standard estimate of the average duration of an untreated episode of wasting is insufficient is supported
113 by both theoretical and quantitative evidence. Intuitively, it would be expected that the average duration
114 of an episode of wasting – a value directly affected by contextual factors such as food availability, disease
115 rates, and treatment accessibility – varies considerably by context. In addition, values derived from the
116 1980s likely cannot even be applied to the regions from which they were derived today. A number of
117 recent studies have confirmed that this value does in fact vary by context. An analysis of cohort and
118 survey data from three West African countries (Mali, Niger and Burkina Faso) between 2009 and 2012
119 showed that the incidence correction factor for severe wasting varies widely by country [9]. More recent
120 studies conducted in Mali, Burkina Faso, Niger and Nigeria have reached similar findings [10,11,12]. In
121 each of these contexts, the 7.5-month value was found to considerably underestimate incidence.

122 Reliable estimates of caseload are needed for effective service planning and are critical in a context
123 where funding and resources are extremely limited; however, the current, standardly-used approach to
124 estimate incidence presents several major limitations. While it is clear that a single k-value cannot be

applied to all contexts, little has been done to explore the incidence of wasting in the context of Yemen. Without an adjusted, context-specific incidence correction factor for Yemen, when Equation 1 is used to estimate incidence, the only source of variance in this calculation from year to year is prevalence, as measured by the SMART survey. Basing all planning decisions primarily on annual estimates of prevalence – a function of not just incidence but also recovery, treatment and fatality rates, which only captures a single snapshot – provides limited insight that can be used to guide policy decisions. In addition to the fact that wasting incidence has been largely unexplored in the context of Yemen, beyond Yemen, past work which has explored context-specific incidence correction factors has focused primarily on severe wasting; little has been done to explore the incidence of moderate wasting or the relationship between moderate and severe wasting in studies of incidence. With severe wasting arising as existing cases of moderate wasting worsen in severity, an understanding of the interplay between them is needed to holistically assess the burden of wasting. Attempting to measure the incidence of moderate and severe wasting while assessing each one independently of the other neglects the known paths between them and ways in which they inherently interact to form a connected system whereby cases of moderate wasting may progress to severe wasting and cases of severe wasting may improve to moderate wasting.

To address these limitations, we aimed to derive context-specific incidence correction factors for moderate and severe wasting for the governorate of Lahj, Yemen. In doing so, we aimed to model the complete system of interactions which determines the burden of moderate and severe wasting by capturing the bidirectional paths between them. We developed a Markov model to represent this system - a model commonly used in epidemiology to model the progression of disease – and derive estimates of the average duration of an episode (and corresponding incidence correction factors) of moderate and severe wasting. Our model examines the governorate of Lahj, Yemen. Lahj was selected in accordance with guidance from UNICEF team members given the severity of the situation and the relative strength of data reporting from the region given that the area is not one of active conflict.

150 The model-derived incidence correction factors provide adjusted, context-specific estimates of incidence
151 which may allow for more effective service planning and policy decisions by providing more accurate
152 estimates of the number of new cases expected to develop. Additionally, the model framework provides
153 a tool for burden estimation and planning which simulates ground realities using routinely-collected
154 data and therefore does not require direct observation, as has been the case for several similar studies
155 in other regions which estimated the average duration of an episode through longitudinal cohort
156 studies. Using cross-sectional prevalence estimates, routinely-collected records of treatment
157 admissions and respective outcomes and other estimates from the available literature, the model
158 simulates ground realities without requiring that additional efforts or resources be allocated toward
159 direct observation. The model also seeks to capture the complete system of interactions between rates
160 of incidence, the various stages in the progression of wasting, as well as rates of treatment and their
161 respective outcomes, which collectively determine the burden of wasting. Because the model captures
162 each of these paths, decision-makers can modify the model's parameters to holistically simulate the
163 long- and short-term consequences of a potential decision, such as scaling up a given intervention,
164 allowing the model's outputs to guide decisions about future interventions.

165 **Methods**

166 The burden of wasting is determined by a set of paths between moderate wasting, severe wasting and
167 severe wasting with complications as well as treatment admissions and outcomes, creating a network of
168 states for children to move between. This system easily maps onto the general framework of a Markov
169 model, which was used to represent this system. These models are commonly used for probabilistic
170 modeling, especially in the field of epidemiology where there are a defined number of outcomes or
171 health states being modeled [13]. To define a Markov model, the following elements are needed: a set of
172 mutually exclusive and exhaustive possible states, the probabilities of initially residing in each of these
173 states, called the initiate state distribution, and the probability of transitioning from any one state to

every other state, called transition probabilities. Transitions within our model were defined at monthly time intervals. Given the initial state distribution and the set of transition probabilities, the model provides a breakdown of the number of children residing in each state each month.

A child can be classified according to their nutritional status as being either non-wasted, wasted but not in treatment, in-treatment for wasting or deceased. The Markov model presented distinguishes between each level of wasting (moderate wasting, severe wasting and severe wasting with complications) and its respective treatment program. It is composed of eight nutritional states: *Healthy, Moderately Wasted, Severely Wasted*, *Severely Wasted with Complications*, $Treatment_M$, $Treatment_S$, $Treatment_{SC}$ and *Deceased*. If a child resides in either the *Moderately Wasted, Severely Wasted, or Severely Wasted with complications* state, they are wasted but not currently in treatment. However, because the model does account for rates of defaulters (children who stop attending treatment appointments before reaching discharge criteria) and non-responders (children who fail to respond to treatment), if a child currently resides in any of these three states, this does not imply that they have never been admitted to treatment and hence these state names do not use the term *untreated*. During the model's simulation, children can move between states at a set of monthly transition rates, representing the probability that a child in one state will move to another (or remain in the same one) from one month to the next. All possible transitions are depicted by the arrows in Figure 1. Given the initial state distribution and the set of transition probabilities, the model provides a breakdown of the number of children residing in each nutritional state each month.

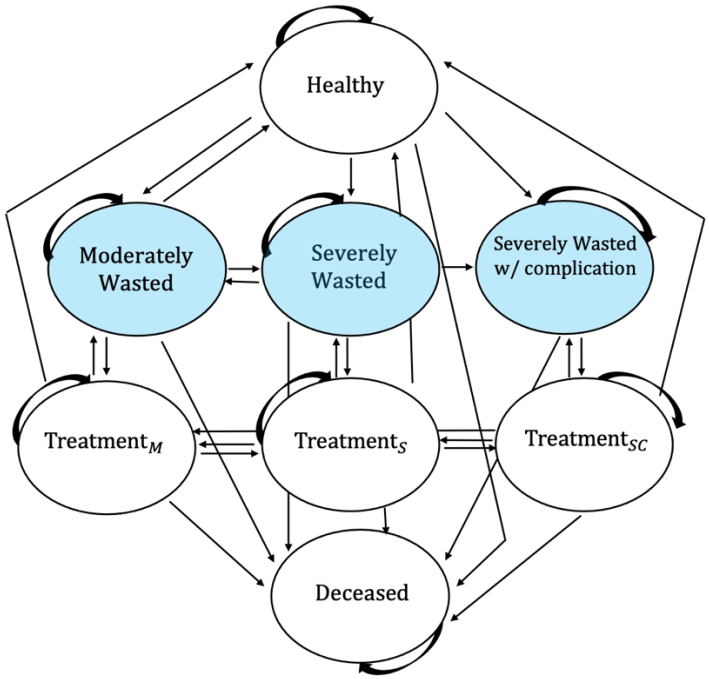


Figure 1. Model State-Transition Diagram. Arrows depict all possible transitions between nutritional states. Blue states indicate a state where a child is wasted but not currently in treatment $Treatment_M$, $Treatment_S$. and $Treatment_{SC}$ refer to treatment for moderate wasting, severe wasting, and severe wasting with complications, respectively.

The model is based on the following assumptions:

1. A child must reside in a wasting state (*Moderately Wasted, Severely Wasted or Severely Wasted with complications*) before entering a treatment state.
2. A child cannot transition from the *Healthy* state directly to the *Severely Wasted* state; a child residing in the *Severely Wasted* state must have previously resided in the *Moderately Wasted* state.
3. Spontaneous recovery can occur among cases of moderate wasting.
4. A severely wasted child will not return to the *Healthy* state without first residing in either the $Treatment_S$ state or the *Moderately Wasted* state. A child cannot transition directly from the *Severely Wasted* state to the *Healthy* state; however, they may transition to *Moderately Wasted* and from *Moderately Wasted*, return to the *Healthy* state.
5. A child in treatment for any form of wasting may default from or fail to respond to treatment, in which case they would transition from the treatment state back to the wasting state (*Moderately Wasted, Severely Wasted, or Severely Wasted with complications*) in which they previously resided.

6. The *Deceased* state is an absorbing state, meaning that once a child enters this state, they cannot transition out of it.

Determining the Initial State Distribution

The model's initial state distribution was informed by 2018 cross-sectional SMART survey data available at the Nutrition Cluster level, reporting the prevalence of moderate and severe wasting among under-five children in Lahj using Weight-For-Height Z-Score as the screening metric [14]. Two separate surveys were conducted in Lahj in August of 2018: one in the highlands region and another in the lowlands region. The two datasets were combined using SMART estimates of the under-five population of each region of Lahj and SMART estimates of the prevalence of moderate and severe wasting. Data from the Yemen Nutrition Cluster was used to estimate the average number of children enrolled in treatment for moderate wasting treatment (Targeted Supplementary Feeding Programs) and treatment for severe wasting (Outpatient Therapeutic Feeding Programs) each month. Because children enrolled in treatment programs would remain in treatment for more than one month, the model aimed to capture the fact that during any given month, among the children currently enrolled in treatment programs, (those currently residing in the treatment state) only some of them would have been admitted in the current simulated month and only some would be discharged in the current simulated month.

Nutritional State	Number of Children	Initial State Probability
Healthy	129581	0.7717
Severely Wasted	4199	0.0250
Moderately Wasted	19224	0.1145
Severely Wasted with Complications	197	0.001174
Treatment$_M$	9987	0.05948

Treatment$_S$	4719	0.02810
Treatment$_{SC}$	0	0.0
Deceased	0	0.0

Table 1. Initial State Distribution. Number of children in each state and corresponding initial state probability at start of model simulation.

While the SMART procedure does not distinguish between untreated wasted children and those who are enrolled in treatment programs, the model framework designated two separate states for treated and untreated children, which required that several simplifying assumptions be made. For severe wasting, it was assumed that among those enrolled in treatment, only those admitted within the past month would still satisfy the Z-Score used to classify severe wasting cases (Z-Score < -3.0) and were therefore included in the estimated number of severe wasting cases produced by SMART [6]. The remaining cases of severe wasting were assumed to be untreated and would be found in the *Severely Wasted* state. The same assumptions were made about cases of moderate wasting (-3.0 < Z-Score < -2.0). In the absence of estimates of the specific prevalence of severe wasting with complications, it was assumed that the ratio of complicated to uncomplicated cases of untreated severe wasting was equivalent to the ratio of uncomplicated treatment admissions to complicated treatment admissions. Because in-patient treatment for complicated severe wasting generally takes less than one month, it was assumed that no children were in treatment for severe wasting with complications to start. The complete initial state distribution is shown in Table 1. Given that the prevalence of wasting varies considerably by season, it was established that the model would begin its simulated year in August – the month during which the 2018 SMART surveys were conducted in Lahj. The model would be run until October 2019 – the date of the subsequent SMART survey in 2019 – in order to provide a basis for comparison for the resulting prevalence of moderate and severe wasting at the end of its simulation [15].

Nutrition State Transition	Interpretation	Transition Probability	Source Data/Notes
From *Healthy* State			
Healthy to Healthy (p_{HH})	Remains healthy	1 – p_{HM} – 0.000750	---
Healthy to Moderately Wasted (p_{HM})	Incidence of Moderate Wasting	**Unknown**	**To be estimated**
Healthy to Severely Wasted (p_{HS})	Develops severe wasting from healthy	0	Model assumption 2
Healthy to Severly Wasted with complications (p_{HC})	Develops severe wasting w/ complication from healthy	0	---
Healthy to Deceased (p_{HD})	General Under-five Mortality Rate	0.000750	2019 Lahj SMART Survey
From *Severely Wasted* State			
Severely Wasted to Healthy (p_{SH})	Severe Wasting Spontaneous Recovery	0	Model assumption 4
Severely Wasted to Moderately Wasted (p_{SM})	Untreated severe wasting improves to moderate wasting	0.0914	Single time point follow-up of severely wasted children – India (Sachdev et al.) [17]
Severely Wasted to Severely Wasted (p_{SS})	Severe wasting remains severe wasting	1 - p_{ST_S} – 0.0724	---
Severly Wasted to Severely Wasted with complications (p_{SC})	Untreated severe wasting develops medical complication	0.01026	Nutrition Cluster OTP/TFC Data
Severely Wasted to Treatment$_S$ (p_{ST_S})	Admitted to OTP	[0.200,0.678]	Nutrition Cluster OTP Data
Severely Wasted to Deceased (p_{SD})	Untreated Severe Wasting Case Fatality	0.00872	Hazard ratios from pooled analysis (Olofin et al.) [16]
From *Moderately Wasted* State			
Moderately Wasted to Healthy (p_{MH})	Moderate Wasting Spontaneous Recovery	0.07814	Randomized control - Burkina Faso (Nikièma et al.) [18]
Moderately Wasted to Severely Wasted (p_{MS})	Untreated moderate wasting progresses to severe wasting (severe wasting incidence)	**Unknown**	**To be estimated**
Moderately Wasted to Moderately Wasted (p_{MM})	Moderate wasting remains moderate wasting	1 - p_{MS} - p_{MT_m}- 0.0807	---
Moderately Wasted to Treatment$_M$ (p_{MT_m})	Admitted to TSFP	[0.0529,0.176]	Nutrition Cluster TSFP Data
Moderately Wasted to Deceased (p_{MD})	Untreated Moderate Wasting Case Fatality	0.00260	Hazard ratios from pooled analysis (Olofin et al.) [16]
From Severely Wasted *with complications* State			
Severely Wasted with complications to Severely Wasted with complications (p_{CC})	Severely wasted w/ complications remains severely wasted w/ complications	1 - p_{CT_C} - 0.00260	---
Severely Wasted with complications to Treatment$_{SC}$ (p_{CT_C})	Admitted to TFC	[0.0,0.229]	Nutrition Cluster TFC Data
Severely Wasted with complications to Deceased (p_{CD})	Severely Wasted w/ complications Untreated Case Fatality	0.00260	Hazard ratios from pooled analysis (Olofin et al.) [16]
From *Treatment$_S$* State			
Treatment$_S$ to Healthy (p_{T_SH})	Cured at OTP	0.307	Nutrition Cluster OTP Data
Treatment$_S$ to Severely Wasted (p_{T_SS})	Defaults from OTP	0.0262	Nutrition Cluster OTP Data
Treatment$_S$ to Treatment$_M$ ($p_{T_ST_m}$)	Referred from OTP to TSFP	0.00503	Nutrition Cluster OTP Data
Treatment$_S$ to Treatment$_S$ ($p_{T_ST_S}$)	Remains in OTP	0.657	Nutrition Cluster OTP Data
Treatment$_S$ to Treatment$_{SC}$ ($p_{T_ST_C}$)	Referred from OTP to TFC	0.004204	Nutrition Cluster OTP Data

$Treatment_S$ to Deceased ($p_{T_S D}$)	In-treatment (OTP) case fatality	0.000156	Nutrition Cluster OTP Data
From $Treatment_M$ State			
$Treatment_M$ to Healthy ($p_{T_m H}$)	Cured at TSFP	0.103	Nutrition Cluster TSFP Data
$Treatment_M$ to Moderately Wasted ($p_{T_m M}$)	Default from TSFP	0.00442	Nutrition Cluster TSFP Data
$Treatment_M$ to $Treatment_M$ ($p_{T_m T_m}$)	Remains in TFSP	0.892	Nutrition Cluster TSFP Data
$Treatment_M$ to $Treatment_S$ ($p_{T_m T_S}$)	Referred to OTP from TSFP	0.000918	Nutrition Cluster TSFP Data
$Treatment_M$ to Deceased ($p_{T_m D}$)	In-treatment (TSFP) case fatality	0	Nutrition Cluster TSFP Data
From $Treatment_{SC}$ State			
$Treatment_{SC}$ to Healthy ($p_{T_C H}$)	Cured at TSFP	0.792	Nutrition Cluster TSFP Data
$Treatment_{SC}$ to $Treatment_M$ ($p_{T_C T_m}$)	Referred from TFC to TSFP	0.0492	Nutrition Cluster TSFP Data
$Treatment_{SC}$ to $Treatment_S$ ($p_{T_C T_S}$)	Referred from TFC to OTP	0.158	Nutrition Cluster TSFP Data
$Treatment_{SC}$ to $Treatment_{SC}$ ($p_{T_C T_C}$)	Remains in TFC	0	Nutrition Cluster TSFP Data
$Treatment_{SC}$ to Deceased ($p_{T_c D}$)	In-treatment (TFC) case fatality	0	Nutrition Cluster TSFP Data
From *Deceased* State			
Deceased to Deceased (p_{DD})	*Deceased* state is absorbing	1	Model assumption 6

Table 2. List of Model's Transition Probabilities, Conceptual Interpretations and Sources. Each transition probability represents the probability that a child in a given nutritional state moves to another within one month. All unlisted transition probabilities have a value of 0, indicating that they are not possible transitions within the model framework.

Estimating Time-Varying Probabilities: Treatment Admission Transition Probabilities

All transition probabilities representing the probability of a child being admitted to a treatment program (including p_{ST_S}, p_{MT_m}, and p_{CT_C}) were time-varying. Given that monthly treatment admission data was available, and admissions varied considerably from month to month, the respective transition probabilities were recalculated for each month during which the model was run to provide time-varying transition probabilities. Though a deeper analysis of the underlying causes of any significant variations observed in each month's recorded admissions would allow the model to operate with a predictive capacity, because the model aimed to retrospectively estimate incidence, time-dependent probabilities were directly estimated to reflect these variations without further consideration of their causes.

Estimating Stationary Transition Probabilities: Treatment Outcomes, General Mortality, Spontaneous Recovery, Untreated Case Fatality

All other transition probabilities were computed as stationary probabilties, meaning they remain unchanged over time. Treatment outcome probabilties (with outcomes including cure, default, non-response, referral to other program, and in-treatment fatality) were estimated from monthly CMAM compiled data provided by the UNICEF Yemen country office. This data included complete records of rates of admission and respective outcomes of children enrolled in Targeted Supplementary Feeding Programs (TSFPs) for moderating wasting treatment, Outpatient Therapeutic Programs (OTPs) for severe wasting treatment and Therapeutic Feeding Centers (TFCs) for complicated severe wasting treatment. This data is available at the Yemen Nutrition Cluster level and includes compiled records of all CMAM nutritional interventions implemented across the governorate. Transition probabilities corresponding to transitions from any treatment state back to the non-wasted state was estimated from respective program cure rates. Transfer between various treatment programs (OTP, TSFP, and TFC) were also considered as shown in Table 2. Transition probabilties corresponding to transitions from any treatment state back to a wasted state were estimated using recorded rates of default and non-response to treatment.

The general mortality rate (p_{HD}) was estimated using estimated using the under-five mortality rate recorded in the Lahj 2019 SMART surveys [15]. Given the scarcity of estimates of untreated wasting case fatality rates specific to Yemen, the model's untreated moderate and severe wasting case fatality rates ($p_{MD,}$ p_{SD}, p_{CD}) were derived from hazard ratios estimated by a pooled meta-analysis using data from cohorts across different contexts before the onset of CMAM [16]. Because it is difficult to observe and measure rates of spontaneous recovery among untreated cases of wasting, both transition probabilities representing a transition of recovery ($p_{MH,}$ p_{SM}) were derived from studies from other contexts [17,18]. The rate of spontaneous recovery for severe wasting was selected from a systematic review by Lelijveld et al. in which they examine a number of studies examining various forms of treatment for moderate wasting [19]. Among those included, the randomized-control trial from Burkina Faso was selected for

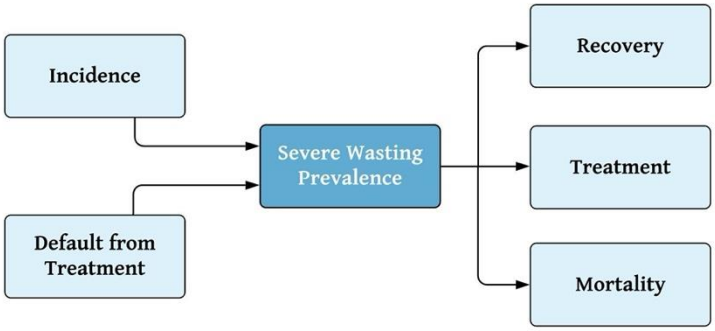
use in the model given that it was the only one where the control group was not provided micronutrient treatment (and this transition probability needed to reflect outcomes of untreated wasting), where the setting was not food secure, and where study definitions aligned with current definitions of moderate wasting [18]. All transition probabilities, as well as their conceptual interpretation and respective sources, are summarized in Table 2.

Estimating Average Duration of An Episode of Severe Wasting

With all other transition rates calculated, the incidence of severe and moderate wasting was found using a process of repeated model calibration. As shown in Figure 2, the prevalence of severe wasting can be understood as a function of several other model rates, including those determining the probability that a child enters the *moderately wasted* state – incidence or default from treatment – and those determining that a probability that a child leaves the *moderately wasted* state – through recovery, treatment or mortality. Thus, in terms of the model's states, children can leave the *Severely Wasted* state either by entering the $Treatment_S$ state, entering the *Moderately Wasted* state (recovery) or entering the *Deceased* state. Children enter the *Severely Wasted* state when they develop severe wasting from moderate wasting, representing the rate of incidence, or transition from $Treatment_S$ back to *Severely Wasted* (default.) Because the prevalence of moderate wasting is directly influenced by the incidence of severe wasting, the incidence of severe wasting needed to first be estimated, before being used to inform the estimation of moderate wasting prevalence.

Given that the incidence of severe wasting was the single unknown in Figure 2, while each of the other transition probabilities as well as the expected prevalence was known, incidence was back-calculated through model calibration. Using the initial state distribution informed by 2018 data shown in Table 1 as well as the model's established non-incidence rates, the model was run for 14 simulated months (until October 2019) and calibrated with a range of estimates of severe wasting incidence, in order to find the value which would result in a prevalence that matched the value reported in the 2019 SMART survey at the end of the model's simulated period [15]. At the end of the simulated period, the number of children

310 in the model's *Severely Wasted* state would represent the prevalence of untreated severe wasting. In
311 order to remain consistent with the original assumptions about the combined prevalence of untreated
312 and currently-in-treatment cases represented by the SMART prevalence, the estimated prevalence used
313 for validation against SMART results was calculated as the sum of the number of children in the *Severely*
314 *Wasted* state at month 14 (untreated case prevalence) and the number of children admitted to treatment
315 within the past month.



316 **Figure 2.** Magnified view of rates determining the prevalence of severe wasting within model framework. With the incidence of severe wasting as the single unknown, repeated model calibration was used to estimate the rate of incidence.

317 Estimating Average Duration of An Episode of Moderate Wasting

318 Model calibration was also used to estimate the average duration of a moderate wasting episode.
319 Because the model framework assumes all severe wasting cases develop from existing cases of
320 moderate wasting, the prevalence of moderate wasting is also directly affected by the incidence of
321 severe wasting. The model-derived incidence rate of severe wasting was therefore used as an input in
322 the process of determining the average duration of an episode of moderate wasting. Spontaneous
323 recovery was also assumed to occur among cases of moderate wasting, where a child with untreated
324 moderate wasting can return directly to the *Healthy* state. It was also assumed that cases of severe
325 wasting could improve to moderate wasting, contributing an additional path of entry into the
326 *moderately wasted* state. Using each of the transition probabilities (either entering or leaving the
327 *Moderately Wasted* state) shown in Figure 3, the model was calibrated to determine the average

duration of an episode of moderate wasting, again using the prevalence recorded in the 2019 SMART survey as the basis of comparison. The same assumptions were made about treated and untreated cases as previously described for severe wasting.

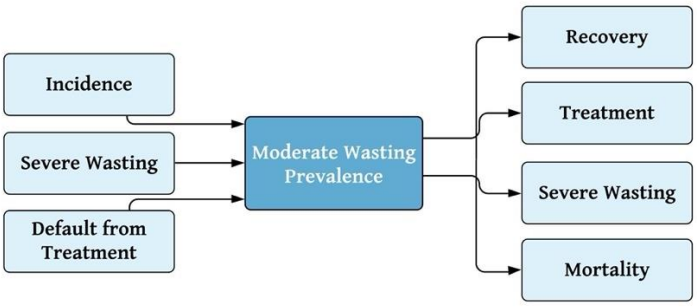


Figure 3. Magnified view of rates determining the prevalence of moderate wasting within model framework. Upon estimating the incidence of severe wasting, the incidence of moderate wasting remained the single unknown and could be estimated through repeated model calibration.

Sensitivity Analysis

In order to quantify uncertainty within the model – either resulting from the general uncertainty within program records or the use of several data sources from contexts outside of Yemen – a one-way, deterministic sensitivity analysis was conducted. Sensitivity analysis puts the probability of variables (transition probabilities) in the model through a range of possible values, and the outcome of the model, in the case, the resulting incidence of wasting, is examined [20]. One-way sensitivity analysis examines one transition probability at a time, while holding all others constant. This was performed for moderate and severe wasting incidence, respectively. Each transition probability directly affecting the incidence of severe wasting – including that of treatment admissions, spontaneous recovery, case fatality, default from treatment and mortality – was allowed to vary between 50% and 150% of its base value. The same analysis was performed for each transition probability directly affecting the incidence of moderate wasting – including severe wasting incidence, treatment admissions, recovery, default from treatment and case fatality – was allowed to vary between 50% and 150% of its base value. Upon modulating each parameter through the defined range, the same process of model calibration was performed in order to

347 produce the corresponding incidence rate. This analysis would reveal which of these rates had the
348 greatest impact on the incidence rate derived by the model.

349

350 **Results**

351 Average Duration of Episode and Adjusted K-values

352 Upon repeated model calibration, it was found that the average duration of an episode of severe wasting
353 was 3.86 months, with a corresponding incidence correction factor *k* of 3.11. Using this value to estimate
354 the incidence of severe wasting (used to calculate the *Moderately Wasted* to *Severely Wasted* transition
355 probability), subsequent model calibration produced an estimate of the average duration of an episode
356 of moderate wasting of 4.64 months, for an incidence correction factor *k* of 2.59. Table 3 presents a
357 comparison of the model's estimated prevalence at the end of its period of simulation in October 2019
358 and the 2019 SMART survey's recorded prevalence, used for validation. The model-derived incidence
359 rates could not be directly validated given that the model aimed to use the available data to estimate a
360 previously unknown value. While caseload may be roughly estimated using treatment admissions data
361 and expected program coverage, in a highly unstable crisis setting such as Yemen where coverage likely
362 varies over time, any information about estimated coverage derived from cluster surveys or other
363 sources likely presents several limitations. In addition, several different methods for estimating program
364 coverage exist and it is often difficult to establish certainty in the denominator of this calculation (the
365 number in the program / the number who should be in the program.) The model aimed to utilize the
366 available data regarding outcomes that are directly observable in order to provide information about
367 outcomes which are not, namely the incidence of wasting. Thus, its estimates of untreated children,
368 along with known values of the number of children enrolled in treatment, can be used in order to refine
369 estimates of program coverage, rather than using uncertain estimates of program coverage to derive or
370 validate information about untreated cases.

371

	SMART 2019	Model Output
Severe Wasting Prevalence	3733	3738.39
Moderate Wasting Prevalence	21358	21374.55

Table 3. Validation of resulting prevalence of moderate and severe wasting in October 2019 using adjusted incidence rates.

As expected, both values of the average duration of an episode of wasting were considerably lower than the originally assumed value of 7.5 months. With caseload defined as the number of prevalent cases at the start of the year plus the number of incident cases over the course of the year, the adjusted annual caseloads for moderate and severe wasting were found to be 36% and 58% higher, respectively, than the originally assumed values as shown in Table 4. A comparison of the monthly number of incident cases of moderate and severe wasting is show in Figure 4. Knowing the incidence of both moderate and severe wasting – where it was assumed all severe wasting cases developed from existing cases of moderate wasting – the frequency at which cases of moderate wasting progressed to severe wasting could be derived. It was found that approximately 27% of children who were moderately wasted developed severe wasting over the course of the model's simulation.

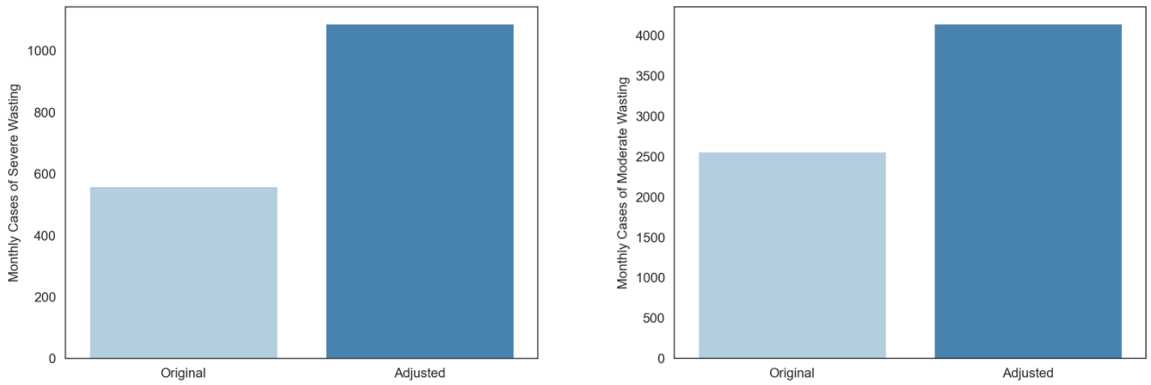


Figure 4. (A) Comparison of monthly number of cases of severe wasting using original approach (k = 1.6) and adjusted (model-derived) monthly number of cases of severe wasting (k = 1.6). **(B)** (A) Comparison of monthly number of cases of moderate wasting using original approach (k = 3.11) and adjusted (model-derived) monthly number of cases of moderate wasting (k = 2.59).

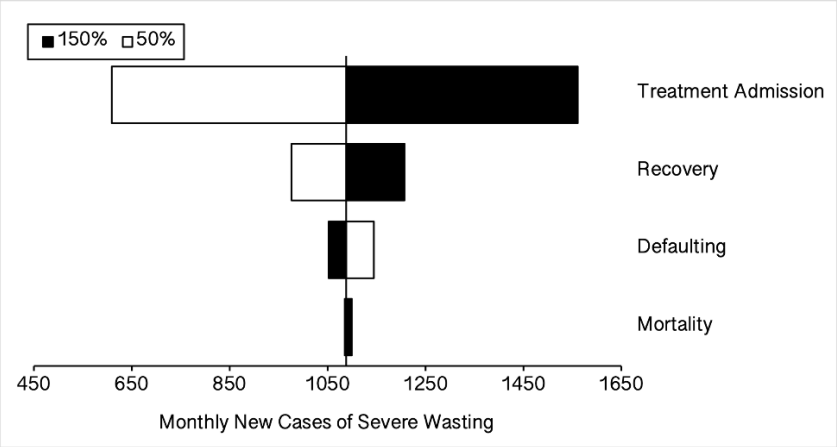
	Original Annual Caseload	Adjusted Annual Caseload	Average duration of episode (months)	Adjusted k-value
Moderate Wasting	49981	67891	4.64	2.59
Severe Wasting	10919	17256	3.86	3.11

Table 4. Summary of main findings. Original caseload refers to the value estimated with k = 1.6 and adjusted caseload refers to model-dervied estimate using adjusted k-value.

Sensitivity Analysis

While the model-derived incidence rates could not be directly validated, the uncertainty within the data used to estimate these values, could be quantified through sensitivity analysis. The results of the sensitivity analysis for moderate and severe wasting incidence are shown in Figure 5. Longer bars indicate that the corresponding parameter had a greater impact on the resulting incidence, expressed as the monthly number of new cases of moderate and severe wasting. For both moderate and severe wasting, transition probabilities for treatment admissions and spontaneous recovery were those the model was most sensitive to. Bars corresponding to the transition probability for defaulting appear inverted in comparison to the others due to the fact that an increase in defaulting, (and subsequent return to the untreated wasting state) where all other rates and prevalence were held constant, would result in a lower incidence rate. The same is true of the bar corresponding to severe wasting recovery in Figure 5B; an increase in the probability of severe wasting recovery would indicate a higher probability of return back to the *Moderately Wasted* state. The range of values swept for each parameter as well as the resulting k-value is presented in Table 5.

(A)



(B)

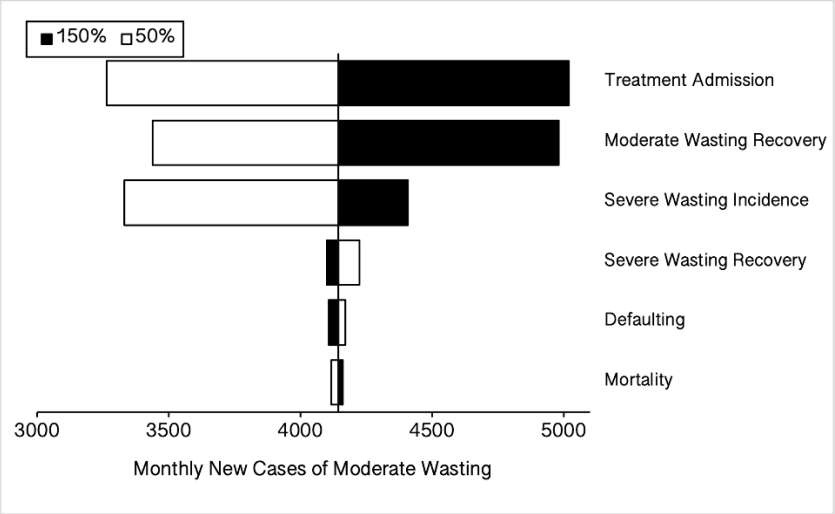


Figure 5. Sensitivity Analysis. **(A)** Sensitivity analysis for transition probabilities directly affecting incidence of severe wasting. **(B)** Sensitivity analysis on transition probabilities directly affecting incidence of severe wasting.

(A)

	Range	Average duration (months)
Treatment Admission	Time-varying	2.69 – 6.89
Recovery	0.0457 – 0.137	3.48 – 4.30
Defaulting	0.0131 – 0.0393	3.67 – 3.99
Mortality	0.00436 – 0.0131	3.82 – 3.87

(B)

	Range	Average duration (months)
Treatment Admission	Time-varying	3.83 – 5.89
Moderate Wasting Recovery	0.0391 - 0.117	3.86 - 5.59
Severe Wasting Incidence	0.0263 - 0.0939	4.36 – 5.77
Severe Wasting Recovery	0.0457 – 0.137	4.55 – 4.69
Defaulting	0.00221 – 0.00663	4.61 - 4.68
Mortality	0.00130 – 0.00390	4.62 – 4.67

Table 5. Range of values and resulting average duration of episode found from sensitivity analysis. **(A)** Sensitivity analysis results for severe wasting incidence. **(B)** Sensitivity analysis results for moderate wasting incidence.

Discussion

In this manuscript, we provide context-specific estimates of incidence for moderate and severe wasting among under-five children in Lahj, Yemen. From this, we provide a framework for holistically assessing the burden of wasting which considers the complete system of bidirectional paths which determine the prevalence and incidence of wasting. Accurate estimates of the incidence of wasting are critical for projecting the needs of a program and planning accordingly. While data from cross-sectional prevalence

surveys such as SMART is available, these estimates provide only a single snapshot using a metric which both varies seasonally and which is dependent on rates of mortality, recovery and treatment coverage. Estimates of monthly incidence – presenting the number of children developing new cases of moderate and severe wasting who will therefore require treatment – provide insights that may be of practical use to decision-makers in their planning of services.

The model-derived incidence rates align with the consensus within the literature that a single incidence correction factor of 1.6 results in underestimates of caseload and cannot be sufficient. As shown in Table 4, previous estimates did in fact lead to considerable underestimates of caseload, leaving populations of children in need of treatment unaccounted for. Thus, when target caseloads are calculated to plan for the coming year, relying on the original estimate to guide the planning of resources and services may lead to potential shortages. To the authors' knowledge, other studies have not explored the incidence of moderate and severe wasting in Yemen, and so our results cannot be assessed against other comparable findings. However, qualitative evidence from Yemen further confirms that previous estimates of caseload were considerable underestimates. First, historical program data from Yemen has shown that when caseload is calculated using $k = 1.6$, the number of children admitted to treatment sometimes surpasses the expected monthly caseload, leading to coverage estimates over 100%. Additionally, when the incidence correction factor is assumed to remain unchanged from year to year, the only source of variance in the annual caseload calculation comes from cross-sectional prevalence data. Because of this, estimated caseloads for wasting in Yemen over the last three years have remained relatively stable, which does not align with the general instability caused by the conflict or extensive reports showing that the nutrition situation has continued to deteriorate over the past years.

Several studies, using data from cohort studies in Mali, Burkina Faso, Niger and Nigeria, have found context-specific incidence correction factors [10,11,12]. All found the estimated duration of 7.5 months resulted in underestimates of caseload. An analysis of cohort and survey data from three West African

countries (Mali, Niger and Burkina Faso) between 2009 and 2012 showed that the incidence correction factor varies widely by country [9]. In each of these contexts, using a k-value of 1.6 was found to considerably underestimate incidence. However, as the authors of these works note, these results are not intended to be generalized to other regions where a number of contextual factors differ greatly. Thus, our results cannot be compared to those found in other contexts. They do, however, confirm the assumption that incidence correction factors vary considerably by context, and a single estimate cannot be appropriate. While it is known that seasonal variations will affect incidence rates of wasting, possible approaches for accounting for seasonal variability have not been extensively explored [21]. Each of the aforementioned studies exploring context-specific incidence correction factors, assumes a constant rate of incidence, though recognizing the limitations of doing so. Our model's ability to assess changes in incidence over time is constrained by the frequency at which prevalence data is collected - in this case, once a year. Thus, it can retrospectively provide incidence estimates on an annual basis, which may provide a basis for understanding changes to incidence on a longer scale. If more frequent cross-sectional prevalence data is available in other contexts, the model may be used to provide estimates of incidence over shorter periods of time and thus reflect changes to incidence throughout the course of the year.

While several other studies have aimed to estimate context-specific incidence correction factors in other contexts, the majority have examined severe wasting, and little work has been done to explore context-specific incidence rates in Yemen. To the authors' knowledge, little work has been done to examine the incidence of moderate and severe wasting together, under the same framework. Rather than considering the development of moderate wasting, severe wasting and severe wasting with complications independently of each other, the model framework allows for a consideration of the complete system of interactions that they form. With more accurate estimates of the incidence of severe wasting, the model captures the rate at which moderate wasting is expected to develop into severe wasting. Deriving this information would generally require direct observation of a cohort of moderately wasting children.

Additionally, by representing the burden of wasting in a model of this form, the model can not only estimate expected caseload, but also be used as a tool to simulate various scenarios in order to guide planning decisions. For example, by adjusting the rate of treatment for moderate wasting and running the model for several months, decision-makers can understand both the long- and short-term effects of doing so on not just the burden of moderate wasting, but also the burden of severe wasting and severe wasting with complications in the long-term. These insights may form the basis of further cost-effective analyses of various programs. Thus, accurate estimates of incidence are not only critical in determining the number of children in need, but also in more holistically assessing the nutrition situation.

The model's outputs may provide a number of insights about program coverage. While an alternative, simple approach to adjusting incidence estimates could entail using expected program coverage and treatment admissions to find the total number of treated and untreated cases of wasting, doing so would assume confidence in current coverage estimates. While coverage may be estimated directly by representative sampling, such estimates remain scarce. Given that a key unknown of the coverage calculation is the number of untreated cases, our model provides a means of estimating this – representing the total number of developing cases which will require treatment – which does not rely on an existing coverage estimate, but which may instead be used to inform more accurate estimates of program coverage.

As is the case with many mathematical models seeking to capture complex processes, our model had several limitations. First, a fundamental property of Markov models is that of "memorylessness" – the assumption that the future states depend only on the current state and not any past states [13]. Though it is known, for example, that a child who spontaneously recovers from an episode of moderate wasting is at a greater risk of developing moderate wasting again, the model cannot consider this as the child would return to the *Healthy* state in its simulation, and the child would therefore have the same probability of becoming moderately wasted as a child who had never previously been moderately

503 wasted. Cases of defaulting from treatment present similar limitations; when children default from
504 treatment and return to a wasted state, though they likely saw some level of improvement during the
505 period in which they attended a treatment program, upon returning to the wasted state, they become
506 indistinguishable from someone who had never before been in treatment. While it is possible to
507 introduce a level of consideration of past states while maintaining the Markovian property of
508 memorylessness, because quantitative information about these particular outcomes (e.g. the probability
509 of becoming wasted again upon recovery) is limited, this could not be considered. However, given that
510 we did not aim to examine these cases at such an individual level and that rates of default and
511 spontaneous recovery were relatively low, the effects of these limitations on the results were likely
512 minimal.
513
514 While the transition probabilities corresponding to treatment admission were time-varying, the
515 assumption that other rates would remain constant presented several limitations. It is likely that
516 mortality rates vary seasonally; however, given the ethical constraints of following a cohort of untreated
517 children, little is known about outcomes of untreated wasting. Existing estimates of untreated case
518 fatality rates for moderate and severe wasting were used for this model which were expressed as a
519 constant rate, and given that this data is limited, variations in these rates could not be explored. Among
520 the most uncertain of the model's transition probabilities is that of spontaneous recovery for moderate
521 and severe wasting. Because spontaneous recovery tends to happen by chance and varies widely by
522 context, with the changing situation in Yemen, there is little data representing the current context.
523 Cohort studies tracking untreated cases of wasting – which monitor rates of spontaneous recovery
524 among other outcomes - are scarce given the ethical limitations of doing so; those available were
525 conducted before the onset of CMAM. Given this, data from other contexts was used to estimate these
526 rates, which posed several limitations given that spontaneous recovery happens unpredictably and is
527 dependent on many contextual factors. Because of this, our model's spontaneous recovery rates were
528 among the most uncertain of the model's rates, but as shown in Table 5, the sensitivity analysis proved

that varying these values by a factor of 50% - 150% would never result in an average duration as high as 7.5. months. The results in Table 5, showing that in the case of both moderate and severe wasting, rates of treatment admission had the greatest impact on the computed incidence rate, provide confidence in the model's findings; while several rates came from other contexts, rates of treatment admission were estimated from comprehensive data sets from Yemen. Thus, this analysis establishes that the rates that most heavily influenced the model's findings were among those with a high level of confidence.

Several limitations were presented by the limited data available for validation. SMART survey results were a primary source of validation of the model's results. However, because SMART relies on representative sampling in order to estimate prevalence for the entire governorate, a level of uncertainty is expected within its results. The 2018 SMART survey also notes that settlements for internally displaced people (IDPs) were excluded from the sampling frame [14]. It is known that internally displaced people in Yemen face comparatively higher levels of food insecurity and lower levels of access to health and basic services, meaning the survey's results likely underestimate the prevalence of wasting by excluding these settlements [22]. Additionally, because SMART surveys in Yemen are conducted annually, the absence of intermediate data points meant that monthly prevalence at each iteration of the model could not be validated. Given that conducting widescale cross-sectional prevalence surveys is costly and humanitarian agencies' face increasingly limited funding, it is expected that this data will be scarce. Despite this, the model aims to make use of and supplement the available data to offer new insights, improve upon the existing approach for estimating wasting and strengthen understandings of the burden of wasting in Yemen.

Despite its limitations, our model can provide decision-makers with important insights about the expected burden of wasting. Additionally, the model's ability to holistically capture all determinants of the monthly prevalence of wasting may provide a potential alternative to conducting in-person cross-sectional surveys such as SMART, allowing humanitarian agencies to direct efforts and funds elsewhere.

555 Future work may entail extending the model framework to other conflict-effected settings in order to
556 produce more accurate caseload estimates and consider the expected instability of conflict settings.
557 Doing so may validate the utility and generalizability of the model and in other contexts. Future work
558 may also entail building upon the model to explore seasonal changes in the incidence of wasting by
559 considering the direct and indirect drivers of wasting. Doing so would allow the model to operate with a
560 predictive capacity; by capturing relationships between the incidence of wasting and its underlying
561 causes, the model may anticipate how a change in ground realities may result in a change in the
562 incidence of wasting. While the adjusted incidence rates provide a more context-specific improvement
563 from the standard, global estimates, this approach assumes the previous year's caseload can be used to
564 anticipate caseload for the following year. Capturing the determinants of wasting within the model
565 framework would further improve upon this approach by allowing incidence estimates to reflect
566 changes on the ground.
567
568 **Conclusion**
569
570 In this manuscript, we present context-specific estimates for the incidence of moderate and severe
571 wasting in Lahj, Yemen. Accurate estimates of incidence are critical in anticipating program needs and
572 holistically assessing the burden of wasting among children. Confirming the assertion that a single
573 incidence correction factor cannot be sufficient, our results show that previous estimates led to
574 considerable underestimates of caseload and left entire populations of wasted children unaccounted for.
575 In addition to providing improved estimates of caseload, the model may also be used as a decision-
576 making tool, allowing users to modify its parameters to understand the long- and short-term
577 implications of a given interventional decision, which may be used to guide future cost-effectiveness
578 analysis. Additionally, by seeking to estimate the total number of cases of wasting – both treated and
579 untreated – the model provides a basis for providing improved estimates of program coverage. In crisis
580 settings such as Yemen where funding and resources are extremely limited, the model's outputs may

help ensure that limited resources are allocated most effectively and holistically capture the burden of wasting in a way that can facilitate effective decision-making and intervention strategies.

Abbreviations

CMAM: Community-based Management of Acute Malnutrition

MAM: Moderate Acute Malnutrition

SAM: Severe Acute Malnutrition

SMART: Standardized Monitoring and Assessment of Relief and Transitions

OTP: Outpatient Therapeutic Feeding Program

TFC: Therapeutic Feeding Center

TSFP: Targeted Supplementary Feeding Program

IPC: Integrated Food Security Phase Classification

Declarations

Ethical Approval and Consent to Participate

All human based data was deidentified and shared by UNICEF following ethical guidelines.

Consent for Publication

Not applicable

Availability of data and materials

The data that support the findings of this study are available from UNICEF but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of UNICEF.

Competing Interests

The authors state that the institutions of Boston University (BU) and the United Nations International Children's Fund (UNICEF) are currently involved in a financial partnership.

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Authors' Contributions

RH was a main contributor to the data analysis and interpretation, designed and coded the model and was a main contributor in writing the manuscript. MHZ provided guidance in the development of the model and the creation of the manuscript. MS assisted in model development and data anlysis. SG and ER provided technical support and nutritional expertise which informed the model's development. NAD compiled and provided data, assisted in developing the model and provided guidance in data interpretation and insight on ground realities.

FS and MKD provided guidance in the study.

MHZ, NAD, MPS, SG, and ER all provided edits to the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable

Authors' Information

NAD, FS and MKD have all worked on the ground in Yemen and are familiar with the country's current realities.

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Figures

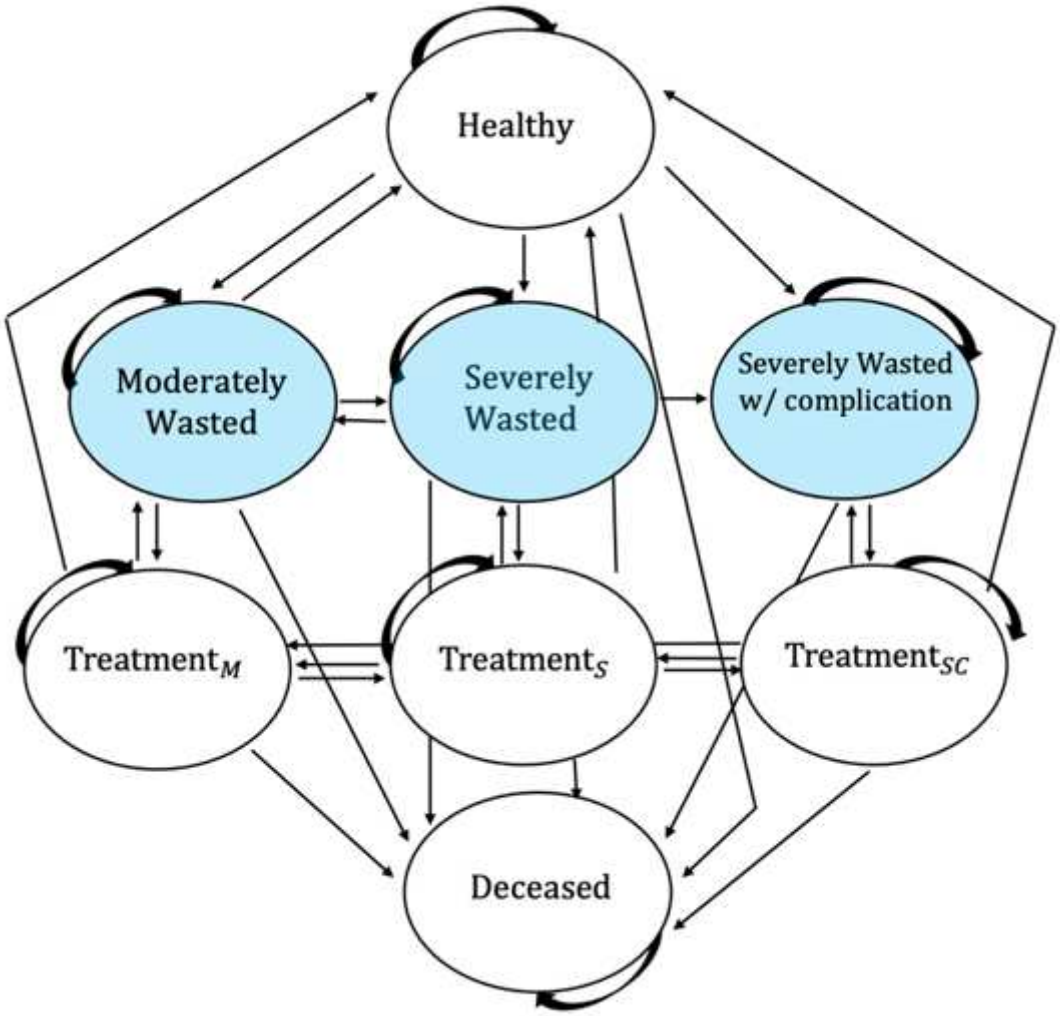

Figure 1

Model State-Transition Diagram. Arrows depict all possible transitions between nutritional states. Blue states indicate a state where a child is wasted but not currently in treatment TreatmentM, TreatmentS, and TreatmentSC refer to treatment for moderate wasting, severe wasting, and severe wasting with complications, respectively.

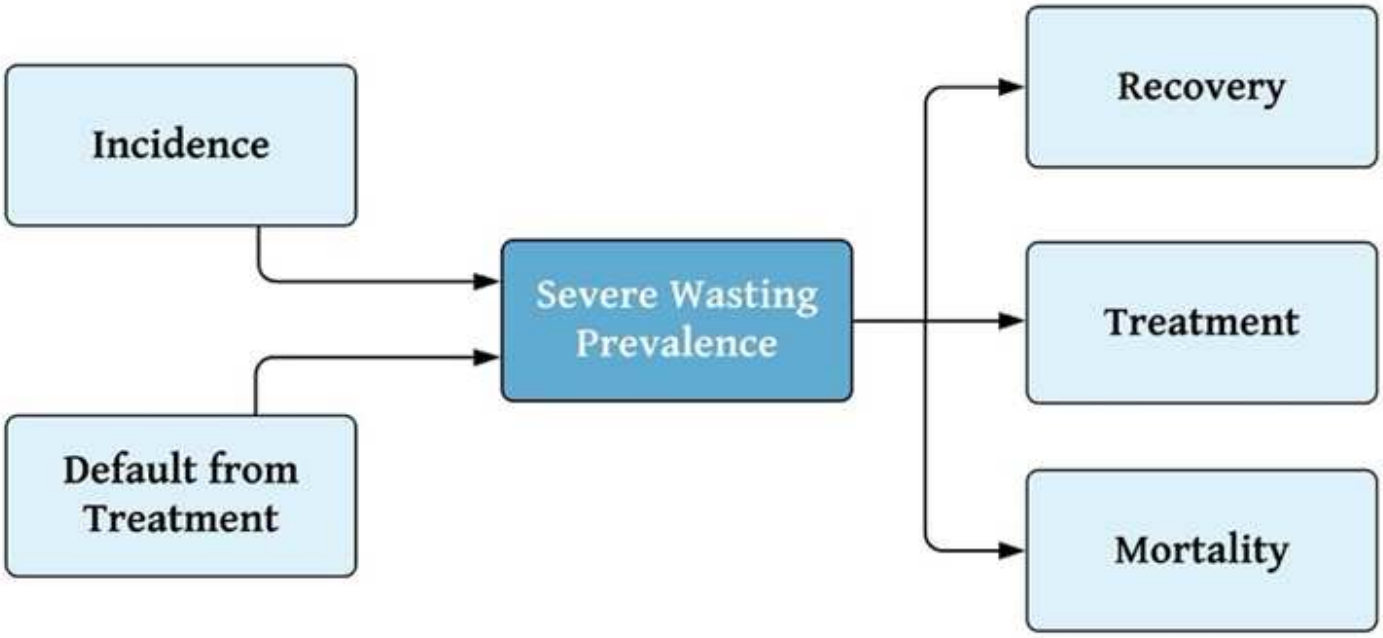

Figure 2

Magnified view of rates determining the prevalence of severe wasting within model framework. With the incidence of severe wasting as the single unknown, repeated model calibration was used to estimate the rate of incidence.

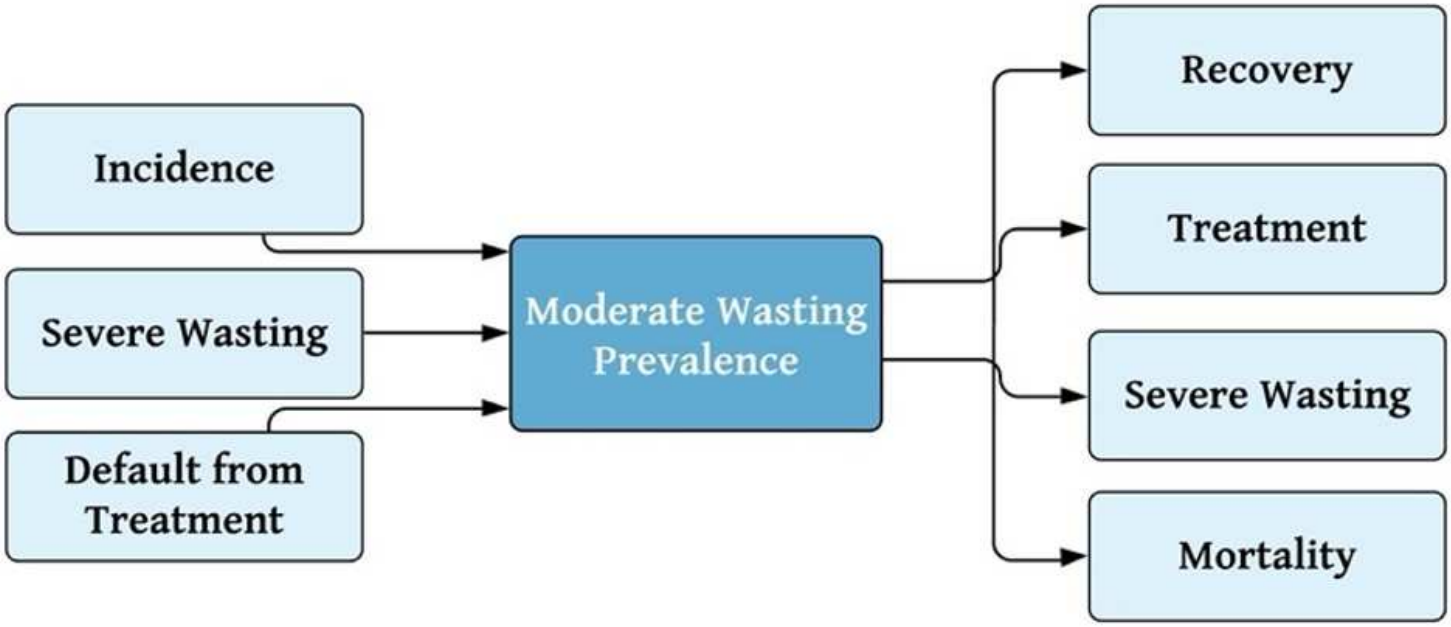

Figure 3

Magnified view of rates determining the prevalence of moderate wasting within model framework. Upon estimating the incidence of severe wasting, the incidence of moderate wasting remained the single unknown and could be estimated through repeated model calibration.

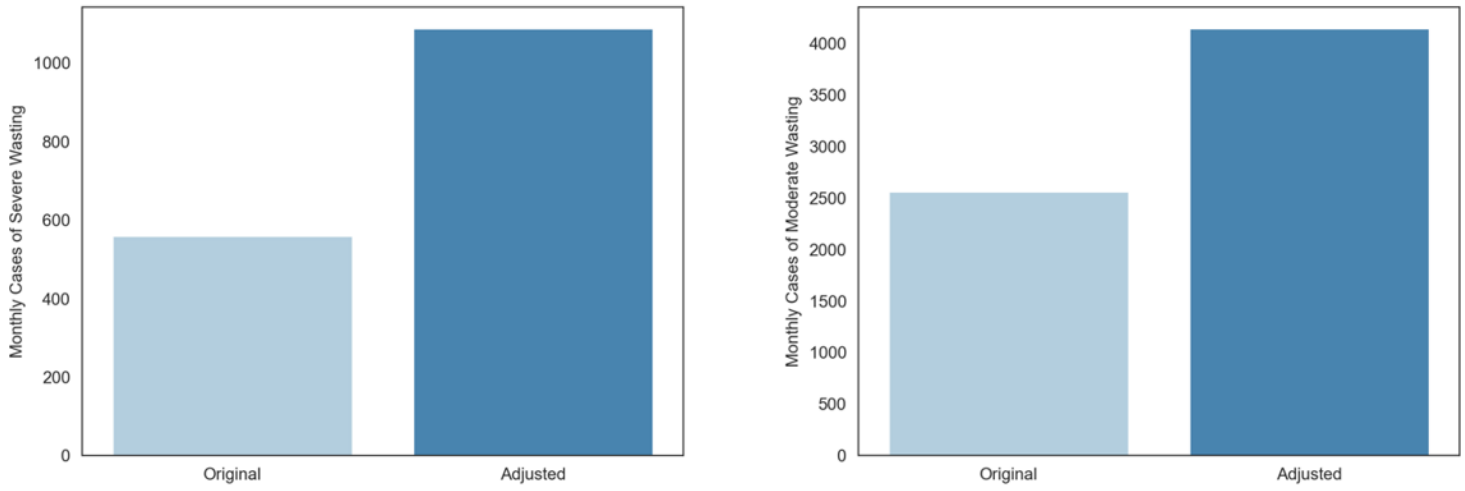

Figure 4

(A) Comparison of monthly number of cases of severe wasting using original approach (k = 1.6) and adjusted (model-derived) monthly number of cases of severe wasting (k = 1.6). (B) (A) Comparison of monthly number of cases of moderate wasting using original approach (k = 3.11) and adjusted (model-derived) monthly number of cases of moderate wasting (k = 2.59).

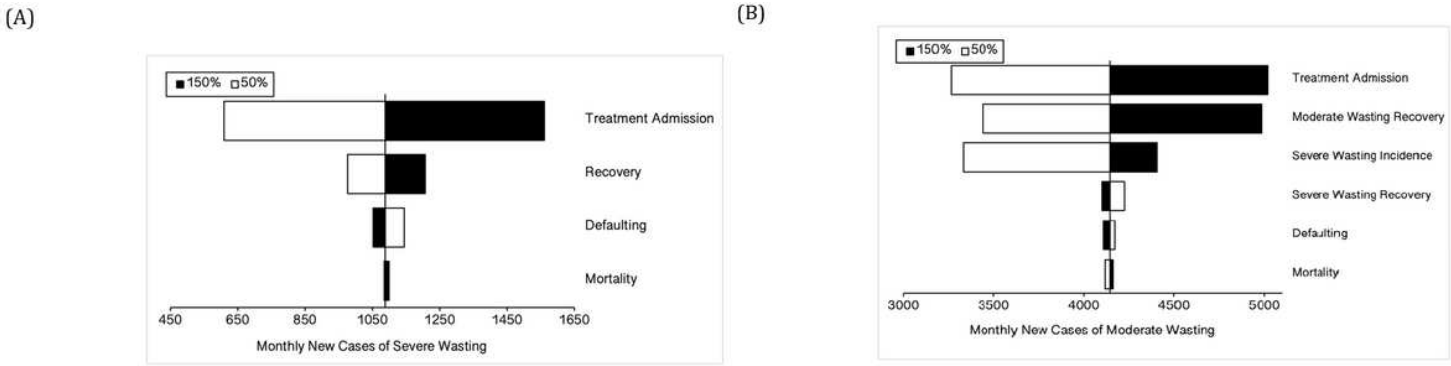

Figure 5

Sensitivity Analysis. (A) Sensitivity analysis for transition probabilities directly affecting incidence of severe wasting. (B) Sensitivity analysis on transition probabilities directly affecting incidence of severe wasting.