# Survival and Recovery in Severely Wasted Under-five Children Without Community Management of Acute Malnutrition Programme

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<b>Objective:</b> To evaluate recovery and survival of severely wasted children without community management of acute malnutrition programme.	children aged between 6 and 24 months. Younger age ( <i>P</i> =0.04), poorer household-head occupation ( <i>P</i> =0.04) and lower enrolment anthropometry (any variable; <i>P</i> <0.001) were significant predictors of mortality. Children below 18 months of age had higher adjusted		
<b>Design:</b> Single time point follow-up (24th December 2013 – 2nd April, 2014) of severely wasted children identified in a community-based cross-sectional survey (September 2012 – October 2013).	mortality risk (HR 4.7; 95% CI 0.95, 22.51; <i>P</i> =0.053). At follow-up, 30% of survivors were still severely wasted, 39% were moderately wasted (weight-for-height -3 to <-2Z) and 31% had recovered		
Setting: Rural Meerut District, Uttar Pradesh, India.	spontaneously. Younger age ( $P$ <0.001), female gender ( $P$ =0.04)		
Participants: 409 severely wasted (WHO weight-for-height <-3Z), 6- to 59-month-old children.	and longer follow-up duration ( <i>P</i> =0.003) were significant independent predictors of recovery. The adjusted OR (95% CI) for recovery <24 months was 2.81 (1.70, 4.65).		
Outcome measures: Survival and recovery (weight-for-height≥-2Z).	Conclusion: Without community management of acute malnutrition in rural Meerut District, severely wasted children had		
<b>Results:</b> Median (IQR) follow-up contact duration was 7.4 (6.6, 10.1) months. Among 11 deaths, there were 5 (case-fatality 1.2%), 6 (1.5%), 8 (2.0%) and 10 (2.4%) events within 1, 1.5, 4	low (1.2%-2.7%) case-fatality with long-term spontane recovery of around 25-30%.		
and 6 months of enrolment, respectively. Ten deaths occurred in	<b>Key words:</b> <i>Mortality, Outcome, Protein energy malnutrition,</i> Severe acute malnutrition.		
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In 2011, the global prevalence of severe acute malnutrition (SAM) below 5 years of age, estimated as severe wasting or weight-for-height ≤3 Z-score of WHO reference, was 3% or 19 million children with the highest burden in South Central Asia (5.1%) and central Africa (5.6%) [1]. In a recent pooled analysis of ten prospective studies recruiting participants between 1977 and 1997, the mortality risk (HR; 95% CI) for severe wasting was 11.63; 9.84, 13.76 [2]. The proportion of total under-five mortality attributable to severe wasting was quantified as 7.4% or between 516,000 and 540,000 deaths [1]. Management of SAM was estimated to be the most important nutrition intervention to scale up; at 90% coverage, this mediation could save between 285,000 and 482,000 lives [3].

The World Health Organization (WHO) recommends inpatient treatment for children with complicated SAM [4], an estimated 15% of the total

burden [3]. Community-based management is recommended for the overwhelming majority (~85%) with uncomplicated SAM, including specially formulated diets like Ready-to-use Therapeutic Foods (RUTF) [4,5]. These recommendations and the aforementioned lives-saved projections have strengthened advocacy for community-based management of SAM, which is still not being practiced in several states in India. Important reasons for this include financial constraints and controversy surrounding the use of commercial products and projected benefits [6,7].

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The lives-saved projections draw upon the mortality risk of untreated severely wasted children, based on 2-4 decades old studies [2]. With advances in socioeconomic profiles, mortality indices and health care, these mortality risks may be overestimates for several regions of modern India. Further, recovery rates (43%-57%) are lower than in African studies, despite longer treatment and greater support for feeding and morbidity management [8]. It is therefore conceivable that the recovery rates and mortality risk of uncomplicated severe wasting in community settings are less dependent upon specially formulated diets than in African regions. This study evaluated recovery and survival of severely wasted children, identified in a community-based survey, under the existing community health care system.

# Methods

This study is an extension of a larger cross-sectional study entitled "Evaluation of midarm circumference for detection of SAM in children aged 6-59 months with weight-for-height Z score below -3 SD as reference", the results of which are being communicated separately. Briefly, this community-based cross-sectional study was conducted between September 2012 and October 2013 in District Meerut, Uttar Pradesh, India. Two adjoining rural blocks were identified and their 70 contiguous villages were selected. House visits were undertaken to locate 6-59 months old children. Children with severe illnesses and physical deformities were excluded. After written informed consent from parents, eligible children were evaluated by the trained research team at local Anganwadi Centers or Health Sub-centres or schools. Socio-demographic profile was recorded on a pretested Anthropometric proforma. measurements were conducted by standard techniques [9]. Length was measured below 24 months of age by an infantometer (SECA, Germany) and height in 24-59 months old by a stadiometer (SECA, Germany) with a least count of 0.1 cm. Weight (with minimal clothing) to the nearest 10 grams was recorded on a digital weighing scale (SECA, Germany). Mid upper arm circumference (MUAC) was measured by fiber glass tape to the nearest 0.1 cm. Technical errors of measurements for inter- and intraobserver variations were below 2%. Each child was also clinically examined for visible severe wasting and bipedal edema. WHO reference Z scores were calculated for the three anthropometric indices (length/height-forage, weight-for-age and weight-for-height) [10]. In the 18463 children with valid measurements, only one child had pedal edema. The prevalence of severe wasting (weight-for-height <-3Z) was 2.2 % (95% CI 2.02%, 2.44%).

Within the backdrop of the main survey, no special efforts were made to sensitize the community or government functionaries (if willing to help) about the importance of identification of SAM children and their further management. Parents or caregivers of severely wasted children were given appropriate nutritional counselling by the project staff, and these children were referred to the nearest Primary Health Center for further management. At the time of conduct of the study, there was no special provision or programme for management of SAM in Uttar Pradesh.

It was considered unethical to prospectively followup all the recruited subjects at repeated intervals without offering continuing management support. Based on ethical, logistic and financial considerations, after completion of the original cross-sectional survey, we attempted home visits only for the 409 severely wasted children to determine their survival status, date of death (if applicable) and repeat anthropometry. Survival status for few migrants was established telephonically but their anthropometry could not be recorded. This repeat follow-up was done between 24th December 2013 and 2nd April, 2014. Contingent upon this design, the follow-up duration from the initial visit varied from 0.6 to 17.8 months among survivors.

Ethical clearance was obtained from the Institutional Ethics Committee of All India Institute of Medical Sciences for both the initial cross-sectional study and the repeat follow-up visit. The study was approved by the Government of India and the Uttar Pradesh State Government. Oversight was provided by the National Research Alliance for SAM established by the Indian Government. An independent institution (Clinical Development Services Agency) periodically audited the study and provided recommendations.

Statistical analyses: Data analysis was performed using SPSS version 20.0. Descriptive statistics were compared with Chi-square and t-test. In children above 5 years at follow-up, weight-for-height Z score was linearly interpolated at exact age of 5 years using the baseline and follow-up anthropometry. Recovery was defined as WHO weight-for-height Z-score  $\geq$ -2 [4]. Univariate and multivariate associations for mortality and recovery were evaluated by Cox Proportional Hazard Model [11] and logistic regression, respectively. The probability of survival and recovery in relation to follow up time was estimated by Kaplan-Meier plot [12].

# RESULTS

Baseline characteristics of 409 severely wasted children are summarized in *Table* I. There was greater representation of 6- to 24-month-old children (55%), boys (63%), nuclear families (62%) and Hindus (53%). Half the households were headed by unemployed or unskilled labourers and a quarter by semi-skilled or skilled workers. Parental literacy was poor; 26% fathers

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Characteristic	Age categ	Total	
	6-24 mo	24-59 mo	
Number (% of total)	226 (55)	183 (45)	409
Age <sup>*</sup> (mo)	14.47 (5.03)	41.98 (10.91)	26.78 (15.96)
Boys	140 (61.9)	118 (64.5)	258 (63.1)
Type of family (Nuclear)	131 (58.0)	121 (66.1)	252 (61.6)
Religion			
Hindu	110 (48.7)	105 (57.4)	215 (52.6)
Muslim	116 (51.3)	77 (42.1)	193 (47.2)
Sikh	0(0)	1 (0.5)	1 (0.2)
Occupation of head of the household			
Professional/ Semi-Professional/ Clerical/ Shop owner/ farmer	42 (18.6)	51 (27.9)	93 (22.7)
Skilled worker/ Semi-skilled worker	68 (30.1)	46 (25.1)	114 (27.9)
Unskilled worker/Unemployed	116 (51.3)	86 (47.0)	202 (49.4)
Father's education			
Illiterate	60 (26.5)	48 (26.2)	108 (26.4)
Primary School	63 (27.9)	48 (26.2)	111 (27.1)
Middle School & higher	103 (45.6)	87 (47.5)	190 (46.5
Mother's education			
Illiterate	121 (53.5)	94 (51.4)	215 (52.6
Literate	105 (46.5)	89 (48.6)	194 (47.4)
Family income <sup>*</sup> (annual) (in ₹) <sup>#</sup>	84,432 (1.61)	81,479 (1.66)	83,100 (1.63)
Baseline height* (cm)	69.69 (6.09)	89.47 (9.62)	78.54 (12.60)
WHO height-for-age Z score*	-2.98 (1.79)	-2.48 (1.55)	-2.76 (1.70)
Stunting (WHO length/height-for-age <-2 Z)	172 (76.1)	117 (63.9)	289 (70.7)
Severe stunting (WHO length/height-for-age <-3 Z)	108 (47.8)	63 (34.4)	171 (41.8)
Baseline weight <sup>*</sup> (kg)	6.14 (1.14)	9.71 (1.83)	7.73 (2.32)
WHO weight-for-age Z score*	-4.04 (1.01)	-3.60 (0.89)	-3.84 (0.98)
Underweight (WHO weight-for-age <-2 Z)	222 (98.2)	178 (97.3)	400 (97.8
Severe underweight (WHO weight-for-age <-3 Z)	200 (88.5)	145 (79.2)	345 (84.4)
WHO weight-for-length/height Z score*	-3.56 (0.49)	-3.40 (0.40)	-3.49 (0.46)
Baseline MUAC <sup>*</sup> (cm)	11.6 (1.1)	13.0 (0.9)	12.2 (1.2)
WHO MUAC-for-age Z score*	-2.90 (1.10)	-2.54 (0.78)	-2.74 (0.99)
WHO MUAC-for-age <-3 Z	90 (39.8)	44 (24.0)	134 (32.8
MUAC <12.5 cm	182 (80.5)	40 (21.9)	222 (54.3)
MUAC <11.5 cm	87 (38.5)	8 (4.4)	95 (23.2)
MUAC <11.0 cm	52 (23.0)	3 (1.6)	55 (13.4)

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<b>TABLE I</b> BASELINE C	CHARACTERISTICS OF 409 (	CHILDREN WITH SEVI	ERE WASTING

Values in n (%) or \*Mean (SD); #Geometric mean (SD) from log transformed values; MUAC: Mid upper arm circumference.

and 53% mothers were illiterate. Co-existence of other anthropometric deficits was common; stunting in 71%, severe stunting in 42%, underweight in 98%, severe underweight in 84% and MUAC <-3 Z in 33%. Only 23% had MUAC <11.5 cm. Except for underweight, other anthropometric deficits were significantly higher in 6-24 months old subjects. Mortality outcome was known with certainty in all while repeat anthropometry for comparison was available for 368 (92.5%) survivors (*Fig.* 1). The median (IQR) and range of follow-up contact duration were 7.4 (6.6, 10.1) months and 3.0 to 17.8 months, respectively.

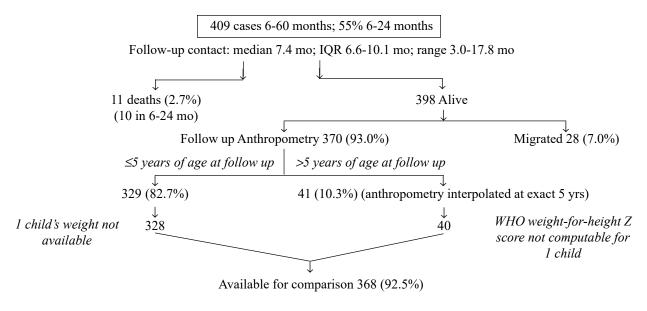


FIG. 1 Flow chart for the follow-up.

There were 11 deaths during 290.5 person-years follow-up with a case fatality of 2.7% (95% CI 1.4, 4.8) and mortality incidence (per thousand person-years) of 37.9 (95% CI 21.0, 68.4). There were 5 (case fatality 1.2%, 6 (1.5%), 8 (2.0%) and 10 (2.4%) deaths within 1, 1.5, 4 and 6 months of enrolment, respectively. Mortality was comparable among boys and girls (6 vs 5) with incidence (95% CI) being 32.5 (14.6, 72.4) and 47.1 (19.6, 113.1), respectively. Younger age (P=0.04), poorer occupation of head of household (P=0.04) and lower enrolment anthropometry (any variable; P<0.001) were significant predictors of mortality in the univariate model (WebTable I). Among anthropometric variables, the effect size of the association was greatest for MUAC followed by MUAC-for-age in both univariate and multivariate (age, sex, socio-economic profile adjusted) models. Ten deaths occurred in younger subjects; the mortality incidence (95% CI) was 63.6 (34.2, 118.2) and 7.5 (1.1, 53.3) in 6-24 and 24-60 months' age groups, respectively. Mortality risk was higher (HR 4.7; 95% CI 0.95, 22.51; P=0.053) in children below 18 months of age even after adjustment for sex, baseline weight-for-length/height Zscore and socio-economic factors.

In survivors, the median (IQR) and range of followup duration were 7.4 (6.6, 10.2) months and 4.1 to 17.8 months, respectively. **Table II** summarizes the change in anthropometric Z-score categories in relation to maximum follow-up duration with six-monthly increments and an additional time window of 8 months for comparison with the multicentric Indian study [8]. The mean (SD) change in weight-for-length/height Z- score increased with follow-up duration, with the overall value being 1.04 (1.09). Overall, among 368 severely wasted children, only 30% were still severely wasted, 39% were moderately wasted and 31% had recovered. In the subgroup with maximum follow-up of 6 months, 56% were still severely wasted but the corresponding figure for 8 months was 33%, which was similar to overall (30%) statistics. Probability of recovery and shifting to weight-for-length/height category  $\geq$ -3Z increased sequentially with follow-up duration (*Web Fig.* 1). Younger age (*P*<0.001), female gender (*P*=0.04) and longer follow-up duration (*P*=0.003) were significant independent predictors of recovery (*Web Table II*). The adjusted OR (95% CI) for recovery below 24 months was 2.81 (1.70, 4.65).

The mean (SD) change in weight-for-age Z-score was lower than weight-for-length/height but this too increased with follow-up duration, with the overall value being 0.59 (0.75). Consequentially, 62% remained severely underweight, 28% were moderately underweight and only 10% had become normal. In contrast, mean (SD) length/height-for-age Z-score decreased with follow-up duration, with the overall value being -0.18 (0.79) (Table II). Thus 46% were severely stunted, 31% were moderately stunted and 23% were normal at follow-up. Using methodology adopted by several African studies [8], namely, height at enrolment to compute weight-for-length/height Z-score during follow-up, enhanced overall recovery to 72%. Conversely, correction for observed height deficit since enrolment, reduced overall recovery from 31% to 26%.

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Characteristic	Baseline		Maximum follow-up duration			
		6 mo	8 mo	12 mo	18 mo	
Follow-up duration statistics						
Range (mo)	NA	0.6-5.9	0.6-8.0	0.6-11.0	0.6-18.0	
Mean (SD)	NA	4.4 (1.5)	6.1 (1.6)	6.7 (1.9)	8.1 (3.4)	
Median (IQR)	NA	4.9 (4.2, 5.6)	6.7 (5.3, 7.3)	7.0 (5.8, 7.6)	7.3 (6.2, 10.0)	
Number available	368	86	244	299	368	
Weight-for-length/height; number (%)						
Severe wasting (<-3 Z)	368 (100)	48 (56)	80 (33)	97 (33)	110 (30)	
Moderate wasting (-3 to -2 Z)	0	27 (31)	98 (40)	123 (41)	145 (39)	
Normal or recovered ( $\geq$ -2 Z)	0	11 (13)	66 (27)	79 (26)	113 (31)	
Change from baseline; Mean (SD) Z score	NA	0.41 (0.94)	0.92 (0.99)	0.93 (1.04)	1.04 (1.09)	
Length/height-for-age; number (%)						
Severe stunted (<-3 Z)	148 (40)	30 (35)	106 (43)	133 (45)	171 (46)	
Moderate stunted (-3 to -2 Z)	112 (31)	26 (30)	80 (33)	96 (32)	113 (31)	
Normal ( $\geq$ -2 Z)	108 (29)	30 (35)	58 (24)	70 (23)	84 (23)	
Change from baseline; Mean (SD) Z score	NA	-0.09 (0.47)	-0.14 (0.53)	-0.17 (0.61)	-0.18 (0.79)	
Weight-for-age; number (%)						
Severe underweight (<-3 Z)	313 (85)	56 (65)	155 (64)	194 (65)	229 (62)	
Moderate underweight (-3 to -2 Z)	47 (13)	23 (27)	64 (26)	76 (25)	102 (28)	
Normal ( $\geq$ -2 Z)	8 (2)	7 (8)	25 (10)	29 (10)	37 (10)	
Change from baseline; Mean (SD) Z score	NA	0.24 (0.54)	0.55 (0.65)	0.54 (0.68)	0.59 (0.75)	
Sensitivity Analyses						
Weight-for-length/height using baseline leng	th/height; numbe	er (%)*				
Severe wasting (<-3 Z)	368 (100)	24 (28)	26(11)	32(11)	32 (9)	
Moderate wasting $(-3 \text{ to } -2 \text{ Z})$	0(0)	30 (36)	59 (24)	69 (23)	70 (19)	
Normal or recovered ( $\geq -2$ Z)	0(0)	32 (37)	158 (65)	197 (66)	261 (72)	
Weight-for-length/height using adjusted leng	th/height; numb	er (%)^				
Severe wasting (<-3 Z)	368 (100)	51 (59)	93 (38)	118 (40)	136 (37)	
Moderate wasting (-3 to -2 Z)	0(0)	24 (28)	97 (40)	117 (39)	137 (37)	
Normal or recovered ( $\geq -2$ Z)	0 (0)	11 (13)	54 (22)	64 (21)	95 (26)	
Change from baseline; Mean (SD) Z score	NA	0.33 (0.94)	0.80 (0.99)	0.78 (1.04)	0.88 (1.09)	

NA: Not applicable; The minimum follow-up duration is truncated till the exact age of five years in subjects requiring interpolation of anthropometry. The actual minimum follow-up duration was 4.1 months in survivors; \*Weight-for-length/height was calculated using follow-up weight and baseline length/height. Sample sizes were reduced by 1, 1 and 5 children at 8, 12 and 18 months, respectively because WHO Z-scores could not be computed with the baseline length/height at follow-up age; ^ Weight-for-length/height was calculated using recorded weight at follow-up. However, the follow-up length/height was adjusted upwards for the marginal average decline from baseline to get an estimate of change in weight-for-length/height assuming that there is no length/height deficit.

#### DISCUSSION

Under the existing community health care system in rural Meerut District, the case fatality for severely wasted children was only 1.2% within 1 month and 2.7% with median follow-up contact of 7.4 months. Only 30% of survivors were still severely wasted, 39% were moderately wasted and 31% had recovered

spontaneously. Younger age, female gender and longer follow-up duration predicted recovery while younger age, lower category of occupation of household-head and poorer anthropometry at enrolment forecasted mortality.

This quality-monitored dataset on a reasonable sample size from rural India provides contemporary

evidence on recovery and survival under the existing community health care system of a poorly performing State. This information is crucial for estimating the costeffectiveness of, and need for, investing in communitybased management of SAM. Biased estimates are improbable because mortality status was available for all and follow-up anthropometry for 93% of survivors. It is unlikely that participants recovered at shorter duration of follow-up became wasted later on, because Kaplan-Meir curves revealed increasing recovery rates with greater follow-up duration. Ethical considerations precluded collection of detailed prospective information on morbidity, treatment and cause of death. Another limitation was that only severely wasted children were followed-up; financial and logistic reasons prevented follow-up of children with MUAC <115 mm.

In this rural setting with no dedicated program for management of SAM, the low case fatality was unanticipated and digressed from the general perception that uncomplicated severe wasting results in high mortality, if left untreated [3-5]. Underestimation of case fatality is unlikely because survival status was available for all participants with a minimum follow-up duration of 4.1 months. Although appetite was not specifically ascertained, exclusion criteria of severe illness suggests that bulk of participants had uncomplicated SAM, which has relatively lower-case fatality. Additional explanatory possibilities include: (i) vulnerability to mortality is reduced above six months, (ii) improvement in access to public and private healthcare, and (iii) provision of additional therapeutic nutritional products may not be critical for survival.

There is paucity of contemporary data from India for direct comparison. In the multicentric efficacy trial [8], case fatality in severely wasted children during the treatment phase (maximum 16 weeks) was lower (3/855; 0.4% vs 2.0%) despite a high morbidity burden (10.3% hospitalizations, 41.5% diarrhea, 13.3% acute respiratory infections and 61.6% fever). This reflects the effect of additional comprehensive intervention package provided free-of-cost, which included antibiotics at initiation of treatment, quality management of intercurrent morbidities with need-based hospitalization, diets of high nutritional value, and peer support for feeding. Among four recently published programmatic experiences [13-16], three necessitating inpatient facility management [13-15] are not directly comparable. In the fourth study from rural Bihar [16], uncomplicated cases of SAM defined as weight-forheight Z <-3 SD and/or MUAC <110 mm (February 2009 to June 2010) or MUAC <115 mm (from July 2010), were treated as outpatients and provided WHO- standard ready to use, therapeutic, lipid-based nutrition product on a weekly basis. Deterioration to complicated SAM during course of therapy was managed through inpatient facility admission. Notwithstanding these supplementary therapeutic inputs, the case fatality during six weeks (66/6184; 1.1%) was broadly comparable to our study (1.5%). In a single follow-up contact similar to ours, the investigators also contacted defaulters, namely, those with MUAC <115 mm failing to attend the ambulatory therapeutic feeding center for two consecutive weeks or children who left the inpatient stabilisation centre and did not return for two consecutive days [17]; 25% had been in the program for >7 weeks. These defaulter criteria selected younger children, girls and few complicated SAM, who were at greater risk of mortality. Their case fatality within 1 and 18 months was 2.9% (20/692) and 5.2% (36/692), respectively; our corresponding rates being 1.2% and 2.7%. Finally, the case fatality rates observed by us (1.2% to 2.7%) were well within the standard of care (4%) established for community-based management of SAM using a Delphi process [5].

In survivors, spontaneous improvement occurred in weight-for-length/height, which increased with followup duration. A similar decline in wasting was reported among untreated defaulters in Bihar program between 3 and 18 months of follow-up [17]. However, our recovery rates (13%-31%) were substantially lower than the proposed [5] standard (80%; range 50-93%) and Bihar programme (53% at mean 7.9 weeks) with slightly different criteria (weight-for-height >-2Z and MUAC>110 mm with no edema). In the multicentric efficacy trial [8] employing identical criteria, recovery at the end of treatment phase (4 months or earlier) was likewise higher (420/855; 49.1%). However, four months later (end of sustenance phase), only 14.7 % remained recovered, 48% were moderately wasted and 37.3% were still severely wasted. Our study documented marginally better figures with follow-up duration ≤8 months. In conformity with earlier observation [8], we also documented a substantial increase in recovery (27% to 65%) if enrolment height was used instead of concomitant height as done in several African studies.

In the multicentric efficacy trial [8], there was a marginal increase in height-for-age (0.04 to 0.08 Z) at the end of sustenance phase. In contrast, we documented a small decrease (0.14 Z), which partly explained spontaneous recovery rates. However, the contribution of decreased height-for-age on recovery rates appeared small in sensitivity analyses (from 27% to 22% at 8 months; *Table* II).

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# WHAT IS ALREADY KNOWN?

• Based on decades old evidence, mostly from African regions, policy stakeholders believe that uncomplicated severe wasting results in high mortality and poor spontaneous recovery, if left untreated in the community.

#### WHAT THIS STUDY ADDS?

 In this era, without community management of acute malnutrition in rural Meerut District, severely wasted children had low (1.2% - 2.7%) case-fatality with long-term spontaneous recovery of ~25%-30%.

The low case fatality and long-term spontaneous recovery rates (~25%-30%) in severely wasted Indian children need confirmation. However, the lower recovery rates than African settings, particularly after cessation of treatment phase [8], and our data suggest that the benefits of investing in community-based management of severe wasting in India are considerably overestimated. Extreme thinness in Indian children could have a different biological and social perspective than in African regions prone to periodic food insecurity. If consensus with this evidence input still favors initiating such a program, we could focus on ages between 6 months and 2 years because of their higher case-fatality and better recovery rates.

In conclusion, without community management of acute malnutrition in rural Meerut District of India, severely wasted children had low (1.2% - 2.7%) case-fatality with long-term spontaneous recovery of around 25-30%.

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