Body composition of adults with a history of severe acute malnutrition during childhood using the deuterium dilution method in eastern DR Congo: the Lwiro Cohort Study

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ABSTRACT

Background: Few studies have evaluated the body composition (BC) of adults who suffered from severe acute malnutrition (SAM) during childhood, a population at risk of long-term noncommunicable diseases.

Objective: We performed an observational cohort study to evaluate BC in a group of young adults aged 11–30 y after nutritional rehabilitation for SAM, in the Democratic Republic of the Congo (DRC).

Methods: We evaluated 151 adults in eastern DRC who were treated for SAM during childhood between 1988 and 2007. They were compared with 120 aged- and sex-matched control adults living in the same community who had not been exposed to malnutrition as children. The main variables of interest were the different compartments of adult BC (fat-free mass [FFM], fat mass [FM], and 2 indices of height-normalized BC: FFM index [FFMI] and FM index [FMI]) measured by deuterium dilution.

Results: The mean age in both groups was 23 y, and females represented 49% and 56% of the exposed and nonexposed groups, respectively. SAM-exposed males had lower mean ± SD weight (53.6 ± 6.4 compared with 56.4 ± 7.9 kg, $P = 0.029$) and lower height (159.9 ± 6.6 compared with 163.6 ± 6.7 cm, $P = 0.003$) compared to unexposed males. SAM-exposed subjects had less FFM (–1.56 kg [–2.93, –0.20]; $P = 0.024$) but this observation was more marked in males (45.4 ± 5.4 compared with 48.2 ± 6.9 kg, $P = 0.01$) than in females. No differences in FM were noted between SAM-exposed and unexposed subjects. Adjusting for height, FFMI and FMI showed no difference between SAM-exposed and unexposed in either sex.

Conclusion: SAM during childhood is associated with reduced FFM in adulthood which is probably due to a shorter height. *Am J Clin Nutr* 2021;00:1–8.

Keywords: acute malnutrition, body composition, long-term effect, deuterium dilution method, DR Congo

Introduction

Acute malnutrition is a major public health problem in low- and middle-income countries (LMICs) (1) accounting for ≥45% of the 5.9 million annual deaths among children aged <5 y (2). In addition to the consequences in terms of mortality, malnutrition has serious adverse effects on physical development leading to growth retardation, mental and physical disability (3), and is associated with a significant risk of developing cardiometabolic diseases in adulthood (4–7). This increased risk of chronic noncommunicable diseases (NCDs) in adulthood is potentially

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Abbreviations used: BC, body composition; CHW, community health worker; CMAM, community-based management of acute malnutrition; DRC, Democratic Republic of the Congo; FFM, fat-free mass; FFMI, fat-free mass index; FM, fat mass; FMI, fat mass index; IAEA, International Atomic Energy Agency; LMIC, low- and middle-income country; NCD, noncommunicable disease; RUTF, ready to use therapeutic food; SAM, severe acute malnutrition; TBW, total body water.

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related to an imbalance in body composition (BC), especially the risk of disproportionate fat accumulation which may or may not be related to subsequent catch-up growth (8).

In recent years, the community-based management of acute malnutrition (CMAM) program, anchored on early case detection, referral, and treatment using energy-dense ready to use therapeutic food (RUTF) formulations that take into account the different pathophysiological changes associated with severe acute malnutrition (SAM) (9–13), has resulted in a greater number of children surviving SAM episodes. Despite the increased survival related to the CMAM program, the long-term metabolic implications of the program, and specifically how the RUTFs influence body compositional changes and the risk of metabolic syndrome, remain largely unknown. Nevertheless, several authors believe that the rapid weight gain observed in malnourished children who consume these foods is more associated with fat mass (FM) accrual (14–16). However, previous studies have shown that appropriately designed nutritional supplements promote the accretion of fat-free mass (FFM) (17, 18).

To date, few studies have examined long-term body compositional changes in individuals exposed to SAM and treatment with RUTFs (19). This issue is of increasing importance in the context of nutritional transition and the increasing incidence of NCDs such as type 2 diabetes, particularly in LMICs (20). The Democratic Republic of the Congo (DRC) is among the countries with high rates of acute malnutrition and stunting (21). According to the latest MICS-2019 report, the rates of acute malnutrition, stunting, and underweight among children aged under 5 y were 6.5%, 41.8%, and 23.1%, respectively (22). In the same report, 48% of children aged below 5 y in South Kivu province were stunted (22). The Lwiro pediatric hospital was one of the pioneer facilities in DRC where CMAM was implemented. A team of medical researchers has been developing a SAM treatment model since the 1980s and began digitizing clinical data as early as 1986.

The aim of our study was to evaluate BC among a group of young adults 11 to 30 y after exposure to SAM and subsequent nutritional rehabilitation. Evidence on the link between previous SAM exposure and adult BC is relevant in a context of perpetual food insecurity such as the one prevailing in eastern DRC.

Methods

The study took place at the "Centre de Recherche en Sciences Naturelles de Lwiro" (CRSN-Lwiro), in the health zones of Katana and Miti-Murhesa, in South Kivu, DRC (23).

The sample size was determined by the number of patients admitted for SAM at Lwiro pediatric hospital between 1988 and 2007, still living in Miti-Murhesa and Katana HZ in 2018, and able to be located (24). A total of 1981 patients were treated for SAM during childhood at Lwiro pediatric hospital during the period of interest. The median age at hospital admission was 41 mo, and 70.8% of patients were aged 6–59 mo (24). The nutrition diagnosis made at the time (based on the weight-to-height ratio plotted on the local growth curve established by De Maeyer in 1959, the presence of nutritional edema, and serum albumin concentrations) (25) was reassessed using the ENA for SMART program, version October 2007, for standardization according to the WHO child growth standards (26). Based on the WHO standards, 84% of the children were classified as having SAM (24). The others, classified as having moderate acute malnutrition or not suffering from acute malnutrition, were hence excluded from subsequent analyses. All hospitalized children were treated according to the guidelines at that time (25).

During the follow-up of these subjects who subsequently became adults, i.e. 11 to 30 y after nutritional rehabilitation, 524 subjects from the initial cohort who were still living in the zones of Miti-Murhesa and Katana were surveyed (24). To assess long-term growth, these survivors (SAM-exposed) were compared with 407 unexposed subjects randomly selected from the community (24).

Unexposed was defined as an individual who had no hospital history of SAM, was of the same sex, was living in the same community, and was ≤24 mo older or younger than the exposed. Unexposed individuals were randomly selected by spinning a bottle at the exposed adult's home and enquiring door to door, starting from the nearest house towards which the bottle pointed (19). Though the optimal study design would be a 1:1 ratio of cases and controls, the unexposed participants were more difficult to recruit than the exposed due to the fear of social stigma associated with childhood malnutrition. The selection of unexposed subjects was also limited by the number of eligible adults in the community (24).

The inclusion criteria for SAM-exposed individuals for this study were: to be aged ≥21 y, to have had SAM before the age of 5 y, and to voluntarily agree to participate in the study.

The following subjects were excluded from our study: breastfeeding women and those who identified themselves as pregnant (>3 mo of amenorrhea or with visible pregnancy). On the basis of these criteria, 151 formerly malnourished people were selected and formed the presentation group (**Figure 1**). Meeting the criteria, 120 nonexposed individuals were selected from 407 potential participants.

Outcomes

The primary outcome variables were BC expressed as FFM and FM in adulthood.

Dependent variables.

FFM, FM, and total body water (TBW) values, expressed in kg, were obtained using the deuterium dilution method (stable nonradioactive isotope administered orally as deuterated water [D_20]). Two indices of height-normalized BC were calculated: the fat-free mass index (FFMI), calculated as FFM/height^2, and the fat mass index (FMI), calculated as FM/height^2 (27). Since humans are characterized by sexual dimorphism in FFM and FM, we thought it wise to present the results separately by sex. BMI was calculated using the formula weight/height^2 (in kg/m^2) and was categorized into 4 groups: <18.5 = thin; 18.5 to 24.9 = normal; 25 to 29.9 = overweight, and ≥30 = obese (28).

Independent variables.

The type and frequency of food consumption were evaluated using a food diversity score created by the World Food Program

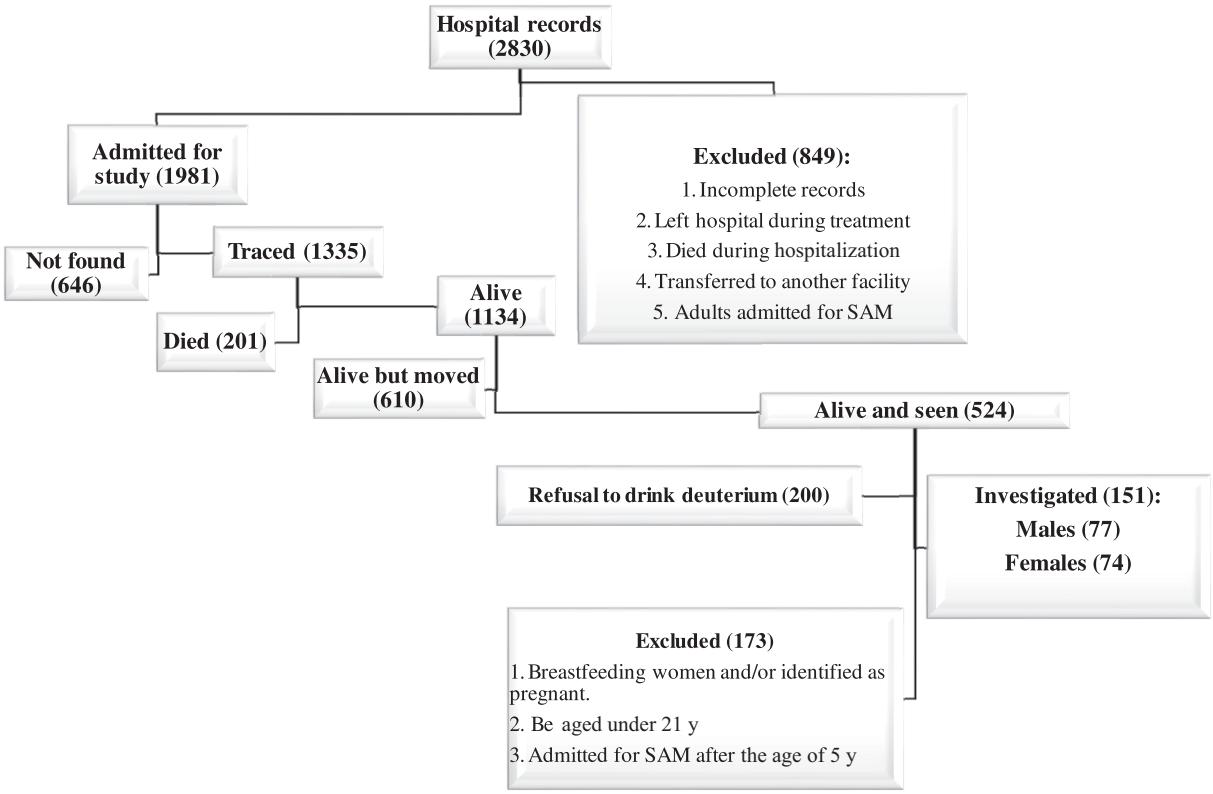

FIGURE 1 Recruitment of exposed group. SAM, severe acute malnutrition.

(29, 30). This score measures the dietary diversity of households, weighted according to frequency of consumption. We asked the head of the household (often the mother) how many days the household had eaten each of the 10 following food groups in the last 7 d: grains, tubers, legumes, vegetables, fruits, meat/fish, milk/dairy products, sugar, oil/fat, and condiments. The frequency with which each food group was consumed was then multiplied by its nutritional value, giving a score for each food group. Lastly, the scores for each food group were added to calculate the overall score. Depending on the total, a subject was considered as having an insufficient or satisfactory diet if his/her score was between 0–42 and >42, respectively (29, 30).

Data collection

Data were collected over a period of 4 mo (January to April 2019), and the collection took place in 2 steps, carried out by 20 trained community health workers (CHWs) and 3 supervisors, assisted by local leaders, qualified nurses, and community liaisons. The CHWs were the same as those who had helped identify the subjects during the gathering of the cohort (24).

During an initial home visit, the CHWs administered a sociodemographic questionnaire translated into Kiswahili (the language spoken in the eastern DRC) to the participants and scheduled an appointment within 48 h at the nearest hospital for the second step. This second stage consisted of recording anthropometric parameters, administering deuterated water, and collecting saliva samples by doctors trained for this purpose and working in the various health facilities in the area. Among all the research team mentioned above, only physicians and laboratory technicians were blinded for the exposure status of the participants, contrarily to CHWs.

The questionnaire covered variables relating to the participant's identity, lifestyle (alcohol and tobacco use, dietary habits), and socioeconomic status (education and occupation).

The anthropometric measurements considered were weight and height. Body weight was measured to the nearest 100 g, with the subject wearing only light clothing, using electronic scales (bathroom scales, Tanita Digital HD-325®). Height was determined using a SECA 206 cm® measuring device with the subject wearing no shoes, to the nearest 0.1 cm. The anthropometric measurements were taken according to WHO guidelines (26) and were quality controlled, meaning that they were taken independently by 2 members of the team.

The final measurement was the average of the 2 measurements. In the event of a discrepancy of >300 g (weight) and/or 0.5 cm (height), a third measurement was taken. The average of the 2 closest measurements was then used.

BC was determined from TBW, calculated from the ratio of the isotope dilution space to the weight of D_2O consumed, corrected for nonaqueous isotope exchange (31). A baseline saliva sample was taken from participants 2 h after their last meal. Each participant was then given an oral dose of 6 g of D_2O (99.8 atom % D, Cambridge Isotope Laboratories Inc.), weighed accurately to the nearest 0.001 g, in sterile, leak-proof, self-cleavable polypropylene dosing bottles on a calibrated analytical balance (Sartorius 0.0001 g; Sartorius AG) at Bukavu Provincial General Reference Hospital Tertiary Level Laboratory. The consumed

dose was recorded to the second decimal of a gram. Two saliva samples were taken 3 and 4 h after D_2O ingestion. To obtain these samples, participants were asked to spin a small cotton ball around the oral mucosa until it was completely soaked in saliva. The cotton ball was then placed in a sterile disposable 10 mL syringe and the plunger was depressed to transfer the saliva into a sterile 3.6 mL Cryo Vial labeled with the subject code, and date and time of sample collection. Finally, the saliva samples were stored at –20°C in plastic vials until analysis, using a Fourier Transform Infrared spectroscopy instrument (FTIR-8400S, Agilent Corporation) in accordance with International Atomic Energy Agency (IAEA) validated protocols (31). The settings of the instrument were as follows: measurement mode: absorbance; apodization: square triangle; number of scans: 32; resolution: 2.0; and range (cm_1): minimum 2300 – maximum 2900.

A "background" scan was performed using the unenriched drinking water that was used to make the calibration standard (zero standard) and the instrument was calibrated using a prepared D_2O standard (1000 mg/kg). The TBW was calculated from the saliva sample using the equilibration technique, assuming that the equilibration peak was reached at 3 to 4 h after deuterium ingestion (31). FFM was determined by dividing the participant's TBW by 0.732 (the hydration factor in adults aged 21 y or older). FM was derived from the difference between body weight and FFM. The fitting of the curves and the calculation of the results was done using a spreadsheet model provided by the IAEA (31). The 2 outcomes were then adjusted for height to give the FFMI (FFM/height^2) and FMI (FM/height^2), both expressed in the same kg/m^2 units as BMI (27).

Ethical standards

Respondents provided signed informed consent for participation in the study, either by written signature or by fingerprints, depending on literacy. All procedures performed in this study were approved by the Institutional Ethics Committee of the Université Catholique de Bukavu and were in accordance with the 1964 Helsinki declaration and its later amendments.

Statistical analysis

We used Stata version 13.1 software for our analyses. Categorical variables were summarized as frequency and proportion. Quantitative data were presented as mean and SD or median and minimum-maximum (min-max), depending on whether the distribution was symmetrical or not. The characteristics of the exposed and unexposed were compared using the chi^2 test (or Fisher's exact when applicability conditions were required) for proportions and student's *t*-test for means (in terms of FFM, FM, TBW, BMI, weight, and height), respectively. We used linear regression models, introducing interactions between sex and exposure into the models. For the interaction effect, we deemed a P value <0.1 as showing a statistically significant difference. Although these interactions were not significant, we decided to present comparisons of the characteristics of SAM-exposed and unexposed stratified by sex due to sexual dysmorphia in terms of BC. Finally, for the whole sample, linear regression models were used to determine the effect of SAM during childhood on TBW (kg) and FFM (kg). The basic models only included the main exposure, SAM, providing an unadjusted difference in the means with a 95% CI between SAM-exposed and unexposed for TBW and FFM. Different models were then constructed in order to analyze the effects of SAM after adjustment. The adjusted model included 3 variables accounting for the fixed effects on TBW and FFM of sex, food diversity, and age. The differences in the means are presented along with their 95% CI. Conditions for applying a linear regression (normality, uniformity of variance, and linearity) were verified via analysis of residuals.

The SD (σ) of TBW in 150 adults was 5 kg in a study conducted in Africa (31). The average body weight of participants was ∼55 kg. An increase in FFM equivalent to 5% of body weight could be considered clinically significant; 2.75 kg of FFM is equivalent to ∼2 kg of TBW (2.75 kg × 0.732). Therefore, assuming that $\sigma = 5$ kg and $\delta = 2.0$ kg of TBW, with a power of 80%, a significance level of 0.05, and the study participants divided into 2 groups (control and intervention), the required sample size (n) can be calculated using the following formula: $N = 2 \times 7.85 \times (5/2)^2 = 98$.

Where 7.85 is the multiplication factor f (α, power) with power = 80% and $\alpha = 0.05$ obtained from statistical tables. Therefore, ≥99 participants in each group are required to achieve statistically significant results. If a higher power or significance is sought, more study participants are required. It is also recommended that a coefficient be applied to this number to account for drop-outs based on local experience. Assuming a drop-out rate of 20%, 119 participants should be recruited into each group.

Results

Demographic and nutritional characteristics of the studied population

Table 1 summarizes the demographic and nutritional characteristics of the studied population. The mean age in both groups was ∼23 y regardless of sex. Females represented 49.8% and 55.8% in the SAM-exposed and unexposed groups, respectively. In terms of anthropometrics, no statistically significant differences were observed between the 2 groups, overall, and in females. However, in males, unlike the unexposed, the SAM-exposed had a reduced weight and height, and these differences were statistically significant. Finally, in terms of diet diversity, no difference was observed between the 2 groups.

Difference in BC between SAM-exposed and unexposed

Table 2 shows the difference in BC between exposed and unexposed. In males, compared with unexposed males, those exposed had lower absolute FFM (45.4 ± 5.4 compared with 48.2 ± 6.9 kg, $P = 0.01$) and lower TBW (33.4 ± 3.9 compared with 35.4 ± 5.0 kg, $P = 0.01$). However, no difference was observed between SAM-exposed and unexposed males in terms of FM (absolute/relative). As far as females are concerned, there was no difference between SAM-exposed and unexposed individuals in terms of FFM (absolute/relative) and FM (absolute/relative). Finally, adjusting for height, FFMI and FMI showed no difference in either sex.

TABLE 1 Nutritional difference between exposed and nonexposed people

	Exposed			Nonexposed			
Variables	*n*	Means ± SD	%	*n*	Means ± SD	%	*P*[1]
Age							
Females	74	23.5 ± 5.2		67	23.1 ± 4.7		0.65
Males	77	22.5 ± 4.5		53	22.5 ± 4.3		0.98
Sex							
Female	74		49.0	67		55.8	0.26
BMI (females)							
<18.5	2		2.7	0		0.0	
18.5–24.9	57		77.0	54		80.6	0.39
≥25	15		20.3	13		19.4	
BMI (males)							
<18.5	8		10.4	2		3.8	
18.5–24.9	67		87.0	49		92.4	0.36
≥25	2		2.6	2		3.8	
Weight, kg							
Females	74	54.0 ± 7.4		67	54.4 ± 7.0		0.79
Males	77	53.6 ± 6.4		53	56.4 ± 7.9		0.029
Height, cm							
Females	74	153.2 ± 6.5		67	154.2 ± 6.0		0.32
Males	77	159.9 ± 6.6		53	163.6 ± 6.7		0.003
Food diversity (females)							
Insufficient	38		51.4	32		47.8	0.67
Satisfactory	36		48.6	35		52.2	
Food diversity (males)							
Insufficient	39		50.6	20		37.7	0.14
Satisfactory	38		49.4	33		62.3	

[1] *P* value calculated using the chi[2] test (or Fisher's exact when applicability conditions were required) for proportions and student's *t*-test for means.

The interaction effects for TBW and FFM with $P = 0.11$ were examined further in stratified analysis. The differences (95% CI) between SAM-exposed and nonexposed means, derived from the regression models including the interactions were for TBW: –0.38 (–1.75 to 0.99) ($P = 0.59$) and –2.06 (–3.54 to –0.60) ($P = 0.006$) for females and males, respectively. The corresponding values for FFM were: –0.54 (–2.42 to 1.34) ($P = 0.58$) and –2.82 (–4.81 to –0.83) ($P = 0.006$).

Adjusted effect of exposure on TBW (kg) and FFM (kg)

As shown in **Table 3**, compared with the unexposed, the SAM-exposed had a significantly lower TBW (–1.13 kg [–2.12, –0.13]; $P = 0.027$) and FFM (–1.56 kg [–2.93, –0.20]; $P = 0.024$). Importantly, these effects did not diminish after adjustment (for sex, food diversity, and age).

Discussion

Our results suggest that survivors of SAM have lower FFM in proportion to their shorter height in adulthood resulting in similar height-adjusted FFMI compared with subjects who were not exposed to SAM in childhood. Nevertheless, they have a similar average FM to that of the general population not exposed to SAM in childhood. To our knowledge, our study is the first in an LMIC to evaluate the long-term BC of survivors of SAM during childhood, at the end of a long-term follow-up (between 11 and 30 y) after hospital discharge, in a context of endemic malnutrition. The originality of our study lies in the following points: *1*) large sample size measured using a state-of-the art technique (deuterium dilution) and *2*) inclusion of subjects who continued to experience an unfavorable dietary environment, without nutritional transition.

In our work, it was observed that SAM-exposed participants had a reduced FFM in comparison to unexposed ones, even after adjustment for sex, food diversity, and age. Indeed, evidence supports that undernutrition in childhood is associated with lower FFM in adulthood independently of potential later catch-up growth (7, 19).

Reduced FFM in adulthood is associated with decreased thermogenesis, insulin resistance/hyper insulinemia, decreased fasting and postprandial glucose uptake, risk of metabolic syndrome and/or type 2 diabetes, and increased incidence of atherothrombotic cardiovascular disease (6, 7). In addition, independent of this lower FFM, exposed individuals are at significantly higher risk of visceral obesity (6, 7, 19, 32). This phenotype of individuals with central obesity puts them at a similar or greater risk of cardiometabolic events as obese or overweight subjects (33). Indeed, visceral fat is considered metabolically less favorable, particularly with regards to the secretion of harmful adipokines. Its presence positively correlates with an increased cardiometabolic risk, particularly atherosclerosis and the damaging effects of chronic insulin resistance and reactive hyperinsulinemia that the latter promotes (33–35).

Despite their low FFM and the tendency of shorter stature (significant in males) with a high proportion of thinness, former

TABLE 2 Difference in body composition between exposed and nonexposed people

	Exposed		Nonexposed		
Variables	*n*	Means ± SD	*n*	Means ± SD	*P*[1]
Males	77		53		
BMI, kg/m^2		20.9 ± 1.9		21.0 ± 2.0	0.81
Fat mass, kg		8.2 ± 3.3		8.1 ± 5.3	0.94
TBW, kg		33.4 ± 3.9		35.4 ± 5.0	0.01
Fat-free mass, kg		45.4 ± 5.4		48.2 ± 6.9	0.01
Fat mass, %		15.1 ± 5.4		14.2 ± 6.6	0.40
Fat-free mass index, kg/m^2		17.6 ± 1.7		17.9 ± 1.7	0.39
Fat mass index, kg/m^2		3.2 ± 1.3		3.0 ± 1.7	0.58
Females	74		67		
BMI, kg/m^2		23.0 ± 2.7		22.8 ± 2.8	0.62
Fat mass, kg		14.4 ± 5.0		14.2 ± 5.2	0.80
TBW, kg		29.2 ± 3.8		29.5 ± 3.9	0.56
Fat-free mass, kg		39.7 ± 5.2		40.2 ± 5.4	0.55
Fat mass, %		26.2 ± 7.0		25.7 ± 7.6	0.65
Fat-free mass index, kg/m^2		16.8 ± 1.5		16.8 ± 1.7	0.94
Fat mass index, kg/m^2		6.1 ± 2.1		5.9 ± 2.1	0.47
All	151		120		
BMI, kg/m^2		22.0 ± 2.5		22.0 ± 2.4	0.83
Fat mass, kg		11.2 ± 5.2		11.5 ± 5.8	0.68
TBW, kg		31.3 ± 4.4		32.1 ± 5.3	0.16
Fat free mass, kg		42.6 ± 6.0		43.8 ± 7.2	0.15
Fat mass, %		20.6 ± 8.4		20.6 ± 9.1	0.96
Fat-free mass index, kg/m^2		17.3 ± 1.7		17.4 ± 1.8	0.82
Fat mass index, kg/m^2		4.6 ± 2.3		4.7 ± 2.4	0.96

[1] *P* value calculated using student's t-test. TBW, total body water.

malnourished people have a similar mean BMI to nonexposed people suggesting possible catch-up growth (weight-for-height) in adulthood, resulting in similar height-adjusted FFMI and FMI between SAM-exposed and unexposed in both sexes, meaning that FFM is reduced in proportion to their shorter height. That is an important finding, as height also matters for health (36–38), but it would suggest that the main pathway of SAM influencing later health is by constraining linear growth, and the associated lower accretion of FFM.

Indeed, our subjects spent their childhood in precarious nutritional conditions before experiencing one or more episodes of SAM, and then continued to live in an unfavorable environment in terms of food quality and security, without nutrition transition, which resulted in stunting but the same amount of FM. It is documented that FFM requires a significant amount of micronutrients for its synthesis, especially type I micronutrients (39). The deleterious effects may be expressed to a greater degree in exposed than in nonexposed even if they live in the same poor environment. However, it was observed that this reduced FFM is more pronounced in males than in females. The sex differences are more likely due to the greater risk of stunting and undernutrition in males than females. Both biological and social mechanisms have been proposed for the observed differences as well as a combination of both (40).

TABLE 3 Adjusted effect of exposure on total body water (kg) and fat-free mass (kg)

	TBW (kg)		Fat-free mass (kg)	
Variable	b (95% CI)[1]	*P*	b (IC95% CI)[1]	*P*
SAM				
Exposed	–1.13 (–2.12, –0.13)	0.027	–1.56 (–2.93, –0.20)	0.024
Nonexposed	0		0	
Age, y	0.10 (–0.01, 0.21)	0.062	0.17 (0.02, 0.31	0.022
Sex		<0.001		<0.001
Female	–5.01 (–6.00, –4.02)		–6.82 (–8.18, –5.47)	
Male	0		0	
Food diversity		0.118		0.136
Insufficient	–0.80 (–1.80, 0.20)		–1.04 (–2.41, 0.33)	
Satisfactory	0		0	
	R^2: 0.28		R^2: 0.28	

[1] Difference with 95% CI calculated by linear regression

b is the regression coefficient. TBW, total body water; SAM, severe acute malnutrition.

At this stage, the SAM-exposed males and females in our study still have a relatively healthy BC (at least, similar to nonexposed individuals). Given the current age of our study population and the unfavorable environment, with no nutrition transition, in which our population continued to live, it is quite possible that some differences have been masked. However, in light of population aging and trends with regards to Western-style diets in many African countries, it is highly possible that, in the future, SAM survivors will experience increased weight gain and therefore potentially greater risks of NCDs later in life (41).

Regardless of sex, BMI was similar in both groups. This normal average BMI in the SAM-exposed group, advantageous at first glance, probably reflects rapid weight gain associated with weak linear growth defining a particular phenotype of subject becoming "obese in relation to themselves" but without having a high BMI in absolute terms, joining the notion of metabolically obese-normal weight (MONW) subjects (42). Consequently, the BMI gain is more about FM than FFM, a relative difference that may explain, in part, the underlying insulin resistance and visceral obesity that may be responsible for the significant risk of metabolic syndrome observed in a study conducted in the same cohort on the association between SAM and the occurrence of NCDs in adulthood (32).

Of note, despite the various insightful results from our study, there are still a number of limitations. A major limitation is survival bias. In fact, only 151 of the 524 subjects of the initial cohort were examined, and they may have different characteristics from those of the unanalyzed, or those lost to follow-up and/or deceased subjects. Nevertheless, we believe that this would not have significantly altered our main conclusions because the characteristics at hospital admission did not differ between the lost to follow-up and traced subjects (24). Second, we did not have health information on early life, including gestational age, birth weight and height, growth rate during the first 2 y of life, HIV status, and data on subjects' progress from hospital discharge to the completion of this work. These variables could be potential confounding factors, as they are related to both malnutrition and its long-term deleterious effects (43). Third, although not malnourished in the past, unexposed subjects lived in the same unfavorable conditions as SAM-exposed, and it is difficult to establish whether they were perfectly healthy on a cardiometabolic level. The continued unfavorable situation in which our 2 groups lived probably helped to significantly reduce any differences in BC and in most cardiometabolic markers studied. Fourth, the study design is unable to separate mechanisms due to SAM per se from mechanisms due to persistent effects of the child's early environment or persistent living in the same poor environment.

In conclusion, our results show that SAM survivors have reduced FFM in proportion to their shorter height in adulthood with the preservation of FM. This suggests that the main pathway of SAM influencing later health is by constraining linear growth, and the associated lower accretion of FFM with preservation of FM. This particular phenotype may contribute to the later onset of NCDs and more research on this topic is needed.

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The authors' contributions were as follows—PM, GB, VOO, and PD: conceived and designed the experiments; PM, CC, and GN: collected data; MD and JW: contributed to specific areas of data analysis and quality control; PM: analyzed the data and wrote the first draft of the manuscript; JW, GM, MPH, EK, JM, ML, MD, PD, and GB: contributed to the writing of the manuscript and agree with the manuscript's results and conclusions; and all authors: read and approved the final manuscript.

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Data Availability

Data described in the manuscript, code book, and analytic code will be made available upon request pending by application to the corresponding author.

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