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Incidence of severe acute malnutrition after treatment: A prospective matched cohort study in Sokoto, Nigeria

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Abstract

Severe acute malnutrition (SAM) among children in Nigeria is tackled through the outpatient therapeutic programme (OTP) of the Community-based Management of Acute Malnutrition (CMAM) programme. CMAM is evidently effective in resolving SAM, but little evidence exists on the remaining risk of SAM relapse for children discharged as cured from the OTP. We aimed to measure and compare the 6-month incidence of SAM among OTP-cured and community control children and identify factors associated with SAM relapse. We conducted a prospective matched cohort study that tracked 553 OTP-cured and 526 control children in Sokoto State, Northern Nigeria. Outcomes and covariates were measured fortnightly in up to 12 home visits. We used multivariate Cox and accelerated failure time models to identify significant risk correlates, where the covariates to be tested for correlation with relapse were selected using domain knowledge and automatic feature selection methods. SAM incidence rates were 52 times higher in the OTP-cured cohort (0.204/100 child-days) than in the community control cohort (0.004/100 child-days). Children with lower mid-upper arm circumference at OTP admission, with lower height/length-for-age *z*-scores, whose household head did not work over the full year, who lived in an area previously affected by environmental shocks, who were female and who had diarrhoea before the visit had a significantly higher relapse risk. Our study shows that OTP-cured children remain at a significantly excess risk of SAM. To improve long-term health outcomes of these children, programmes adopting a CMAM approach should strengthen follow-up care and be integrated with other preventive services.

KEYWORDS

associated factors, Community-based Management of Acute Malnutrition, Northern Nigeria, outpatient therapeutic programme, relapse, severe acute malnutrition

1 | INTRODUCTION

Acute malnutrition is an important concern for children aged under 5 years, both globally and in Nigeria. In 2018, the Global Nutrition report estimated that Nigeria had the second highest wasting burden (a form of acute malnutrition) worldwide with 3.4 million afflicted children under 5 years (Development Initiatives, 2018). Severe acute malnutrition (SAM) represents most life-threatening form of acute malnutrition. SAM is defined by a weight-for-height *z*-score (WHZ) < −3 standard deviations (SD) from the World Health Organization (WHO) reference median, and/or a mid-upper arm circumference (MUAC) < 115 mm, and/or the presence of nutritional oedema (United Nations Children's Fund [UNICEF], WHO, & World Bank Group, 2017). In Nigeria, most of the SAM cases are clustered in the north (ACF International, 2015). In 2018, the prevalence of severe wasting among children under 5 was around 2% in Nigeria, and almost twice as high in the North-East and North-West regions compared with that in the southern regions (National Population Commission [NPC] & ICF, 2019).

Since the 2000s and the advent of ready-to-use therapeutic foods (RUTF), SAM has been commonly addressed through the WHO-recommended approach of Community-based Management of Acute Malnutrition (CMAM) (WHO, 2013). CMAM programmes provide treatment for children aged 6–59 months through an outpatient therapeutic programme (OTP) service for uncomplicated cases and an inpatient service for complicated cases. Volunteers are tasked with actively finding and referring wasting cases in their communities and with following-up children when they either drop out or complete the programme, to minimize the likelihood of relapse. In some contexts, treatment and support for moderate acute malnutrition (MAM) are also provided. MAM is defined by a −3 SD < WHZ < −2 SD and/or MUAC 115–125 mm (UNICEF, WHO, & World Bank Group, 2017).

In Nigeria, the CMAM programme was introduced in 2009 in Gombe and Kebbi States by development partners, including UNICEF, Save the Children, Valid International, Médecins Sans Frontières and Action Against Hunger, to find innovative ways of introducing the CMAM approach to the routine health system (ACF International, 2015). By 2017, it was scaled up to 12 states in Northern Nigeria that together host a population of more than 12 million children under age 5 (ACF International, 2015; UNICEF, 2020).

In Nigeria, children are admitted and discharged from the CMAM programme using MUAC as the main criterion (Chitekwe, Biadgilign, Tolla, & Myatt, 2018). Children with a MUAC < 115 mm and no apparent health complications are admitted into the OTP (Federal Ministry of Health [FMOH], 2010), in line with the WHO MUAC criteria (WHO, 2013). After initial diagnosis, children are treated on a weekly basis at health facilities for up to 12 weeks. At each visit, the child is examined by health facility staff; their MUAC and weight are measured, and the child is provided with essential medicines, vaccines and supplementation (including Vitamin A) and enough RUTF rations to last until the following visit. A child is discharged as cured when their MUAC is >125 mm for two consecutive weeks with signs of sustained weight gain (FMOH, 2010). Children who do not recover after 12 weeks are either referred to the inpatient service or discharged as nonrecovered. Beyond providing nutrition counselling, treatment for MAM is not covered by the CMAM programme in Nigeria outside of emergency zones.

Key messages

- The risk of developing severe acute malnutrition is significantly higher among children treated at the community-based management of acute malnutrition (CMAM) programme than among community control children. Thus, the CMAM programme needs to be integrated with other preventive services to improve long-term outcomes of children.
- The relapse risk is the highest in the 2 months after discharge. Post-discharge follow-up is necessary to minimize the relapse risk.
- A set of observable characteristics, such as being female and having lower anthropometric measurements at CMAM admission, are risk factors for relapse and can be used to easily identify high-risk groups.

The literature strongly suggests that CMAM programmes are effective in achieving 'nutritional recovery in a timely manner' (Lenters, Wazny, Webb, Ahmed, & Bhutta, 2013). However, to maximize impact, programmes working to treat SAM should improve long-term outcomes of survivors by minimizing relapse, defined as a new episode of SAM after discharge, persistent excess morbidity and mortality. A systematic review by Stobaugh et al. (2019) shows that the evidence surrounding postdischarge outcomes after initial recovery from SAM is still limited but tends to highlight poor health and nutrition outcomes, including relapse.

Evidence on SAM relapse is sparse with a high variation in estimates because of both contextual and methodological differences (Stobaugh et al., 2019). This makes it difficult to understand the persistent risk of a SAM episode after initial recovery from the CMAM programme, as well as the associated risk factors. Another important gap in the literature is the absence of comparison groups, making it difficult to determine the excess risk for SAM associated with a recent SAM episode. Additionally, to our knowledge, only one study explored the issue of relapse in Nigeria and did not include a control group (Begashaw, 2013; Stobaugh et al., 2019).

To fill this gap in the literature, the primary objective of this study was to assess the persistent and excess risk of SAM among children treated by the CMAM programme. The persistent risk was assessed by measuring the 6-month incidence rate of relapse among children discharged as cured from the OTP services of the CMAM programme. Excess risk was assessed by comparing this rate of relapse with the 6-month incidence rate of SAM in a cohort of community controls. Our secondary objective was to identify factors that are associated with the risk of relapse.

2 | METHODS

2.1 | Study design

This prospective matched cohort study was conducted from September 2018 to May 2019 in five rural local government areas (LGAs) in Sokoto State, Northern Nigeria. Nine out of the 23 LGAs in Sokoto State hosted the CMAM programme. Of these, four were excluded because they were either hosting another study looking at improving CMAM delivery, were periurban, or not easily accessible. In the selected five LGAs, the CMAM programme had been running since 2010 and was being implemented throughout the study period. Within each LGA, five health facilities were hosting the CMAM programme, and the study covered this exhaustive list of 25 health facilities.

The study followed two cohorts of subjects: first, a cohort of children who were discharged from OTP as cured and were aged 6–59 months at admission into the OTP, who had not previously been admitted to the OTP or inpatient care and whose households resided in the catchment area of the selected health facilities and were not planning to move out—subsequently referred to as 'OTP-cured children'—and second, a cohort of children from the same communities as OTP-cured children who had no history of SAM, no treatment for SAM and no anthropometric or clinical signs of MAM (MUAC < 125 mm) or of severe stunting (height/length-for-age *z*-score [HAZ/LAZ] < −3 SD) at the time of recruitment into the study. Each community control child was matched to an OTP-cured child based on the following criteria: residence (living in the same community), age (allowing up to 3-month difference), sex, age of the mother (below or above 20 years of age) and level of education of the mother (no education, completed primary and completed secondary or above). These children are subsequently referred to as 'community control children'.

Exclusion criteria for both cohorts of children for enrolment into the study included the presence of disability or any congenital disease (after clinical examination) that affects growth or prevents accurate anthropometric measurement and/or prevents the child from eating normally, a sibling already enrolled into the study, the biological mother of the child having passed away or having a mother <15 years old.

2.2 | Sample size

The minimum sample size required for this study was calculated to be 500 OTP-cured and 500 community control children across the 25 facilities. This sample size would allow us to detect a 4% point difference in SAM incidence between both cohorts with 95% confidence. Calculation parameters were chosen conservatively and assumed an incidence of SAM among community controls of 1%, a total number of 25 clusters (health facilities), a coefficient of variation of cluster sizes of 0.9 and an intracluster correlation of 0.02. Sample size calculations were implemented using the *clustersampsi* tool in Stata (version 15, StataCorp LLC, College Station, Texas). With an anticipated loss to follow-up of 20%, the study therefore aimed to recruit 600 children per cohort.

2.3 | Cohort timeline

OTP-cured children were recruited at health facilities on a rolling basis between September and November 2018. There, the study team screened all children who had been discharged as cured for eligibility and consent to participate in the study. Following recruitment into the study, each OTP-cured child was visited at their home within 2 weeks of their initial recruitment. Immediately after the first home visit, a search for a community control was conducted using a snowball approach that relied on referrals from the mother of the OTP-cured child. Only children who met the matching and eligibility criteria were recruited into the study. Afterwards, both cohorts were followed-up fortnightly for a total of 12 home visits. Participation in the study ended at the 12th visit, or if the child developed SAM, had died, or the family no longer consented to participation in the study or moved out of the community.

2.4 | Data collection and tools

A questionnaire was administered to the mothers of OTP-cured children at the health facility to locate the children's homes. Data on children's health status at admission and discharge from the OTP were also collected from registration and treatment tracking cards kept at the facility by staff. A questionnaire was administered to the mothers of the community control children to assess eligibility and matching criteria.

At the first home visit, a questionnaire was administered to the mother and household head to collect information across several domains related to the child, mother and household (Table 1). Children's MUAC was measured using the WHO/UNICEF-recommended MUAC tape and measurement protocol (WHO, 2013), whereas height and length were measured with a precision of 0.1 cm, using boards manufactured by SECA: standing boards for children who were able to stand and lying-down boards for children unable to. At each follow-up visit, the child's MUAC was measured and a short questionnaire was administered to collect child-level co-morbidity data in the previous 2 weeks.

In each health facility, a survey was conducted using direct observation and interviews with staff to assess adherence to the Nigeria CMAM national guidelines (FMOH, 2010) and availability of OTP-related drugs and equipment. The survey also collected data on shocks that affected the catchment area of facilities in the year prior to the survey, such as drought, floods, sandstorms and security-related events.

All questionnaires were administered using the Computer-Assisted Personal Interviewing software CSPro (version 7.1.3, U. S Census Bureau, Washington, DC), and health facility cards were

TABLE 1 Domains included in first home visit questionnaire

Level	Dimension
Child level	Height/length, mid-upper arm circumference
	Demographics
	Breastfeeding history
	Co-morbidities in the 2 weeks prior to the survey
	Immunization status
	Dietary diversity (24 h prior to survey)
Mother level	Demographics
	Economic activity and education status
	Knowledge on child-feeding and health-seeking behaviour
	Reproductive history and care
	Perceived outpatient therapeutic programme experience
	Networks in community
Household level	Household demographics and composition
	Economic activity and education of household head
	Household assets and wealth
	Water, sanitation and hygiene infrastructure
	Household food security and dietary diversity
	Deaths in the household in the year prior to the survey

scanned and data entered digitally using the SurveyCTO software (Dobility, Inc., Cambridge, Massachusetts).

2.5 | Definition of variables

SAM was determined using the WHO and national MUAC criteria of MUAC < 115 mm (FMOH, 2010; WHO, 2013). To account for measurement error and identify definite relapse, a child was classified as having SAM if his/her MUAC was ≤112 mm at any visit, or if his/her MUAC was 112–115 mm for two consecutive visits.

Stunting was defined using the WHO methodology and reference tables (WHO, 2013). A child was classified as stunted if his/her HAZ/LAZ was <−2 SD from the WHO reference median and as severely stunted if his/her HAZ/LAZ was <−3 SD.

Basic immunization was defined by the minimum immunization package recommended by WHO; a child was classified as having received basic immunization if they had taken one BCG vaccine, one measles vaccine, three polio vaccines (excluding polio at birth) and three DPT/PENTA vaccines (Brown & Gacic-Dobo, 2015). We applied this basic immunization package criterion to all children, irrespective of age. Information was based on the vaccination card, if available, and on the mother's recall otherwise.

Child appropriate feeding, defined in terms of continued breastfeeding, dietary diversity and meal frequency, was measured using the age-specific Infant and Child Feeding Index (ICFI) score (Guevarra et al., 2014). A child was classified as having appropriate feeding if his/her ICFI score was ≥6. Child dietary diversity was assessed using a score that ranged from 0 to 3, assigned based on the number of food groups consumed by the child in the 24 h preceding the survey and the child's age (Guevarra et al., 2014). Child meal frequency was assessed using a score that ranged from 0 to 3, assigned based on the number of snacks or meals fed to the child in the 24 h preceding the survey and the child's age (Guevarra et al., 2014). A child was classified as having ever been exclusively breastfed if they received only breast milk for at least the first 3 days of life, with the exception of oral rehydration solution, drops/syrups of vitamins, minerals or medicines (WHO, 2010).

Household socio-economic status was measured using the Demographic and Health Surveys Wealth Index (NPC & ICF, 2014). Using principal component analysis, a wealth index standardized score was constructed, and the sample was then divided into population quintiles. Households were classified as having a 'low socioeconomic status' if they fell in the bottom two quintiles.

Households were classified as having unimproved sanitation if they did not have access to a flush toilet or latrine, ventilated improved pit latrine, pit latrine with slabs or composting toilet (NPC & ICF, 2019). Households were classified as having unsafe drinking water if they did not have access to piped water, public taps, standpipes, tube wells, boreholes, protected dug wells and springs and rainwater, or safe drinking water was more than a 30-min round-trip walk from home (NPC & ICF, 2019). Households were classified as having inadequate flooring if they had an earth, sand or dung floor.

Household dietary diversity was assessed by summing the total number of food groups consumed by the household in the 24 h preceding the survey (Swindale & Bilinsky, 2006). The validated Household Food Insecurity Access Scale (Coates, Swindale, & Bilinsky, 2007) was used to measure the degree of food insecurity in the household in the 4 weeks preceding the survey. Based on the scale, households were categorized into four categories: food secure, mild, moderately and severely food insecure.

The delivery of the OTP services was assessed using data from the health facility survey and the household questionnaire: a score ranging from 0 to 6, measuring the availability of nonexpired medicines essential to treat SAM and co-morbidities, an OTP implementation score ranging from 0 to 13, measuring the adherence to the OTP protocol as outlined in the Nigeria CMAM national guidelines (FMOH, 2010) and a perception-based score ranging from 0 to 16, recording the mother's satisfaction with the OTP service. Each dimension in a score was given equal weight. Higher scores reflect better availability, quality and perceptions of the service.

2.6 | Statistical analysis

The dependent outcome variable was time to incidence of SAM, which was determined by calculating the differences—in days—from the child's recruitment into the study until development of SAM. SAM incidence rates for OTP-cured and community control children were

calculated as the number of SAM cases per 100 child-days of observation. Kaplan–Meier survival curves were also plotted for each cohort and tested for equality using the log-rank test. The characteristics of both cohorts were compared using a Wald test.

We used multivariate regressions to identify risk factors associated with relapse and restricted this analysis to the OTP-cured children. Our analysis estimated a relationship between relapse and covariates measured at one point in time. As recruitment and first home visits were about 2 weeks apart, some children already experienced relapse at the first home visit. Because we were interested in identifying risk factors for relapse prior to the SAM occurrence, we limited the analysis to the covariates that could reasonably be assumed to be time-invariant between recruitment and the first home visit, in order to minimize the risk of endogeneity in our regressions.

We estimated hazard ratios using Cox proportional hazards models and adopted four methods for the selection of covariates. The first was based on theoretical priors and was derived from a literature review and contextual knowledge of OTP and SAM in Northern Nigeria. The other three used automated feature selection techniques, including forward and backward stepwise regressions with threshold significance levels set at $P = 0.05$ (James, Witten, Hastie, & Tbishirani, 2014) and cross-validated Lasso regressions (Tibshirani, 1997). We used these four approaches because of the large number of potential covariates that could be used in our regressions and the need to systematically check alternative specifications to the theory-driven one. We considered variables to be significantly and robustly related to the relapse risk if they were identified to be significant correlates in at least three of the four models that we ran. For each model, the proportional hazards assumption, assessed using Schoenfeld residuals (Kleinbaum & Klein, 2012), was not violated.

We also conducted additional analyses using data collected in the fortnightly follow-up visits to estimate a model with time-varying variables. To avoid introducing endogeneity, we defined the time origin as the first home visit and restricted the analysis to the subsample of children not experiencing relapse at that time. Child morbidity covariates were lagged by one time period to ensure that the parents' recall refers to a period prior to the SAM assessment. Since specification tests on a Cox model using this set up indicated that the proportional hazards assumption is violated, we estimated a parametric accelerated failure time model using maximum likelihood estimation. We ran several models with different assumed survival distributions and selected the lognormal survival distribution, which was the model with the lowest Akaike Information Criterion (George, Seals, & Aban, 2014; Kleinbaum & Klein, 2012). For this model, covariate selection was theoretically based and included the covariates found to be significant in our main analyses, as well as additional time-varying covariates measured at the first visit only or repeatedly at the follow-up visits.

Robust standard errors clustered at the health facility level were used throughout. Analysis was performed on the subsample of children with complete data (no imputation for missing values was done). Statistical significance was defined by P values <0.05. Data cleaning and analyses were performed using Stata (version 16, StataCorp LP, College Station, Texas), with the exception of the Lasso variable selection, which was implemented using R (version 3.6.0, R Foundation for Statistical Computing, Vienna, Austria) in RStudio.

2.7 | Ethical considerations

Verbal informed consent was sought and recorded in the questionnaire from mothers during recruitment of children into the study and from household heads at the first home visit. All children who experienced SAM during the study were referred to the nearest OTP services. This study met the ethics criteria of the Sokoto State Health Research Ethical Committee and approval was received on 12 March 2018.

3 | RESULTS

Out of a total of 645 OTP-cured children who were recruited into the study, 553 were found at the first home visit and deemed eligible, 83 were not found and nine were not eligible (Figure 1). Our analysis sample consisted of these 553 OTP-cured children, as well as the 526 community control children who were successfully matched and deemed eligible. Throughout the study, 134 (24%) OTP-cured children experienced relapse, whereas only three (0.6%) community control children developed SAM. Across the two cohorts, 14 (1%) children died, including nine OTP-cured and five community control children ($P = 0.326$), and 62 (6%) children were lost to follow-up, including 32 OTP-cured and 30 community control children. The remaining 378 (68%) OTP-cured and 488 (93%) community control children were still alive and free of SAM at the end of the study. The median time for follow-up was 153 days.

3.1 | Characteristics of children, mothers and households

Table 2 presents key background characteristics of children, mothers and households included in the analysis, across the two study cohorts. We found some differences between the two cohorts. First, OTP-cured children were significantly more likely to be stunted than community control children. Notably, severe stunting was an exclusion criterion for community controls. Second, households of OTP-cured children were more likely to be in the lowest two wealth quintiles than households of community control children. Third, heads of households of OTP-cured children were less likely to work than those of community control children. Finally, mothers of community control children had a lower mean number of live births than mothers in the OTP-cured cohort.

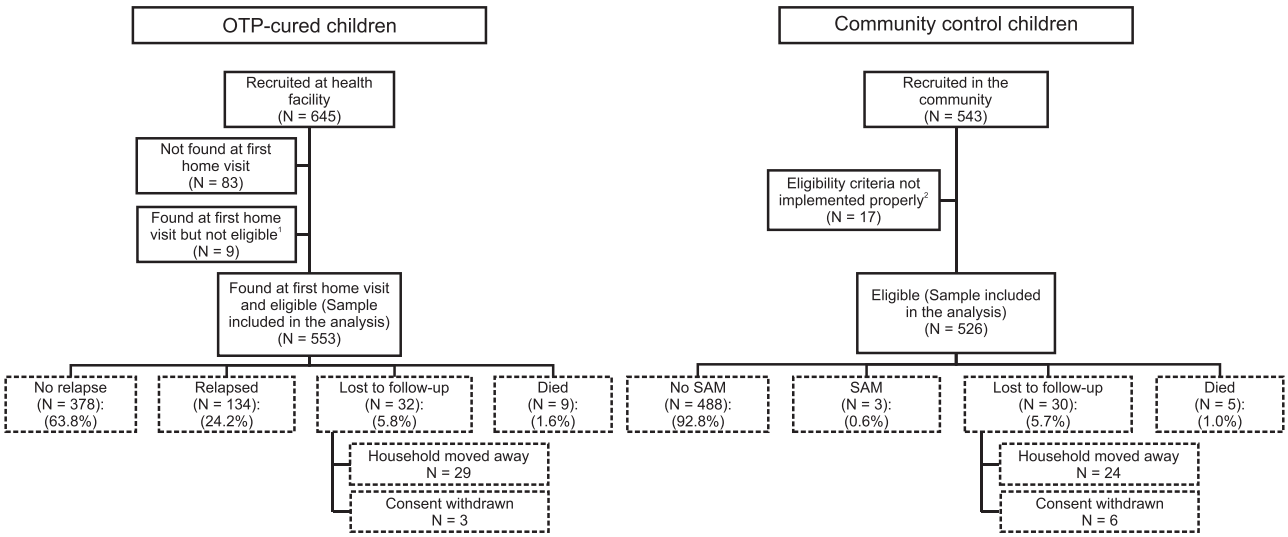

FIGURE 1 Monitoring of children after enrolment into the study. Notes: (1) Eligibility of OTP-cured children was re-assessed at the first home visit. (2) These 17 community control children were discovered at analysis stage to not have passed the eligibly criteria and hence were excluded from the analysis. The boxes with the dashed lines represent the outcomes of children in the two cohorts at the end of the study. Abbreviations: OTP, outpatient therapeutic programme; SAM, severe acute malnutrition

TABLE 2 Key background characteristics of children included in the study

Variable	OTP-cured		Community controls		
	Estimate	*N*	Estimate	*N*	Difference
Child level					
Male, % (CI)	52.3 (48.1–56.4)	553	52.5 (48.2–56.7)	526	–0.2
Age in months, mean (SD)	19.2 (7.5)	553	18.9 (7.6)	526	0.2
Appropriately fed, % (CI)	18.5 (15.5–22)	551	20.0 (16.8–23.6)	526	–1.5
Had diarrhoea in the 2 weeks preceding the first home visit, % (CI)	53.0 (48.8–57.1)	553	51.5 (47.2–55.8)	526	1.5
Received basic immunization, % (CI)	5.6 (4–7.9)	553	3.8 (2.5–5.8)	526	1.8
Stunted, % (CI)	87.3 (84.2–89.9)	535	46.3 (42–50.6)	523	41.0***
Mother level					
No education, % (CI)	95.3 (93.2–96.8)	553	96.0 (94–97.4)	526	–0.7
Age in years, mean (SD)	28.5 (7.2)	553	27.5 (6.4)	526	1.0*
Attended antenatal care for study child, % (CI)	55.9 (51.7–60)	553	56.3 (52–60.5)	526	–0.4
Age at first birth in years, mean (SD)	17.6 (2.2)	553	17.7 (2.4)	526	–0.1
Number of live births, mean (SD)	4.7 (2.7)	553	4.2 (2.4)	526	0.5***
Household level					
Number of household members, mean (SD)	7.3 (3.9)	553	6.9 (3.6)	526	0.3
Age dependency ratio, mean (SD)	149.2 (81.1)	541	138.5 (75.3)	509	10.7*
Household head works, % (CI)	96.0 (94–97.4)	553	98.1 (96.5–99)	526	–2.1**
Household head has no education, % (CI)	78.1 (74.5–81.4)	553	75.1 (71.2–78.6)	526	3.0
Household in lowest two wealth quintiles, % (CI)	47.4 (43.2–51.6)	553	40.5 (36.4–44.8)	526	6.9**
Severely food insecure, % (CI)	26.0 (22.5–29.9)	553	25.9 (22.3–29.8)	526	0.2

Note: Significance stars correspond to *P*-value ranges for a Wald test.
Abbreviations: CI, confidence interval; SD, standard deviation; OTP, outpatient therapeutic programme.
*$P \leq 0.05$.
**$P \leq 0.01$.
***$P \leq 0.001$.

3.2 | SAM incidence rates and probabilities of remaining SAM-free during follow-up

The relapse incidence rate in the OTP-cured cohort was 0.204 per 100 child-days, and the SAM incidence rate in the community control cohort was 0.004 per 100 child-days. The crude rate ratio between cohorts was 52, meaning that OTP-cured children had a SAM incidence rate 52 times higher than the community controls and hence were at excess risk of SAM. The Kaplan–Meier curves presented in Figure 2 show that for OTP-cured children, most relapse cases occur within the first 60 days post-OTP discharge. For OTP-cured children, 75% remained without SAM up until day 159. We conducted a log-rank test and found that the difference between the survival curves for the two cohorts was statistically different (χ^2 = 135.1, P < 0.001).

3.3 | Relapse risk factors

Multivariate Cox regressions for the sample of OTP-cured children showed strong evidence that being a male, having higher LAZ/HAZ and a larger MUAC at admission into the OTP are significantly related to a lower relapse risk (Table 3). Regular and nonseasonal economic activity of the household head was also associated with a lower relapse risk. Environmental shocks, and particularly sandstorms, that affected health facilities' catchment areas in the 12 months prior to recruitment were associated with higher relapse risk. Other indicators presented in Table 3 did not consistently correlate with the likelihood of relapse (Models A–D).

After controlling for time-varying covariates, including household and child dietary diversity, food security and co-morbidity data, the three child-level indicators identified as significant in our main analyses were still significantly and inversely related to the relapse risk: being male, higher LAZ/HAZ and higher MUAC at admission into the OTP. In addition, children who lived in a moderately food insecure household were less likely to experience relapse than children who lived in a severely food insecure household. Similarly, a higher child-level dietary diversity score was associated with a lower relapse risk. A set of covariates measured repeatedly at each follow-up was also significantly related to the relapse risk. Most importantly, children with diarrhoea in the 2–4 weeks prior to the follow-up visit were significantly more likely to experience relapse at any given visit (Model E).

Because we conducted the risk factor analysis on the subsample of children with nonmissing data, this meant that the number of observations in our Cox models was lower than that of the 553 OTP-cured children (ranging from 447 to 464 for the different specifications of Models A to D, as shown in Table 3). In particular, MUAC at admission into the OTP was missing for 11% of the sample. We conducted sensitivity analysis by estimating a Cox model without MUAC at admission as a covariate and found that our results were robust to this specification (Table A1). Note also that the smaller sample size for Model E resulted from restriction of our analysis to the subsample of children not experiencing relapse by the first home visit.

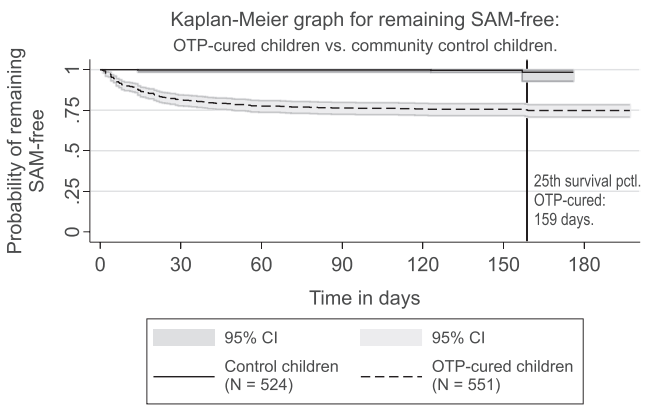

FIGURE 2 Kaplan–Meier curves for remaining SAM-free: OTP-cured versus community control children. Notes: Two OTP-cured children passed away before the first home visit and hence are not included. Two community control children dropped out of the study before the second home visit and are not included. Vertical black line indicates the 25th percentile SAM-free time for the OTP-cured cohort = 159 days. Abbreviations: OTP, outpatient therapeutic programme; SAM, severe acute malnutrition; CI, confidence interval

4 | DISCUSSION AND RECOMMENDATIONS

Our main finding was that children discharged as cured from the OTP remain at persistent and excess risk of SAM. In the 6-month study period, 24% of the OTP-cured children experienced relapse, whereas less than 1% of the community control children developed SAM. The incidence rate of SAM was 52 times higher among the OTP-cured cohort than among the community control cohort. Most of the relapses occurred within the first 2 months of discharge.

These results are comparable with other findings in the literature. The only other study, to our knowledge, on post-OTP discharge SAM relapse in Nigeria found that 25% of their study population experienced relapse, although the study used a coverage survey and relied on mothers' recall of the first episode (Begashaw, 2013). Other studies in sub-Saharan Africa and Asia reported a range of 2%–37% (Ashraf et al., 2012; Bhandari et al., 2016; Binns et al., 2016; Dale et al., 2018; Grellety et al., 2017; Stobaugh et al., 2019) and found that relapse was the highest in the first 3–6 months after discharge (Burza et al., 2016; Tsinuel, Alemseged, Philips, Paluku, & Team, 2015). Finally, Tsinuel et al. (2015), the only other study we are aware of that compared relapse after OTP treatment with SAM incidence in a control group found an incidence rate of 1% in their control group and 15% in their post-OTP group in Ethiopia.

Assessment of the risk factors of relapse revealed that being female, having a lower LAZ/HAZ at recruitment, a lower MUAC at admission into the OTP and a household head without stable employment throughout the year were all related to a higher likelihood of relapse. Similarly, increased occurrence of sandstorms around the

TABLE 3 Multivariate regression analysis of factors associated with relapse

	Cox models										AFT model	
	Model A			Model B			Model C			Model D			Model E	
Covariate selection method	Theory-based			Backward stepwise			Forward stepwise			Lasso			Theory-based	
Variable	HR		CI	HR		CI	HR		CI	HR		CI	TR	CI
(LGA controls: included)	(Yes)			(Yes)			(Yes)			(Yes, some)			(Yes)	
Child level														
Male	0.49	**	[0.31, 0.76]	0.46	***	[0.30, 0.70]	0.58	***	[0.39, 0.84]	0.54	**	[0.35, 0.81]	2.44	** [1.25, 4.79]
LAZ/HAZ	0.70	***	[0.59, 0.83]	0.69	***	[0.58, 0.83]	0.71	***	[0.61, 0.84]	0.74	***	[0.63, 0.87]	1.49	*** [1.20, 1.84]
MUAC at admission into the OTP	0.58	**	[0.39, 0.86]	0.49	***	[0.36, 0.65]	0.52	***	[0.38, 0.71]	0.56	***	[0.41, 0.77]	2.73	** [1.37, 5.42]
Age, months	0.98		[0.94, 1.02]										1.01	[0.91, 1.12]
Put to the breast immediately after birth	1.01		[0.58, 1.76]											
Ever exclusively breastfed	0.95		[0.46, 1.94]											
Received basic immunization	0.82		[0.39, 1.72]											
Received at least three DPT Penta vaccines				0.39	*	[0.18, 0.86]								
Received at least three polio vaccines (excluding polio at birth)				1.77	*	[1.05, 2.97]								
First born in the household							0.62		[0.41, 0.94]					
Mother level														
No education	1.02		[0.18, 5.74]											
Age, years	0.97		[0.90, 1.06]											
Does not work	0.93		[0.60, 1.43]											
Talks about child feeding and care with other mothers	1.39		[0.77, 2.51]							1.49		[0.89, 2.49]		
Attended antenatal care for study child	1.23		[0.86, 1.75]											
Attended postnatal care for study child	1.40		[0.81, 2.41]	1.73	*	[1.04, 2.86]								
Number of live births	1.11		[0.96, 1.30]											
Number of children that died				1.19	***	[1.09, 1.31]				1.07		[0.96, 1.20]		
Age at the birth of the study child, years	0.99		[0.92, 1.07]											
OTP perceived experience score given by mother										0.94		[0.81, 1.08]		
Perceived experience of OTP programme was poor	1.40		[0.78, 2.53]											
Household level														
Household size	0.95		[0.87, 1.04]											
Age dependency ratio	1.00		[1.00, 1.01]	1.00	**	[1.00, 1.01]								
Female headed	1.37		[0.39, 4.81]											
Age of household head, years				0.97	**	[0.96, 0.99]								

TABLE 3 (Continued)

	Cox models										AFT model	
	Model A			Model B			Model C			Model D			Model E	
Covariate selection method	Theory-based			Backward stepwise			Forward stepwise			Lasso			Theory-based	
Variable	HR		CI	HR		CI	HR		CI	HR		CI	TR	CI
Household head's main work activity is not seasonal	0.70	*	[0.51, 0.98]	0.60	**	[0.44, 0.82]	0.72	*	[0.55, 0.95]	0.64	***	[0.49, 0.83]	1.72	[0.85, 3.48]
Household head has no education	1.21		[0.59, 2.46]											
Unimproved sanitation	1.21		[0.64, 2.26]	2.09	*	[1.09, 4.00]								
Unsafe drinking water source	1.51		[0.89, 2.56]	1.64	*	[1.06, 2.53]								
Inadequate flooring				0.53	*	[0.29, 0.98]								
No electricity										1.37		[0.74, 2.52]		
Household in the lowest two wealth quintiles	0.97		[0.63, 1.51]											
Wealth index score (standardized)										0.90		[0.67, 1.19]		
OTP Centre 30 min or more away (one way)				1.51	*	[1.08, 2.11]								
Health facility 30 mins or more away (one way)							1.50	*	[1.04, 2.17]	1.53	**	[1.13, 2.09]		
Health facility level														
OTP implementation score	0.86	*	[0.76, 0.98]	0.84	***	[0.75, 0.93]							1.13	[0.87, 1.47]
OTP key medicine score	1.42	**	[1.14, 1.76]	1.36	**	[1.11, 1.66]							0.76	[0.48, 1.21]
Catchment area was severely affected by …														
Drought (last 12 months)	2.28	***	[1.42, 3.65]	1.69	*	[1.03, 2.76]							0.99	[0.18, 5.35]
Floods (last 12 months)	1.76		[0.89, 3.46]							1.23		[0.71, 2.13]		
Sandstorms (last 12 months)	2.23	**	[1.27, 3.92]	2.15	**	[1.32, 3.49]				1.47		[0.79, 2.73]	0.88	[0.22, 3.53]
Insecurity (last 12 months)	0.45	***	[0.28, 0.72]	0.57	**	[0.38, 0.85]							1.20	[0.53, 2.74]
Time-varying covariates measured at first visit only														
Child was breastfed yesterday													0.17	[0.01, 4.59]
Interaction term: child breastfed yesterday with child age													1.17	* [1.01, 1.35]
Household is food secure													1.79	[0.72, 4.46]
Household is mildly food insecure													1.07	[0.28, 4.15]
Household is moderately food insecure													3.39	** [1.40, 8.21]
Household is severely food insecure													(ref)	[1.00, 1.00]
Number of food groups household consumed in last 24 h													0.83	[0.64, 1.06]
Child-level dietary diversity score													1.66	* [1.06, 2.61]
Child-level meal frequency score													0.72	[0.49, 1.05]

(Continues)

TABLE 3 (Continued)

	Cox models								AFT model	
	Model A		Model B		Model C		Model D		Model E	
Covariate selection method	Theory-based		Backward stepwise		Forward stepwise		Lasso		Theory-based	
Variable	HR	CI	HR	CI	HR	CI	HR	CI	TR	CI
Child is appropriately fed									1.24	[0.61, 2.52]
Time-varying covariates measured at each visit—lagged by one time period										
Child had diarrhoea in the last 2 weeks									0.25***	[0.14, 0.47]
Child had diarrhoea with blood in the last 2 weeks									0.69	[0.30, 1.57]
Child had illness with fever in the last 2 weeks									0.52*	[0.28, 0.94]
Child had illness with cough in the last 2 weeks									0.79	[0.42, 1.48]
Child was taken to the clinic/health facility/hospital for any other reason in last 2 weeks									0.54	[0.11, 2.63]
Number of subjects	460		447		447		464		391	
Number of relapses	107		103		103		107		39	
Time at risk	55,141		53,618		53,618		55,735		3,769	

Note: Coefficients for models A to D are HRs estimated using a multivariate Cox proportional hazards regression on time-invariant covariates. HRs below zero indicate a lower risk of relapse, whereas HRs above zero indicate a higher relapse risk. Coefficients for model E are TRs estimated using an AFT regression allowing for time-varying covariates and assuming a lognormal survival distribution. TRs below one indicate that covariates are associated with shorter time to relapse (i.e., higher risk of relapse), whereas values above one indicate that covariates are associated with longer time to relapse (i.e., lower risk of relapse). Significance stars correspond to *P* values in a *t*-test. Standard errors are clustered at the health facility level. Note that numbers of observations differ from the full sample of OTP-cured children included in the study (553) because of missing values in covariates included in the regressions. We did not perform any imputations. Empty cells in the table mean that the relevant variable (in the respective row) was not included in this model (in the respective column).

Abbreviations: HR, hazard ratio; TR, time ratio; AFT, accelerated failure time; CI, confidence interval; LGA, local government area; LAZ, length-for-age *z*-score; HAZ, height-for-age *z*-score; MUAC, mid-upper arm circumference; DPT, diphtheria, pertussis and tetanus; OTP, outpatient therapeutic programme.

*$P \leq 0.05$.

**$P \leq 0.01$.

***$P \leq 0.001$.

health facility and having an episode of diarrhoea were related to an increased relapse risk.

Our findings have important implications for the CMAM programme in Northern Nigeria.

First, the high rate of relapse among OTP-cured children indicates that relapse cases must account for a significant proportion of all SAM cases. Hence, tackling relapse would help reduce the SAM burden generally in Northern Nigeria.

Second, the fact that relapse risk was the highest in the period shortly after discharge means that many children, at discharge, were at the risk of experiencing imminent relapse. Possibly, this indicates insufficient recovery for some children and that OTP discharge criteria are not adequate to ensure full long-term recovery from SAM. To tackle relapse, it is important to understand why the current criteria might be inappropriate in some cases and whether changes or additional criteria could be used to reduce the relapse risk.

Third, the high rate of relapse and the fact that children were most vulnerable shortly after discharge, indicate that some form of follow-up care after OTP treatment is needed to tackle the issue of relapse. Support for MAM should be an integral part of treatment for acute malnutrition, and its absence in Nigeria is an important gap (Lelijveld et al., 2020). Given that lower MUAC at admission is a risk factor for SAM relapse, integrating MAM treatment into CMAM programmes in Nigeria would catch children earlier in their deterioration in MUAC, thereby potentially lowering the relapse risk. Examples exist from other contexts where MAM treatment has been successfully integrated into CMAM programs, such as the integrated management of acute malnutrition in Kenya (UNICEF, 2012).

Fourth, some risk factors that we identified, including being female, having lower MUAC at admission and lower LAZ/HAZ, provide a set of easily observable criteria that could offer a way to identify children who are at the highest risk of experiencing relapse. Efforts to tackle the risk of relapse could focus on those children.

Fifth, the fact that lower LAZ/HAZ and MUAC measurements at admission into the OTP were significantly correlated with a higher relapse risk points to the important vulnerability nexus that exists between stunting and SAM. Understanding the relationship between these anthropometric measures might be essential to determine how to improve the treatment of SAM and how to prevent relapse. Research efforts, such as the Wasting and Stunting research programme, are generating more evidence to show how those two factors interact (Angood, 2014). Better understanding of this relationship might be the key to understanding how to refer, treat and follow-up children with the highest relapse risk.

Finally, our study has identified other significant risk factors of relapse that point to the multiple drivers of malnutrition and highlight that CMAM on its own is not sufficient to tackle SAM. It is becoming increasingly important to address malnutrition through broader multisectoral approaches. While evidence on the costs and benefits of multisectoral actions for nutrition, particularly nutrition-sensitive ones, is limited, there are promising findings from the experience of The Working to Improve Nutrition in Northern Nigeria (Visram et al., 2017) and The Nigeria Child Development Grant Programme (Carneiro, Rasul, Mason, Kraftman, & Scott, 2019) pilots, and ongoing research initiatives such as the Strengthening Economic Evaluation for Multisectoral Strategies for Nutrition (Global WACh, 2019).

4.1 | Strengths and limitations

Our study has a number of strengths: (1) the prospective nature of the design that comprised fortnightly home follow-ups, which minimizes the risk of missing short episodes of relapse and is one of the very few such studies in Nigeria; (2) the inclusion of a healthy community control group, which allows assessing the excess risk of SAM following OTP treatment, and (3) the inclusion of indicators measuring the OTP standard of care.

However, it is important to recognize the contextual nature of this research. Our study was restricted in evaluating post-discharge outcomes in the rainy season, and it therefore did not investigate seasonal effects. We also cannot generalize our findings to the population of children in Northern Nigeria or even Sokoto State as the children in our study were recruited from health facilities in a purposefully selected set of LGAs in Sokoto and were selected following specific exclusion and inclusion criteria mentioned above.

5 | CONCLUSION

SAM survivors are at significant risk of relapse in the 6 months following discharge from treatment, with 24% relapsing in this context. Therefore, reducing relapse would substantially reduce the SAM burden in Northern Nigeria. Periodic monitoring of children who have been discharged from the CMAM programme as cured is needed to ensure early detection of at-risk cases. Using key observable characteristics such as sex or MUAC at admission into the OTP could provide a cost-effective way to identify those high-risk cases. CMAM programmes need to include treatment of MAM and need to be integrated with other social services to reduce the likelihood of relapse and improve longer-term outcomes of children.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTIONS

PB, AV, JHug, OA and GO conceived and designed the study. GO, OA, SA, JHug, AV, PM and SN led the primary data collection. JHarb, JHug and PJ analysed the data. JHug, PJ and JHarb wrote the first draft of the paper. All authors critically revised the paper and approved the final version.

ETHICAL STATEMENT

The study was approved by the Sokoto State Health Research Ethical Committee (Reference SMH/1580/V.IV). Furthermore, informed consent was sought from all study participants prior to conducting interviews and observations.

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APPENDIX A.

TABLE A1 Cox regression analysis of factors associated with relapse, excluding MUAC at admission into the OTP

	Cox model		
Covariate selection method	**Theory-based**		
Variable	**HR**		**CI**
(LGA controls: included)	(Yes)		
Child level			
Male	0.46	***	[0.32, 0.65]
LAZ/HAZ	0.69	***	[0.58, 0.81]
Age, months	0.96	**	[0.93, 0.99]
Put to the breast immediately after birth	0.86		[0.52, 1.42]
Ever exclusively breastfed	0.75		[0.37, 1.54]
Received basic immunization	0.72		[0.35, 1.49]
Mother level			
No education	0.96		[0.18, 5.06]
Age, years	1		[0.94, 1.07]
Does not work	0.91		[0.65, 1.28]
Talks about child feeding and care with other mothers	1.38		[0.82, 2.32]
Attended antenatal care for study child	1.2		[0.86, 1.66]
Attended postnatal care for study child	1.4		[0.90, 2.18]
Number of live births	1.12		[0.96, 1.31]
Age at the birth of the study child, years	0.97		[0.91, 1.05]
Perceived experience of OTP programme was poor	1.3		[0.78, 2.17]
Household level			
Household size	0.97		[0.90, 1.05]
Age dependency ratio	1		[1.00, 1.00]
Female headed	1.77		[0.69, 4.54]
Household head's main work activity is not seasonal	0.77		[0.54, 1.09]
Household head has no education	1.37		[0.68, 2.75]
Unimproved sanitation	0.95		[0.54, 1.67]
Unsafe drinking water source	1.43		[0.88, 2.34]
Household in the lowest two wealth quintiles	1.05		[0.66, 1.65]
Health facility level			
OTP implementation score	0.92		[0.83, 1.03]
OTP key medicine score	1.41	**	[1.14, 1.75]
Catchment area was severely affected by …			
Drought (last 12 months)	1.62	*	[1.02, 2.57]
Floods (last 12 months)	1.37		[0.76, 2.47]
Sandstorms (last 12 months)	2.21	**	[1.35, 3.63]
Insecurity (last 12 months)	0.55	**	[0.38, 0.79]

TABLE A1 (Continued)

Covariate selection method	Cox model Theory-based	
Variable	**HR**	**CI**
Number of subjects	513	
Number of relapses	123	
Time at risk	61273	

Note: Coefficients are HRs estimated using a multivariate Cox proportional hazards regression on time-invariant covariates and excluding MUAC at admission into the OTP as a covariate (as a sensitivity check given that MUAC at admission into the OPT was missing for 11% of the sample). HRs below zero indicate a lower risk of relapse, whereas HRs above zero indicate a higher relapse risk. Significance stars correspond to *P* values in a *t*-test. Standard errors are clustered at the health facility level. Note that number of observations differ from the full sample of OTP-cured children included in the study (553) because of missing values in covariates included in the regressions. We did not perform any imputations.

Abbreviations: MUAC, mid-upper arm circumference; OTP, outpatient therapeutic programme; HR, hazard ratio; CI, confidence interval; LGA, local government area; LAZ, length-for-age *z*-score; HAZ, height-for-age *z*-score.

$^{*}P \leq 0.05$.

$^{**}P \leq 0.01$.

$^{***}P \leq 0.001$.