



Bayesian mixed effect models to account for environmental modulators of acute malnutrition treatment in children

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Received: 11 November 2024 / Revised: 14 July 2025 / Accepted: 30 July 2025
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Abstract

Acute child malnutrition is not only a global public health problem influenced not only by very diverse factors, including socioeconomic and dietary aspects, but also by seasonal and geographic factors. The present study is a secondary analysis that attempts to characterize which variables have influenced the Middle Upper-Arm Circumference (MUAC) upon admission and the Length of Stay (LOS) for treatment recovery. The sample of children analysed was 852. Initially, data cleaning and a reduction of the dimensionality of dietary diversity were carried out. A selection of the importance of the variables using the Watanabe Akaike Information Criteria (WAIC) was carried out prior to the adjustment of Bayesian mixed effects models, with the variables of travel time to health site and week of admission as random factors, on the MUAC and LOS variables. Clear differences were seen between both contexts, highlighting significant interactions of travel time in Niger while the seasonal effect stood out in Mali. The MUAC models identified a positive effect of age in both contexts, and in Niger, influences of diet diversity, comorbidities, breastfeeding and vaccination appeared. On the other hand, the LOS models highlighted the severity upon admission, and, in Niger, also factors related to the treatment protocol and the distance to the water source, while in Mali, the quality of water was more decisive. The present study shows the importance of considering acute child malnutrition from a multidimensional and complex approach, where diverse factors (biological, socioeconomic, ecological, etc.) can influence directly or as modulators of the disease and its treatment.

Handling Editor: Jorge Augusto Navarro Alberto.

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Published online: 05 September 2025

Keywords Bayesian models · Child wasting · INLA models · MUAC · Travel time · Undernutrition

1 Introduction

“Every child has the right to good nutrition. Well-nourished children grow and develop to their full potential. They are better equipped to lead healthy lives, to be free from poverty, to learn and participate, and to continue thriving across the life course, with benefits that continue over generations”. This is how the latest worldwide report on levels and trends in child malnutrition published by the United Nations Children’s Fund (UNICEF), the World Health Organization (WHO) and The Bank World (UNICEF et al. 2023) begins. One of the main messages to take into account in this report is that millions of children under five years do not achieve the aforementioned right of having a good nutrition. Of them, 45 million are affected by wasting, the form of malnutrition that poses the greatest risks to health (Black et al. 2008; McDonald et al. 2013; Thurstans et al. 2022). However, the values provided by recent cross-sectional surveys may not faithfully reflect the actual figures, which could be much higher (cumulative incidence) throughout a year (Isanaka et al. 2021; Mertens et al. 2023).

Furthermore, the anthropometric criteria for diagnosing and treating acute malnutrition have varied over the decades, with each employed indicator showing a different relationship with body composition and clinical indicators (Bhutta et al. 2017). First, weight-for-age began to be used ($< 60\%$ of a reference value), later the WHO, to avoid including children with growth retardation, established Weight-for-Height Z-score (WHZ) < -2 as a criterion (Waterlow et al. 1977), and afterwards, with the aim of simplifying the protocols, the Middle Upper-Arm Circumference (MUAC) was introduced (WHO, 2007). Currently, the WHO recognizes two well-differentiated states of severity within wasting: Moderate Acute Malnutrition (MAM) and Severe Acute Malnutrition (SAM). The latter is characterized by greater anthropometric severity: $WHZ < -3$ and/or $MUAC < 115$ mm and/or nutritional oedema (WHO, 2023).

To prevent and effectively ameliorate levels of child wasting, it is essential to know the causes and main risk factors associated with it. Although poor infant feeding practice is usually pointed out as the main determinant of nutritional status, the complex reality is that there are multiple factors that interrelate with each other and have an important impact on it. These factors include socioeconomic status, level of food insecurity, burden of comorbidities, and access to water and sanitation, among others (Rodríguez et al. 2011; Vollmer et al. 2017; van Cooten et al. 2019). A holistic point of view to understand these underlying causes allows a better approach to the problem to achieve lasting and sustainable solutions in the real world (Agostoni et al. 2023). In this sense, there are other external factors that are neither biological, nutritional, nor socioeconomic on their own but that also influence the levels of child malnutrition in a region over time. From an epidemiological point of view, environmental exposures can be broadly categorized into those that are proximate (e.g. directly leading to a health condition) and those that are distal (e.g. indirectly leading to a health condition), such as socioeconomic conditions and climate change.

Other broad-scale environmental aspects can cause adverse health conditions directly by altering proximate exposures and indirectly through changes in ecosystems and other systems related to human health (Merrill 2008). These concepts have recently been introduced into the conceptual framework of maternal and child nutrition by UNICEF (2020a).

In this sense, the aforementioned trends report also highlights that nearly 90% of all global child wasting cases are concentrated in the tropical areas of Africa and Asia (UNICEF et al. 2023). These regions experience marked periods of dry seasons and floods, which negatively affect various aspects such as agriculture, economic production, and access to drinking water (Asmall et al. 2021). A strong negative association has been documented between child weight and the average monthly variation in temperature across Sub-Saharan region, indicating a mean loss of 0.1 WHZ for every 1 °C increase (Baker and Anttila-Hughes 2020). To these annual effects, other climatic phenomena with a more stochastic occurrence are added, such as the El Niño Southern Oscillation (ENSO). Studies have highlighted that warmer conditions during ENSO are globally accompanied by an increase in the severity of child malnutrition in the tropics (Anttila-Hughes et al. 2021). Additionally, studies have shown significant associations between drought conditions and both wasting and underweight prevalence (Lieber et al. 2022).

The most recent evidence on the study of child wasting seasonality, considering 15 years of Standardized Monitoring and Assessment of Relief and Transition (SMART) surveys from 19 countries in the northern region of the African continent, points out to the existence of two wasting peaks during the year. The highest peak of prevalence is estimated to begin in April to May, coinciding with the first increase in temperatures. A second peak of wasting is observed from August to October, coinciding with the primary peak of rainfall (Venkat et al. 2023). A local study in eastern Chad also identified two annual peaks of wasting and severe wasting at the end of the dry season. The smaller peak corresponds to the start of the harvest period, with the lowest prevalence occurring during the start of the dry season (Marshak et al. 2023). This research demonstrates the importance of being cautious regarding the child wasting seasonality in a region, since the existence of a wet and dry season will not necessarily translate into a single hunger season, as has been accepted in previous scenarios (Vaitla et al. 2009; Nonterah et al. 2022).

Environmental geographic variability also directly affects the availability, access, and utilization of basic services, such as health service around the world (Weiss et al. 2018). Various studies have focussed on mapping the levels of child acute malnutrition in countries such as Ethiopia and South Africa using data from national surveys. These studies demonstrate a non-uniform distribution of its prevalence across the country, highlighting the existence of specific spatial patterns and inequalities between administrative areas that respond to different factors (Sartorius et al. 2020; Atalell et al. 2023). Moreover, a cross-country study found an association, at the population level, of a higher prevalence of wasting in rural versus urban areas in 13 countries from the East and southern African region, also relating it to socioeconomic inequalities at the household level (Caleyachetty et al. 2023).

Concerning child wasting, an aspect repeatedly identified as a barrier to accessing correct diagnosis and treatment is the distance to the health site (Puett and Guerrero

2015; Rogers et al. 2015). Consequently, some geospatial analyses in various regions have highlighted this problem and its association with the burden of wasting. In Niger, the geographic distribution of community health posts was reported as inefficient. An estimated 58.5% of its population, which is 10.4 million people predominantly living in rural areas, remained beyond a 60-min catchment of community health posts (Oliphant et al. 2021). Additionally, a geospatial coverage analysis conducted in the three largest districts of the Kayes Region in Mali revealed that there exists a high proportion of children living more than 5 km from the nearest health site, estimated at 70.4%. Moreover, a high proportion of children in rural communities were not screened for SAM, estimated at 52.2% (Charle-Cuéllar et al. 2022).

Traditionally, these analyses and studies have been based on association models typical of classical frequentist statistics. However, the complexity of the contexts being studied, the rapid and abrupt changes that occur in them, as well as the underlying interrelationships between variables require more complete approaches. In this sense, the Bayesian approach is especially interesting and has been widely used in recent studies (Sartorius et al. 2020; Adhikari et al. 2022; Atalell et al. 2023), since they provide the advantages of being able to integrate prior knowledge with the observed data and are more flexible when it comes to updating the results as more data are obtained. Additionally, they explicitly incorporate uncertainty by providing posterior probability distributions for the parameters, which facilitates decision-making, allowing risk assessment and optimization of results.

The objective of the present study is to determine, in an explanatory manner, which variables, incorporating seasonality and travel time to the treatment provider, are associated with greater severity upon admission and a longer stay in treatment for children diagnosed with acute malnutrition in rural regions of Niger and Mali, considered emergency contexts.

2 Material and methods

2.1 Study design

The present study is a secondary analysis derived from controlled trials, which aimed to test different protocols for the treatment of acute child malnutrition (6–59 months) (Charle-Cuéllar et al. 2023; Sánchez-Martínez et al. 2023; López-Ejeda et al. 2024). The intervention was carried out in the Diffa region, in Niger, during the months from December 2020 to April 2021, including a total of 6 different health sites. Meanwhile, in the Gao region, in Mali, the intervention spanned from June 2020 to June 2021, involving a total of 27 health sites. Further details regarding the spatial distribution of the considered health site are found in Figure S1. Both regions are declared emergency zones, characterized by the presence of natural disasters and armed conflicts, which has a negative impact on interventions and field studies (OCHA, 2024a; 2024b).

A three-arm cluster randomized controlled trial was applied in Mali. In the control group, children were treated by specialized health personnel in health sites, using the standard protocol approved by the Ministry of Health of Mali (Community Manage-

ment of Acute Malnutrition (CMAM) group). The first intervention group applied the same treatment protocol but added Community Health Workers (CHWs) as treatment providers in villages, at a minimum distance of 30 km from the reference health site (Integrated Community Case Management (iCCM) standard group). The second intervention group included, in a decentralized manner, both types of treatment providers (nurses and CHWs) but applied the combined-simplified protocol known as the ComPAS protocol (Bailey et al. 2020). On the other hand, a non-randomized controlled trial with only two groups was conducted in Niger, both of them including nurses and CHWs. The control group was treated under the country's standard protocol (CMAM protocol), while in the intervention group the combined-simplified ComPAS protocol was applied.

In addition to measuring anthropometric variables for diagnosing acute malnutrition (MUAC and WHZ), several information was collected, including sex and age, the presence of comorbidities (fever, vomiting, diarrhoea, malaria, acute respiratory infection), and their vaccination status. Furthermore, the present study was based on a subsample of treated children on which a socioeconomic survey was carried out. Specifically, a total of 676 families in Mali and 771 in Niger were interviewed. The socioeconomic survey was conducted by interviewing the child's caregiver at the treatment facility upon admission, covering 58 variables organized into four dimensions of living conditions: demographics (9), livelihoods (14), food security and diversity (26), and access to healthcare (9). Dietary diversity survey aimed to reflect the diversity of the diet and the frequency with which food groups were consumed in the last week as proposed by World Food Programme (WFP, 2008). After the completion of each child's treatment, information regarding the treatment outcome was also collected (recovery, default, discharge error, etc.) which then enables to select only recovered children. Only cured children were included in the present study.

2.2 Data cleaning and exploratory analyses

Data analysis was carried out using R software v. 4.3.2 (R Core Team 2023). Initially, data cleaning was performed, by considering negative numbers or values beyond four standard deviations away from the mean as transcription errors or extreme outliers, and, hence, being replaced by NA. In addition, for categorical variables, those categories showing less than five observations were either eliminated or combined with another if there was an ordinal relationship. Afterwards, missing values were handled, to reach comparable datasets for the model building step. First, variables with total missing values equal to or greater than 10% (12) were removed from the analysis, remaining a total of 46 (Table S1). Subsequently, individuals with any missing values were also removed. This procedure ensures that all participants have information on the same variables without missing values. Finally, after cleaning the data, the total sample set consisted of 413 children from Mali and 439 children from Niger with a mean age of 13.89 ± 7.07 months (Figure S2).

The dependent variables modelled were Mid-Upper-Arm Circumference (MUAC) at admission (millimetres) and Length of Stay (LOS) in treatment for recovered patients only (days), as proxies of severity and treatment effectiveness, respectively. As a temporal variable, the day of the child's admission to treatment was included,

which was later grouped into a new variable indicating the week (starting from the day of the beginning of the study of Mali in June) on which each child was admitted to treatment. Regarding the spatial variable, information is available on the travel time from the child's home to the health site where treatment was provided, grouped into 7 categories progressively increasing travel time (1: Less than 15 min, 2: 15–30 min, 3: 30–90 min, 4: 90–120 min, 5: 120–150 min, 6: 150–180 min, 7: more than 3 h). These temporal data are considered the most suitable proxy for operationalizing accessibility (Weiss et al. 2018). Initially, an exploratory analysis was conducted to examine the relationships between this set of variables in both contexts.

An initial descriptive graph was created using a locally estimated scatterplot smoothing (LOESS) function to model the relationship between the MUAC and LOS variables over time (weeks) and travel time to the health site. In this sense, Pearson correlation coefficients were calculated, stratified by key variables, to better understand the underlying interrelations and modulation effects. Following this, with the objective of reducing the dimensionality of the data, a Principal Component Analysis was conducted separately in each study region on the frequency values of the dietary diversity survey. The calculation was performed by a singular value decomposition of the centred and scaled data, retaining the first four Principal Components, which became new variables in the dataset. To interpret the relationships in the diet data, it was represented a correlation matrix along with its dendrogram, generated through a Hierarchical Cluster Analysis (HCA) using Euclidean distances as metrics.

2.3 Order of importance of the variables

Prior to modelling, the covariates were ordered based on their importance in analysing each dependent variable. For this purpose, several univariate models were built, one for each covariate and country independently. The Watanabe Akaike Information Criteria (WAIC) were then calculated for model comparison. The models with the lowest WAIC values were chosen to establish the order of importance among the covariates. Moreover, the WAIC value is considered a measure of model accuracy (Watanabe and Opper 2010). All univariate models were performed using the subsample of individuals without missing values, incorporating the temporal variable of week and the spatial variable of travel time to the health site as random effects. The models were specified with a hierarchical structure, including the health facility as a random effect, reducing residual spatial dependence, this ensured homogeneity in the information available for each model, enabling their WAIC values to be comparable.

2.4 Defining a Bayesian model

Bayesian inference is a valuable method for data modelling that allows to estimate posterior distributions of model parameters β by updating prior distributions with information from recorded observations y using Bayes' Theorem (Moraga et al. 2021):

$$\pi(\beta|y) = \frac{\pi(y|\beta)\pi(\beta)}{\pi(y)} \propto \pi(y|\beta)\pi(\beta).$$

Mixed-effects models were specifically chosen for their ability to model and incorporate complex relationships between variables, as they allow the inclusion of both linear fixed effects and random effects of different natures (Gómez-Rubio 2020).

Regarding the Bayesian parameters of the model, the prior distribution for fixed effects (regression coefficients and global intercept) was specified as Gaussian $N(0, \sigma^2)$, centred on 0, and with a large variance (minimally informative). Specifically, we set $\beta \sim N(0, \sigma^2)$ chosen to be sufficiently large to avoid imposing strong constraints on the parameter estimates. For health site variables, travel time to the health site and week of admission, we assumed nonlinear relationships with the response variable by including them in the model as random effects. To evaluate what type of random effect to implement for the temporal and travel time variables in each model, the WAIC of the possible combinations was calculated (Table S2). The priors considered included first-order and second-order random walk processes (rw1 and rw2). For the health site variable, an independent and identically distributed (iid) prior structure was used. These random walk processes are very suitable for modelling biological and natural processes, allowing a certain degree of randomness while maintaining dependence on previous values (Codling et al. 2008). Finally, the prior distribution for the precision parameters of the random effects was specified as a Half-Cauchy distribution:

$$\tau \sim \text{Half-Cauchy}(0, s),$$

where s was selected to balance regularization and flexibility. The Half-Cauchy prior yielded a better WAIC than the default multivariate Gaussian distribution with zero mean and precision matrix $\tau\Sigma$, where τ is a generic precision parameter and Σ is a matrix that defines the dependence structure of the random effects.

The statistical models specified in the present study were estimated through the Integrated Nested Laplace Approximation (INLA) approach, implemented via the open-source R-INLA package (Rue et al. 2009). INLA avoids sampling by accurately approximating posterior marginal distributions, making it an efficient alternative to Markov Chain Monte Carlo (MCMC) methods (Lindgren and Rue 2015).

Therefore, in the present study, the INLA models were fit for each variable of interest as follows:

$$\eta_i = \alpha + \sum_{j=1}^{n_\beta} \beta_j \cdot x_{ij} + \sum_{k=1}^{n_f} f^{(k)}(u_{ki}); i = 1, \dots, n$$

where η_i is the linear predictor, α is the intercept, $\beta_j x_{ij}$ are the covariate parameters and covariates, $f^{(k)}$ are the random effects terms on some covariates $\{u_k\}_{k=1}^{n_f}$, and $i = 1, \dots, n$ are the variables of interest.

The selection of the final model was carried out in a stepwise manner to optimize prediction error. Therefore, variables were introduced one by one according to the order of the lowest WAIC established previously by the univariate models. When introducing a new variable into the model, if the WAIC of this expanded

model decreased by more than three units compared to the previous one, the variable remained in the model. Otherwise, the variable was removed from the model, and the next one was tested. This procedure was repeated until two of these stepwise phases were completed to reach the final model.

3 Results

Preliminary exploratory analysis suggests that MUAC values and LOS for recovery differ across the categories of the variables of time from the health site and week of child's treatment admission. Likewise, a difference is also noticeable in the behaviour of the data in both contexts, as shown in Fig. 1. This variation between the data from Mali and Niger appears to be particularly pronounced in the LOS values, both along the travel time and for the week variable categories, with higher values recorded in individuals from Mali.

Next, to quantify the observed relationships graphically in Fig. 1, the sample set was stratified based on certain key factors (protocol, sex, age, severity, comorbidities and vaccination) that may affect the variables of interest. Table S3 shows the

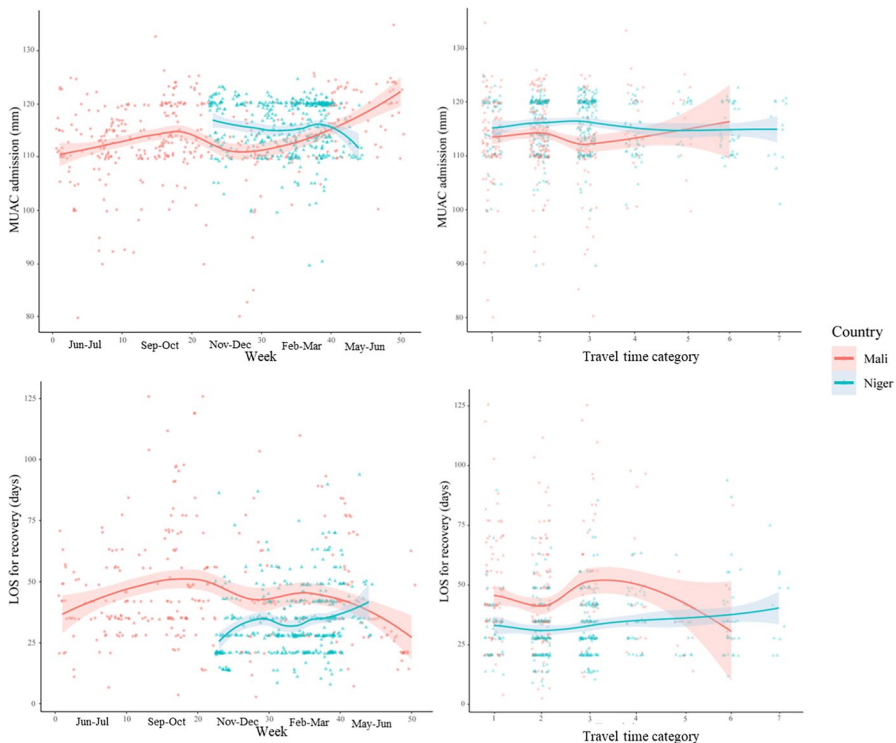


Fig. 1 Scatterplots showing the relationship between MUAC upon admission and LOS with the *Week* and *Travel time category* variables for Mali and Niger. Locally estimated scatterplot smoothing (LOESS) was applied to each country data. *MUAC* Mid-Upper-Arm Circumference, *LOS* Length of Stay

results of these correlations, and despite the limitation that only linear relationships have been evaluated, some relevant results that are worth highlighting were observed when comparing both countries and the categories of the stratification variables. In general, we observe that all the values obtained show weak linear relationships (<0.4), and in many cases, they are not significant. However, we found interesting differences between the categories of some key variables. Firstly, in Niger, we observed an initial effect of severity on the relationship established between MUAC and LOS with *Week*, such that MAM children present significant correlations while SAM do not. There is also a quite notable effect of the presence of comorbidities, with significant effects observed in individuals who presented any. On the other hand, Mali stands out compared to Niger for presenting a large number of significant correlations between the MUAC and *Week* variables. Therefore, it seems to exhibit a fairly evident temporal effect in its evolution. Likewise, we found differential relationships between groups of categories in the treatment protocol, in the degree of severity, in the presence of comorbidities and in the fact of being vaccinated or not. However, the sex and the age of the individual did not appear to have any effect, as the relationships were significant in both groups.

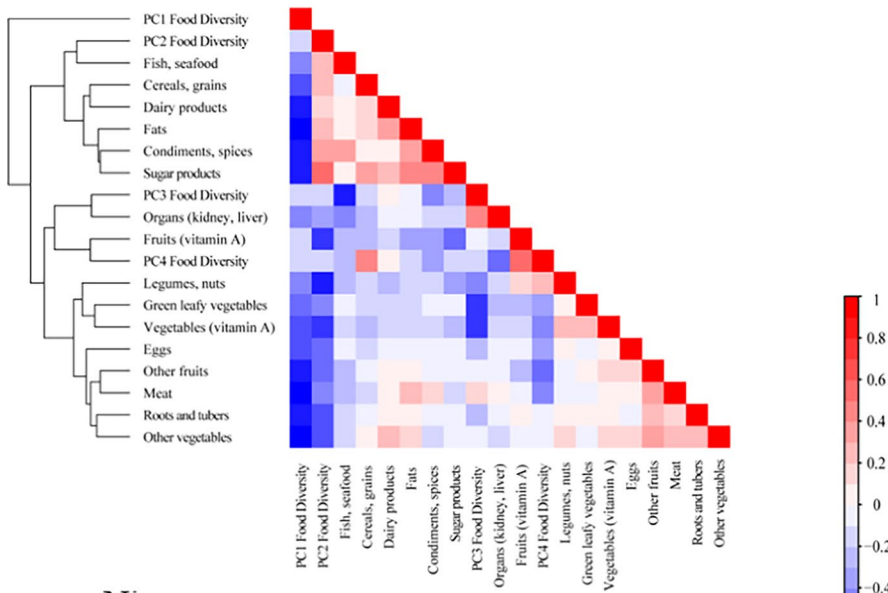
Figure 2 shows the interrelations established in Mali and Niger between the variables of food consumption frequency and each of the first four Principal Components (PC) computed with Principal Component Analysis. The correlations between all these pairs of variables were placed in a correlation matrix, and then a dendrogram was constructed, which showed relevant groups according to the dietary pattern in the population:

In Mali, a pattern in the consumption of certain foods is associated with PC2, indicating a relationship in the consumption of fish and seafood, dairy products, fats, condiments, and sugar products. On the other hand, PC3 is associated with a greater consumption of animal organs such as kidney or liver and PC4 with the consumption of cereal, legumes, nuts and fruits rich in vitamin A. Another interesting association in the dendrogram on the left margin is found with the consumption of meat, eggs, other fruits, roots and tubers, and other vegetables. Finally, it should be noted that PC1 presents negative correlations, pointing that an increase in its values would result a general reduction in the frequency of food consumption.

If we pay attention to the relationships of food consumption in Niger, we find slightly different associations. First of all, PC1 is associated with the consumption of fruits rich in vitamin A, vegetables especially rich in vitamin A, roots and tubers, and legumes. Another interesting association in the dendrogram on the left margin is found with PC2 and the consumption of fats, dairy products, sugar products, and condiments. Finally, PC3 is associated with the consumption of vegetables and fruits not rich in vitamin A and PC4 with the consumption of cereal, legumes and nuts consumption and negatively associated with the rest. A final interesting pattern indicates a group of children who have increased their protein consumption, with a higher frequency of eggs, meat, fish, seafood, animal organs, and other fruits and vegetables in their diets.

Table S4 summarizes the component loadings of each food group in each Principal Component for both Mali and Niger. This allows for a quantitative and independent

Mali



Niger

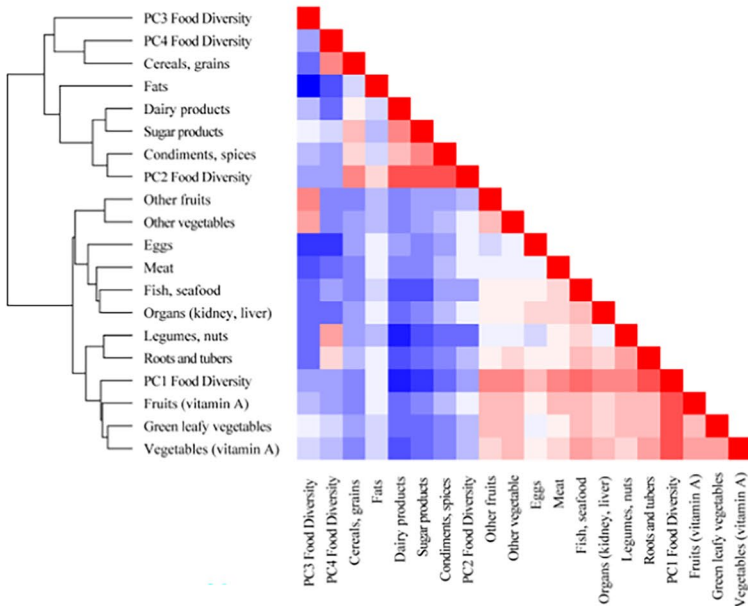


Fig. 2 Relationships between the Principal Components (PC) and the frequency variables of consumption of food groups. The side legend shows the numerical correspondence of the correlation value with a colour gradient

assessment of both the degree of influence and the direction (positive or negative) of each group on the respective Components.

3.1 Final models for MUAC

The parameters of the final models on the MUAC upon admission for Mali and Niger are presented in Table 1. The number of variables introduced in the final model for Niger was five, and this model reached a WAIC of 2617.18. On the other hand, in the case of Mali, the final model was simpler, containing two variables, with a corresponding WAIC of 2691.22. Although one variable is shared in both models, our results seem to indicate two different situations to understand the severity (MUAC) of children upon admission to treatment depending on the context.

If we pay attention to the Niger model, we find variables of different nature involved in determining the MUAC upon admission. A first group seems to be related to the health status of the individual. Presenting any comorbidity negatively affects the MUAC, modifying its values by -2.529 mm (CI: -3.657 ; -1.402). Likewise, the vaccination has a positive effect on the MUAC value, increasing it on average by 1.365 mm (CI: 0.442 ; 2.290). A second group of variables is associated with the child's diet. Firstly, breastfeeding is a quite positive factor according to the model on the MUAC value, if it is present in the child's diet, it causes the MUAC to increase on average by 3.329 mm. (CI: 1.173 ; 5.485). Furthermore, dietary diversity also seems to have an interesting effect. Since PC1 (vegetables and fruits) and PC2 (fats and dairy products) are present in the model, the first one seems to have a negative effect on the MUAC, since for each unit that increases its value, the MUAC is reduced in the individual by 0.508 mm (CI: -0.765 ; -0.252). On the other hand, the effect of the PC2 is positive on the MUAC value, so that for each unit that increases its value, the MUAC increases by 0.544 mm (CI: 0.222 ; 0.867). Another variable present in the

Table 1 Final model of MUAC upon admission in Niger and Mali: INLA posterior mean estimates (including standard deviations) and its credible intervals are presented

Country	Parameter	Mean	SD	CI
Niger	Intercept	109.713	1.788	(106.188; 113.240)
	Comorbidities Yes	-2.529	0.575	(-3.657 ; -1.402)
	Food Diversity PC1	-0.508	0.131	(-0.765 ; -0.252)
	Age Admission (months)	0.145	0.047	(0.052 ; 0.237)
	Receiving breast-feed now Yes	3.329	1.099	(1.173 ; 5.485)
	Vaccination Yes	1.365	0.471	(0.442 ; 2.290)
	Food Diversity PC2	0.544	0.164	(0.222 ; 0.867)
Mali	Intercept	107.739	1.773	(104.265; 111.219)
	Age mother pregnant (years)	0.139	0.051	(0.040 ; 0.238)
	Age Admission (months)	0.160	0.038	(0.086 ; 0.235)

PC Principal Component,
SD Standard Deviation, CI
Credible Interval

model in the case of Niger is the age of the individual, which has a positive effect on the MUAC, observing an average increase of 0.145 mm (CI: 0.052; 0.237) for each month.

Regarding the final model of MUAC upon admission in Mali, which stands out for being much simpler than the one of Niger, we can highlight the shared presence of the variable age upon admission, which acquires a very similar effect, so that for each month that the child turns, his MUAC upon admission increases by 0.160 mm (CI: 0.086; 0.235). Another variable that participates in the model is the age at which the mother began her pregnancy with the treated child, which also appears as a positive factor on the MUAC value. For each year that the mother's age increases, the child's MUAC upon admission increases on average by 0.139 mm (CI: 0.040; 0.238).

3.2 Final models for LOS

Table 2 shows the parameters of the final models of LOS for recovery in Niger and Mali. Once again, the Niger model presents a greater number of variables. It reaches a WAIC of 3269.66 with these five variables. On the other hand, the model in Mali with three variables shows a WAIC of 2952.29. In the case of the LOS for recovery variable, both the Niger and Mali models seem to identify very similar factors related to the study variable in both contexts.

In Niger (see Table 2), the protocol variable stands out with the highest value of posterior mean estimate. So, when the child is treated with the simplified protocol, its LOS is reduced by 10.849 days (CI: -13.719; -7.980) compared with the national standard protocol. Another relevant variable is that referring to the travel health site, which seems to indicate that being able to travel on the same day would have a positive effect on the shortening of the time in treatment, modifying the LOS on average by -3.726 days (CI: -7.075; -0.377). On the other hand, we found the MUAC upon admission, which reflects the severity with which the child began treatment. This last variable indicates in the model that a greater MUAC participates favourably in shortening the time in treatment, since for each millimetre that it increases, the LOS for recovery decreases by 1.061 days (CI: -1.270; -0.853). We also see how the PC4 of diet diversity intervenes to lengthen the LOS for recovery in Niger; according to the model, for each unit that increases this variable, it results in an increase in the LOS of 1.801 days (CI: 0.703; 2.899). Finally, the distance to the drinking water source also has an important influence. Being 100–300 m or 300–500 m compared to the reference category, which is less than 100 m, causes an increase in LOS of 3.756 days (CI: 0.824; 6.690) and 5.372 days (CI: 1.911; 8.835), respectively. However, for the longest distance category, the impact was not significant, possibly because of a small sample size.

The final LOS for recovery model in Mali includes very similar variables to those selected in the case of Niger. Firstly, MUAC upon admission also has a positive effect in reducing LOS for recovery, so that for each millimetre of increase, the reduction is 0.407 days (CI: -0.734; -0.078). A second variable shared in both models is the fourth Principal Component of dietary diversity, which in the case of Mali, an increase also has a negative effect on the LOS, since for each unit of increase, the LOS increases by 2.402 days. (CI: 0.321; 4.480). Analysing the loadings in Table S4, in both countries,

Table 2 Final model of LOS for recovery in Niger and Mali: INLA posterior mean estimates (including standard deviations) and its credible intervals are presented

Country	Parameter	Mean	SD	CI
Niger	Intercept	166.883	12.208	(142.934; 190.835)
	MUAC Admission (mm)	- 1.061	0.107	(- 1.270; - 0.853)
	Protocol Simplified	- 10.849	1.463	(- 13.719; - 7.980)
	Food Diversity PC4	1.801	0.560	(0.703; 2.899)
	Distance to collect water 100—300 m	3.756	1.495	(0.824; 6.690)
	Distance to collect water 300—500 m	5.372	1.764	(1.911; 8.835)
	Distance to collect water more than 500 m	1.839	2.101	(- 2.282; 5.961)
	Travel Health site one day Yes	- 3.726	1.707	(- 7.075; - 0.377)
Mali	Intercept	83.646	19.634	(45.084; 122.141)
	MUAC Admission (mm)	- 0.407	0.167	(- 0.734; - 0.078)
	Food Diversity PC4	2.402	1.060	(0.321; 4.480)
	Water supply other	7.584	11.00	(- 14.009; 29.163)
	Water supply water tanker	1.822	16.917	(- 31.372; 35.004)
	Water supply rain water	21.651	9.907	(2.207; 41.085)
	Water supply surface water	- 4.922	4.366	(- 13.494; 3.640)
	Water supply unprotected well	11.762	3.830	(4.241; 19.273)
	Water supply protected well	8.545	3.278	(2.109; 14.974)
	Water supply community tap	6.180	3.807	(- 1.293; 13.647)

MUAC Mid-Upper-Arm Circumference, *mm* millimetres, *PC* Principal Component, *SD* Standard Deviation, *CI* Credible Interval

PC4 is positively associated with the consumption of cereals, grains, roots, tubers, and legumes but negatively associated with the consumption of meat, liver, kidney, heart, fish, seafood, and eggs, indicating a dietary pattern rich in carbohydrates and low in protein. Finally, the third variable considered in the model is related to drinking water, in this case, its source. We observe how the categories of rain water, unprotected well, and protected well have an appreciable effect, compared to the reference category which is home tap, they increase the LOS for recovery, with the first of them being the most harmful since they represent an average increase of 21.651 days (CI: 2.207; 41.085), followed by unprotected well that increases LOS by 11.762 days (CI: 4.241; 19.273), and protected well by 8.545 days (CI: 2.109; 14.974), respectively.

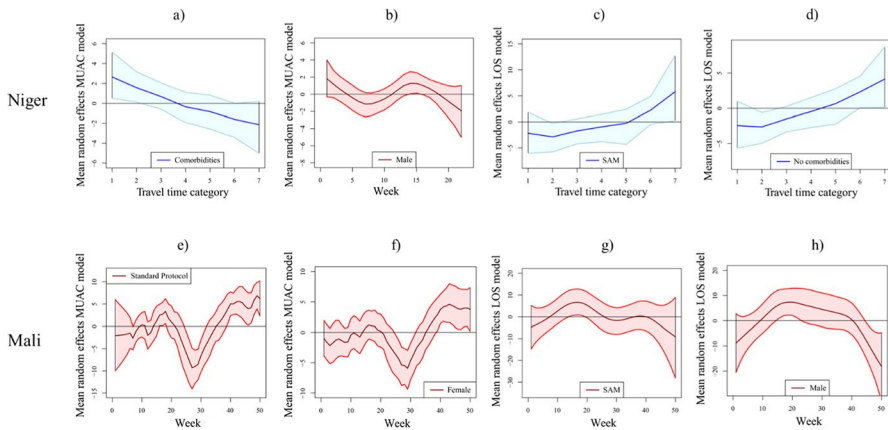


Fig. 3 Behaviour of mean random effects in different categories of interest in the final MUAC and LOS models for Mali and Niger. *MUAC* Mid-Upper-Arm Circumference, *LOS* Length of Stay, *SAM* Severe Acute Malnutrition

3.3 Interactions with random effects

Next, it is relevant to test in the final models built whether the effects of the random factors introduced are homogeneous or if, on the contrary, there are interactions. These interactions could lead to a modulation in a variable's effect, which may be interesting to interpret. Figure 3 shows a collection of graphs that reflect the interactions found between some interesting variables (protocol, the presence of comorbidities, sex, severity) with the *Week* (in red) and *Travel time* (in blue) variables, which were introduced as random effects in the final models. Tables S5-S10 provide a complete view of the numerical evolution of the mean random effects in each category.

It is worth noting that the importance that both random factors acquire in the models seems to be very different between both contexts. This fact is contrasted by the number of interactions found; while, in Niger, the interactions are mostly with the *Travel time* variable, in Mali, it is rather with the *Week* variable that we find a greater number of interactions. Therefore, while, in Niger, the factor of travel time to the health site seems to have an appreciable weight, in Mali, a more noticeable seasonal effect on the variables of interest is present.

For the interactions found in Niger, first, we highlight an effect of *Travel time* in the MUAC model upon admission of individuals who present a comorbidity at the time of their diagnosis of acute malnutrition (Fig. 3a). Thus, those individuals whose travel time to the health site is less than 15 min (category 1), see their MUAC increase on average by 2.65 mm (CI: 0.52; 5.14) compared to the rest of the individuals with a comorbidity. That is, being closer to the health site when they are sick seems to imply arriving with less severity. Nevertheless, the trend of the graph shows that the MUAC decreases when the *Travel time* increases; the confidence intervals, however, do not allow us to be really sure of this effect of increased severity. A second interaction affecting MUAC was found between *Week* and sex (Fig. 3b), indicating that boys recorded an improvement in their severity of 1.26 mm (CI: 0.05; 2.63), an effect that was not recorded in girls.

Another interesting effect observed in Niger occurs in the LOS for recovery model (Fig. 3c), where individuals diagnosed with a higher degree of severity of acute malnutrition (SAM) reduce on their LOS by an average of 2.80 days (CI: 0.23; 5.70) when they are 15–30 min from the health site (category 2), while those individuals who are at the greatest travel time category, more than 2 h from the health site, see an increase in their LOS by an average of 5.49 days (CI: 0.21; 12.67). This effect was not found among the group of treated children diagnosed with a lower severity (MAM) at the beginning of their treatment. Another interesting interaction in Niger, which corresponds to the LOS for recovery model, involves the presence of comorbidities (Fig. 3d). In this case, the behaviour of the random effects in the *Travel time categories* indicates that being 15–30 min from the health site (category 2) reduces the time in treatment in a child with no comorbidities by an average of 2.65 days (CI: 0.49; 4.97). No significant effects were found for the other *Travel time categories*, nor in any of the children with comorbidities.

Mali results show for the MUAC upon admission model, a temporal effect in the individuals who were treated with the Standard Protocol iCCM (Fig. 3e). This effect was not found in individuals treated with either the Control CMAM Protocol or the Simplified Protocol. In this graph, it can be seen that around week 18 after the start of the intervention (October), the average MUAC value upon admission declines, reaching its lowest value at week 27 (November), with an average decrease of 9.29 mm (CI: 4.91; 14.08). At this point, the trend reverses, and the value begins to increase until weeks 40–50 (April–May), where it stabilizes with an average MUAC increase of around 5 mm (CI: 3.90; 9.86) compared to the rest of the weeks. A second interaction found in the MUAC upon admission model in Mali shows a pattern very similar to the one previously described. In this case, the category involved is the female sex (Fig. 3f). It can be seen how the temporal effect on the MUAC value in the group of girls is very clear throughout the study. In such a way that by week 29, the lowest value is reached, with an average reduction in MUAC of 5.91 mm (CI: 2.95; 9.37), and from this moment, the trend of the effect reverses until week 39 (April) when the effect becomes positive, reaching the highest average value in week 43 with 4.60 mm (CI: 1.62; 8.00). This pattern of change was not found in the group of boys.

Regarding the interactions to be highlighted in the Mali model of LOS for recovery, the first of them involves the category of greatest severity (SAM) (Fig. 3g), where a temporal effect of increasing LOS for recovery was observed for boys and girls who began their treatment at weeks 15–19 (September–October), resulting in the greatest effect being about 6.34 days longer on average (CI: 0.65; 12.55). This pattern was not found in MAM individuals. However, the MAM group showed a significant decrease in LOS for recovery from week 45 (May), reaching values of up to 20 days less for LOS on average (CI: 11.55; 32.76) (Table S9). Another interaction found in the LOS for recovery model in Mali, and that combines the different behaviours of SAM and MAM children, is the one that involves in the boys (Fig. 3h). Therefore, they present a temporal effect during weeks 15–22 (September–November) of increase in LOS about 6.95 days on average (CI: 1.64; 12.50), with a subsequent decrease starting at week 45.

4 Discussion

To fully address a global public health problem as serious as acute child malnutrition, understanding its causes and the health-disease process requires a multidimensional approach. The classic models proposed by Laframboise (1973) and Lalonde (1974) point out the involvement of four main groups of health determinants: human biology, the health system, environment, and lifestyle. Following these theories, approaching and identifying these determinants of acute child malnutrition in each context, in addition to using biological (anthropometric) diagnostic criteria, will allow for a greater knowledge of the disease and increase the effectiveness of future interventions.

The final models for MUAC upon admission have shown a mixture of factors of different nature associated with the severity of the treated child, in addition to differences between the contexts of Mali and Niger. In general, the age of the individual seems to be a decisive factor in both cases, which is reflected in the WHO growth standards which show an increase in MUAC with age (WHO, 2006). Age is a key variable in humanitarian interventions, influencing diet, vaccination, and health risks. The Bayesian model confirms its importance, showing that younger children are at higher risk of severe conditions. Therefore, prioritizing their care is essential. While in the Mali model only the age of the mother is added as another determining factor in the severity of the child, it is in younger mothers where the levels of severity increase, as has been confirmed in a broader analysis that included a total of 55 low- and middle-income countries. This analysis associated a higher risk of infant mortality and poor child health outcomes with children of adolescent mothers (Finlay et al. 2011).

In the case of Niger, the final model describes a more complex reality, aiming to understand the influences on MUAC upon admission of treated children. Healthcare-related aspects such as the presence of comorbidities (diarrhoea, vomiting, acute respiratory infections (ARI)) and correct vaccination appear as determining factors. In scientific literature, the vicious circle between infectious comorbidities and acute child malnutrition is well known, mediated by a series of physiological and immune reactions in the body (Humphries et al. 2021). Vaccination is a palliative measure that can help break this vicious circle, a protective effect that has also been proven in previous studies across different scenarios (Altare et al. 2016; Ambadekar and Zodpey 2017). Strikingly, another variable that accumulated greater importance is breastfeeding. This scenario has been identified in different studies and systematic reviews as a protective factor against morbidity and mortality in the first two years of a child's life. Numerous interventions have focussed on promoting its adequate practice based on its positive effects at a nutritional and immunological level (Horta and Victora, 2013; Khan and Islam 2017). Finally, different consumption patterns in dietary diversity also appeared to be linked to MUAC upon admission. Various studies have shown that poor dietary diversity is associated with higher odds of wasting (Li et al. 2020; Aboagye et al. 2021). There are different factors such as socioeconomic level, food security, and childcare, which are related and all of which, in turn, further shape dietary intake and diversity. Moreover, another recent study better characterized this association, stating that the likelihood of wasting was 0.22 times lower for children who received minimum dietary diversity (MDD) and minimum meal frequency

(MMF) (Sheikh et al. 2020). Specifically, in our model, Food Diversity PC1, which has a negative effect on MUAC, was related to greater consumption of fruits rich in vitamin A, vegetables especially rich in vitamin A, roots and tubers, and legumes, while Food Diversity PC2, which has a positive effect, was related to greater consumption of fats, dairy products, sugar products and condiments. These very different effects, depending on the pattern, are supported by a better quality in terms of caloric density and macro- and micronutrient content of the foods included in PC2. This nutritional concept, used by quantitative indices of dietary diversity (WFP, 2008), assigns greater importance to foods such as meat, fish, and dairy products.

LOS modelling has enabled the identification of factors associated with individuals taking longer to achieve recovery, which can be very useful in prioritizing and improving their care. In both the Niger and Mali contexts, individuals with greater severity upon admission, as identified by the MUAC, presented longer LOS. The relationship between anthropometric severity upon admission and treatment outcome is widely documented (Collins et al. 2006; Dah et al. 2022). Studies such as that of Mamo et al. (2019), using another statistical approach, highlight that comorbidities and routine medicine provision are factors that impact time to recovery. Our models also reach this result, linking it through the MUAC upon admission. Another aspect associated with LOS in both contexts was related to the source of water consumption. In the case of Niger, greater distance was associated with an increase in LOS. On the other hand, in Mali, the quality of water was the most relevant variable. This highlights the great importance of having good access to a safe water source that is not only accessible but also drinkable and of high quality. Such quality water aids children in treatment to respond better to it. This deficiency in access to drinking water has been associated in numerous studies with child malnutrition (Kamiya 2011; Bitew et al. 2022). Likewise, there is a great consensus that good quality of consumed water reduces the incidence of comorbidities that impair recovery, especially diarrhoea (Bhutta et al. 2013). There is also consensus in both contexts regarding dietary diversity, as both models indicate that Food Diversity PC4 contributes to an increase in LOS. This can be explained by the negative association of this component with the consumption of eggs and meat. These animal products are energy-dense and contain multiple micronutrients such as iron, zinc, vitamin A, and vitamin B12. Their consumption is associated with improved nutritional status outcomes in observational studies (Hetherington et al. 2017; Larson et al. 2019).

The LOS values of children treated in Niger were found to be influenced by the simplified treatment protocol. This protocol stands out compared to the conventional CMAM protocol, used mostly in the country, for decentralizing treatment and bringing it closer to families and a series of simplifications in the diagnosis and management of cases (Charle-Cuéllar et al. 2023). The WHO, in its most recent guideline on the prevention and management of wasting (WHO, 2023), recognizes CHWs as an effective tool based on currently existing evidence. Different studies have demonstrated its effectiveness in improving treatment coverage, a reduction in severity upon admission and an increase in the recovery rate (Álvarez-Morán et al. 2018; Charle-Cuéllar et al. 2018; Wilunda et al. 2021). Moreover, CHWs will lead to moderate savings in terms of resources (Rogers et al. 2018; Cichon et al. 2023). The great advantage of CHWs is that they reduce the distance to treatment. With health sites

being less saturated, there is more time to treat each individual, allowing comprehensive treatment of other comorbidities such as diarrhoea, ARI, and malaria, which negatively affect severity and LOS (López-Ejeda et al. 2020). A previous study by Dougnon et al. (2021) in rural Niger also found a shorter LOS in SAM children treated by CHWs, attributing it to earlier detection of cases, as their severity was lower.

The developed models not only identify and quantify risk factors related to our variables of interest but can also be used for predictive purposes. They allow us to estimate, with a certain level of confidence, the value an individual may exhibit based on their covariates at the time of diagnosis. This capability is especially useful for predicting the LOS for recovery. In this regard, different profiles could be established to identify children at a higher risk of inadequate treatment response, and consequently, of remaining malnourished for a longer period, with adverse consequences for their health. The utility of its application in the field is evident through the detailed examples used for analysing and comparing various factors associated with each case. These examples involve crossing them with probability distributions and understanding the practicality of applying it in the field.

These models are of great interest because they incorporate the week of admission to treatment (reflecting seasonality) and travel time to the health site (reflecting accessibility to treatment) as random factors in their adjustment. This allows the incorporation of potential interactions they may have with other key factors. In Mali, a clear seasonal influence was observed, while the analyses did not indicate this in Niger, possibly due to the narrower time frame of their data. Specifically, in the case of Mali, the highest severity levels (lowest MUAC upon admission) were observed in weeks 0 and 24 of the study, coinciding with children admitted to treatment in June and November. This result aligns with a recent secondary analysis of 15 years of SMART survey data, indicating two peaks of wasting in African drylands such as Mali. The primary peak occurs in April to May, and the second peak occurs in September to October, influenced by peaks in temperature and precipitation (Venkat et al. 2023). This temporal difference with the identified prevalence peaks could respond to the time necessary for these most critical situations of food insecurity to be reflected in an increase in the severity of MUAC.

It is important to take this seasonality into account in African drylands, where production systems highly depend on climatic conditions characterized by extreme and erratic rainfall. Seasonal temperatures are consistently above 20°C and can reach as high as 40 or 50°C (Young 2020). Furthermore, considering these data will be particularly relevant in the future context of climate change, which is expected to worsen water scarcity and accelerate desertification, thereby influencing food production and nutrition security, which will amplify health challenges (Agostoni et al. 2023). In this sense, the study carried out by Baker and Anttila-Hughes (2020) estimated the effect of temperature on key child nutrition outcomes through a pooled statistical model that controlled for household and regional characteristics. They then forecasted the impact of future warming on child malnutrition levels, determining that the western Africa region would see a 37% increase in the prevalence of wasting by 2100.

The random effects models presented significant interactions within the study sample in each context. In Niger, we observed that children with comorbidities expe-

rience a reduction in their severity on admission (MUAC) if they are very close to treatment. This benefit of proximity to treatment over severity has already been evidenced in studies that included CHWs as treatment providers outside health centres closer to the communities (López-Ejeda et al. 2020; Dougnon et al. 2021). The results of our study seem to indicate that this effect could be especially important when comorbidities are present, as reducing the distance, one of the greatest barriers to accessing treatment, would lead to earlier detection and treatment of comorbidities, potentially reducing their severity upon admission. Another significant interaction detected in severity in Niger was between week and sex, with boys showing a greater MUAC compared to girls. This finding appears somewhat contradictory to the existing literature (Myatt et al. 2018; Costa et al. 2021). In a recent meta-analysis of 44 studies, Thurstans et al. (2020) demonstrated that boys are more likely to be wasted than girls (odds ratio: 1.26 [95% CI: 1.13–1.40]). This is biologically explained by the sexual differences that already exist from the first months of life, both in growth patterns and body composition, with less adipose accumulation and gain in boys (Davis et al. 2019). All of this is influenced by hormonal differences already noticeable in infants and affect their metabolism (Kiviranta et al. 2016).

Regarding the LOS in Niger, an effect of travel time was also observed in the SAM group. Those further away from treatment had a greater LOS, which is directly related to the effect already observed on MUAC in this context. This effect, reflected in the LOS, suggests that in a treatment involving weekly visits, greater distance may impact the effectiveness of treatment adherence, leading to increased missed visits, which could ultimately result in default (Hitchings et al. 2022). This same explanation can be applied to the interaction observed between *Travel time* and the non-comorbidities group, as their LOS is reduced when near treatment but increases when distant. The lack of an effect seen on LOS in the comorbidities group may be attributed to the reduced sample size.

In the context of Mali, interactions were observed in the MUAC model, with very similar behaviours, between the *Week* and the treatment protocol, and, on the other hand, between the *Week* and the sex variable. Firstly, individuals treated with the standard protocol experienced a decrease in their MUAC between weeks 20 and 30 of the study (November–December), coinciding with one of the wasting peaks identified in the literature. The very similar behaviour observed in the values of the group of girls indicates that these seasonal effects were also associated with sex, as they were not appreciated in the group of boys. Both contexts have shared an association between sex and seasonality in MUAC, with a negative effect observed only for girls, which has already been mentioned as biologically contradictory. Therefore, it is necessary to consider the possible presence of social factors related to gender in both contexts, which may explain these results. Previous studies have demonstrated this influence in Southeast Asian countries (Raj et al. 2015), wherein having more brothers increased the odds of severe wasting (AOR: 1.31 [CI= 1.11, 1.55]) for girls but not boys. This is likely due to situations of food insecurity, where there is a preference for feeding male children over female children (Biswas and Bose 2011). A recent study by Thurstans et al. (2023) indicated a greater average daily weight gain in girls. However, in many settings, the adjusted odds ratios (AORs) noted that girls were less likely to recover than boys. Likewise, a study based on big data by country

identified a strong and statistically significant association of the Gender Inequality Index with excess under-five female mortality in low-income and middle-income countries, including the Sahel region (Iqbal et al. 2018).

In terms of LOS in Mali, a seasonal effect was also detected, with the group of SAM males showing an increase in LOS in specific weeks of the study (14–23) during September to November. These findings are based on the characteristics of this specific group of individuals, as it comprises the most severe group of boys (SAM). Therefore, this increased severity is added to the already mentioned disadvantageous biological characteristics of sexual dimorphism (Davis et al. 2019). Furthermore, being admitted to treatment during this time frame means that individuals have to undergo treatment during the second wasting peak of the year identified in the Sahel drylands (Venkat et al. 2023). This period coincides with worsening food security due to increasing temperatures and reduced access to sufficient, safe, and nutritious food to meet their dietary needs, which directly affect the nutritional status of individuals, resulting in longer LOS values comparable to those recorded in our study, where some SAM boys required more than 100 days to achieve recovery. Therefore, this period is particularly critical, requiring heightened attention to the most vulnerable groups, who suffer for an extended period from severe malnutrition.

Finally, there are some issues that need to be stated as potential limitations of our approach. The most obvious is that the Niger data presented a narrower time frame and could not cover an entire year, limiting the results in correctly identifying the possible effect of seasonality on the variables of interest in this context. Another limitation would be the lack of response in some variables and the handling of missing values. In light of the results obtained, it is appropriate to highlight the need for further research, applying an integrative approach involving various biological, socioeconomic, ecological and clinical aspects related to the disease, but in different contexts from those analysed here. This responds to the requests made by international organizations regarding the need to adapt acute malnutrition treatments to the conditions and barriers existing in each context (UNICEF, 2020b; 2022). Therefore, caution is important when attempting to extrapolate the results obtained here to regions that may present very different characteristics.

5 Conclusions

The present study has quantified, using a Bayesian approach, the association of the variables with an increase in severity on admission (MUAC) and Length of stay (LOS) of children treated for acute malnutrition in two rural contexts in Niger and Mali. We showed how aspects such as seasonality and time to the treatment site can act as modulators, interacting differently among groups of individuals.

Relevant differences were shown between contexts, apart from the greater influence of seasonality in Mali and travel time to treatment in Niger. First, regarding severity, in both contexts, there was an influence of the child's age, and it was in Niger that factors such as comorbidity, dietary diversity, and breastfeeding were influential. Second, for the LOS, in both contexts, the severity of admission and dietary diversity

were relevant. In Niger, we found the distance to the water source and the protocol, but in Mali, the quality of the water source was more important.

This study highlights the importance of applying a multidisciplinary analysis to encompass various factors that may have a more or less significant influence, directly or indirectly through interactions, on child malnutrition in different contexts. This approach allows for a better understanding of the environmental factors surrounding the disease.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s10651-025-00674-6>.

Acknowledgements The authors would like to express their gratitude to all medical staff and patients who participated in this study at Niger and Mali.

Author contributions Conceptualization: LJS-M, NL-E, CLH and CF; Methodology: LJS-M and CF; Formal analysis and investigation: LJS-M and CF; Writing—original draft preparation: LJS-M; Writing—review and editing: NL-E, CLH and PC-C; Funding acquisition: NL-E and PC-C; Resources: SS, MNS, AB, MB, AAG, AS, NO and RHL; Supervision: SS, MNS, AB, MB, AAG, AS, NO and RHL.

Funding Open Access funding provided thanks to the CRUE-CSIC agreement with Springer Nature. This research project was funded by Elrha's Research for Health in Humanitarian Crisis (R2HC) programme. R2HC aims to improve health outcomes for people affected by crises by strengthening the evidence base for public health interventions. The R2HC programme is funded by the UK Foreign, Commonwealth and Development Office (FCDO), Wellcome and the UK National Institute for Health Research (NIHR). LJ S-M was granted with a predoctoral fellowship from the Complutense University and Banco Santander.

Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

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Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

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