# PREDICTIVE FACTORS OF TIME-TO-RECOVERY IN CHILDREN WITH SEVERE ACUTE MALNUTRITION TREATED IN RURAL AREA IN MALI: AN APPLICATION OF COX REGRESSION

ALE BONI MAXIME

W62/6503/2016

# A THESIS SUBMITTED AS A PARTIAL FULFILMENT FOR A MASTERS OF

## SCIENCE DEGREE IN MEDICAL STATISTICS AT THE UNIVERSITY OF

NAIROBI

December 2017

# **DECLARATION AND AUTHORSHIP**

In submitting this thesis, I declare that I am the sole author of this thesis and it contains no material previously published or written by another person except where acknowledgement has been made in the text.

I certify that the work in this thesis has not been previously submitted as part of requirements for a degree.

Boni Maxime Ale

Signed ...... Date .....

# **CERTIFICATE OF APPROVAL**

This thesis is approved for submission in partial fulfilment for the award of the degree

in Masters of Science in Medical Statistics at the University of Nairobi.

Boni Maxime Ale

Signed...... Date.....

## Supervisors

 Mrs Anne Wang'ombe, MSc Senior Lecturer School of mathematics University of Nairobi

Hangombe

Signed..... Dat

Date.....

# DEDICATION

To the Lord Jesus, in whose name all our steps are ordained.

To my father, Jules Ale, who taught me to put God first in all my enterprises; Dad you will always be my role model.

To my mother, Rachel Ali, who was a constant personal prayer covering; Mum you taught me resilience, you are my hero.

To my siblings who were constantly supporting me from childhood; I could not be there without you. You were a blessing for me.

To my fiancée, Nelly Njeri Wakaba "Foumilayo" who was a constant personal prayer covering. Since I met you, my life has never been the same. You are my cheerleader.

## ACKNOWLEDGEMENTS

I wish to thank my beautiful fiancée, Nelly Njery Wakaba "Foumilayo" who always pushes me beyond my limits. Thank you for cheering me to get this done.

To Franck Guy Ale, PhDs, my dear brother and mentor. Thank you for always showing me the way.

To my fellows Dr Andrew Mwale (Malawi), Dr Suleiman Hudu (Nigeria) and Dr Adisa Abdul Afeez (Nigeria) who were my family in Nairobi. Your company sharpened my English skills. Thank you "brothers".

To Intra ACP Academic Mobility Scheme who funded this training through Postgraduate Academic Mobility for African Physician-Scientists Project.

To my supervisor, Ann Wang'ombe. Thank you for not being just an excellent teacher

but a "mother" as well. Thank you for pushing me to finish this work.

To UNITID especially Prof. M'Imunya J. Machoki, Dr Julias Oyugi, for making it possible for us to complete the coursework and this thesis.

# **TABLE OF CONTENTS**

Declaration and authorship	 ii
Certificate of approval	 iii
Dedication	 iv
Acknowledgements	 V
Table of contents	 6-7
List of tables	 8
List of figures	 9
Abbreviations	 10
Abstract	 11
CHAPTER ONE	 12-15
INTRODUCTION	 12
Problem statement	 13
Justification	 14
Research question	 15
Hypothesis	 15
Objectives	 15
CHAPTRE TWO	 16-17
LITTERATURE REVIEW	 16-17
CHAPTER THREE	 18-21
MATERIEL AND METHODS	 18
Data source	 18

Study design and settings	 18
Study population	 18
Variables	 19
Sample size calculation	 19
Sampling	 19
Data collection and Management	 19-20
Statistical method used	 21-22
Data analysis	 23
Ethical considerations	 23
CHAPTER FOUR	 24-33
RESULTS	 24-33
Characteristics of the sample	 24
Anthropometric characteristic of	 25
children with uncomplicated SAM	
Treatment outcome of children	 25
Recovery time of children	 26-31
Multivariate analysis using Cox Model	 32-33
CHAPTER FIVE	 34-35
DISCUSSION	 34-35
STRENGTHS AND LIMITATIONS	 35
CONCLUSION	 36
RECOMMANDATIONS	 36
REFERENCES	 37-40

# LIST OF TABLES

Table1		23
Table 2	·	24
Table 3		26
Table 4	·	32

# LIST OF FIGURES

Figure 1	 25
Figure 2	 27
Figure 3	 28
Figure 4	 29
Figure 5	 30

## ABBREVIATIONS

- AHR Adjusted Hazard Ratio
- **CHW** Community Health Worker
- CI Confidence Interval
- **OTC** Outpatient Therapeutic Care
- RUTF Ready to Use Therapeutic Food
- **SAM** Severe Acute Malnutrition
- **iCCM** Integrated Community Case Management
- SQUEAC Semi Quantitative Evaluation of Access and Coverage

## ABSTRACT

**Background:** Malnutrition is a serious public health issue in Africa. West Africa has the highest prevalence of malnutrition. In Mali, access to care is a challenge in remote areas. Thus, the mortality rate of severe acute malnutrition (SAM) is high. The aim of this study was to access outcomes mainly time-to-recovery in children with uncomplicated SAM treated in traditional health facilities compared to community health workers (CHWs) management and identify its predictive factors. **Methods:** A multicentre, randomised intervention study which followed up

prospectively two groups of children between February 2015 and February 2016 in Kita. The intervention group was exposed to treatment delivered in traditional health facilities or CHWs and the control group was exposed to the treatment delivered in traditional health facilities only. Recovery time was determined using Kaplan Meier curves and compared between strata (intervention group, age group and gender). Cox proportional-hazard analysis was used to identify independent predictive factors.

**Results**: Median recovery time of the entire cohort was 42 days (95 % CI: 39–42). There was no significant difference in median time-to-recovery between control group and intervention group (p-value=0.124). After adjustment, independently significant predictive factors of recovery time were weight (AHR = 1.767, 95% CI: 1.47-2.12) and height (AHR = 0.917, 95% CI: 0.89-0.95).

**Conclusion:** Recovery rate was higher than the minimal international standard. Predictive factors of time to recovery were weight and length/height and treatment group was not found significant factor. Thus, including management of uncomplicated SAM would be a good alternative to improve access to care and reduce mortality due to the disease.

**Key words**: uncomplicated severe acute malnutrition, community health workers, time-to-recovery

#### CHAPTER ONE:

#### **1.0 INTRODUCTION**

Malnutrition is a condition that results from eating a diet in which nutrients are either not enough or are too much such that the diet causes health problems (1). There are broadly two types of malnutrition: under nutrition and over nutrition. Under nutrition includes stunting which means low height for age, wasting meaning low weight for height, underweight which means low weight for age and micronutrient deficiencies which implies lack of important vitamins and minerals (2). Over nutrition implies overweight and obesity (2).

Commonly the term malnutrition refers to undernutrition. Undernutrition is a cause of nearly half of all deaths in children under 5 meaning that around 3 million of these children die every year (3). It puts children at greater risk of dying from common infections, increases the frequency and severity of such infections, and has an impact on their recovery. Undernutrition threatens the futures of more than hundred million children by compromising the development of their brains which leads to reduced performance in school and eventual poor economic productivity in the future as an adult (3,4). Therefore, undernutrition does not just affect only the health and well-being of individual children but also the strength of the whole society.

Globally, wasting or acute malnutrition (moderate and severe) affects nearly 52 million of children under 5 (3). Among these wasted children, 17 million are suffering from severe acute malnutrition (SAM) (3). Seventy - five percent (75%) of all children suffering from malnutrition live in lower- middle - income countries while only one percent (1%) live in high income countries (3).

Africa is one of the continents that bears the greatest number of malnutrition in the world after Asia (3). The joint estimate of malnutrition by UNICEF, WHO and World Bank Group reported that children affected by acute malnutrition in Sub-Saharan Africa are 14.0 million of which 4.1 million are SAM (3). These statistics show that malnutrition is a serious public health issue in Africa.

#### **1.1 Problem statement**

Western Africa has the highest prevalence of malnutrition in Africa (3) and Mali is the second largest country in West Africa after Niger. According to Mali Demographic and Health Survey V (DHS V), 13 % of children under 5 are suffering from malnutrition of which 5 % have moderate acute malnutrition (MAM) and 8% have SAM (5). Therefore, in Mali, SAM is a serious public health concern which needs to be addressed properly.

SAM is a life-threatening condition. WHO estimates suggest that SAM contributes to 1 million child deaths per year worldwide. Thus, in Africa where the prevalence of the disease is high and less than 10 per 10 000 population have access to hospital beds, the impact of SAM in children mortality is high (6, 7, 8).

Until recently the WHO recommendation was to refer SAM to hospital to receive therapeutic food together with medical care. However, due to the high mortality rate, and the advent of ready to use therapeutic food (RUTF), there is a shift on the management of this disease with the community management care model (9,10). Nevertheless, studies showed recently that the low coverage of this communitybased therapeutic care model is still a big challenge (11). Despite the significant success of this outpatient model in improving the availability of effective treatment

for uncomplicated SAM cases, recently available evidence shows that on average treatment services reach less than 40% of affected cases within their target area (11). Therefore, there is a need to improve this traditional model of care to ameliorate the survival of these children with uncomplicated SAM.

#### 1.2Justification

In multiple contexts, studies have indicated that community health workers (CHWs) can properly identify danger signs and managed correctly malaria, diarrhoea, and pneumonia (12,13,14). Several studies conducted in Africa (Malawi and Ethiopia) suggested that management of SAM using Integrated Community Case Management (iCCM) method was not inferior to other methods of management of SAM (15,16). It was also recently proved that CHWs can manage uncomplicated SAM (17,18). However, the level of standard of care delivered by the CHWs in the management of SAM is still questionable especially their capacity to correctly identify oedema (19).

In Mali's rural areas, there were CHWs network that is used to deliver iCCM package called SEC (Soins Essentielles dans la communauté) from 2012. This strategy proved to be effective in a context of limited access to care to reduce the gap in access to care by the community especially children younger than 5 years (20,21,22). The iCCM package includes timely and effective treatment of malaria, pneumonia and diarrhoea (22). The CHWs also provide screening, nutritional key advices, and referring severe malnutrition cases to the health facility for treatment (22). To provide access to care for a larger number of children in the population, the Ministry of Health of Mali and Action Against Hunger examined the impact of

incorporating the identification and early treatment of uncomplicated SAM in the iCCM package delivered by CHW by conducting a large clinical prospective multicentre cohort study between February 2015 and February 2016. From this study, they showed that the quality of management of uncomplicated SAM by CHWs was satisfactory at 79.5 % but their analysis did not evaluate recovery time from SAM and associated factors in this context (17).

# **1.3 Research questions**

Is there any difference in the recovery time between children with uncomplicated SAM treated by health facility based staffs (HFBS) and those treated in a model of care which combined CHWs and HFBS?

# 1.4 Hypothesis

There is no difference in median time of recovery from uncomplicated SAM between children treated by HFBS and those treated in a model of care which combined CHWs and HFBS?

# 1.5 Objectives

# 1.5.1 Overall objective

To assess time-to-recovery in children with uncomplicated SAM treated in rural area in Mali.

# 1.5.2 Specific objectives

- To calculate the median time of recovery of children with uncomplicated SAM treated by health facility based staffs (HFBS) and those treated in a model of care which combined CHWs and HFBS.
- 2. To determine factors associated with time-to-recovery of children with uncomplicated SAM.

#### CHAPTER TWO:

#### 2.0 LITERATURE REVIEW

Several studies have been conducted in Sub-Saharan Africa to assess the outcome of children with uncomplicated SAM treated in outpatient health facilities (23,24,25,26). Most of these reported the outcome as proportion of recovery, death and defaulters (23,24). However, very few studies considered time-to-recovery of these children and applied survival analysis methods in analysing their data (25,26). No literature was available on time to recovery and predictive factors in children with uncomplicated SAM treated by CHWs.

A retrospective cohort study was conducted in Southern Ethiopia within outpatient therapeutic care (OTC) and revealed a recovery rate at 64.9% with 95% CI (61, 68) and a length of stay at 6.8 weeks. A multivariable logistic regression was used to determine factors affecting treatment outcomes. These factors were distance from OTC, use of amoxicillin and type of malnutrition (23).

In another study conducted in Northern Ghana, 348 cases of SAM in outpatient care were enrolled the recovery proportion obtained was 33.6 % and the length of stay was 7.0  $\pm$  5.4 days. A logistic regression was used to determine factors associated with recovery rate. These factors were adherence to treatment, age between 24 and 59 months and weight gain more than 20 % (24).

A retrospective study was conducted in Northern Ethiopia within OTC to assess outcomes and determinants of SAM. Recovery rate was estimated at 83.95% and the length of stay was 6.24 days for uncomplicated SAM. Survival analysis

techniques including Kaplan-Meier curves, log rank test and Cox model were applied to determine predictive factors of treatment outcome. Factors significantly and positively associated with recovery rate were use of amoxicillin, de-worming and Plumpy'Nut. The presence of diarrhea, vomiting, negative test of appetite with Plumpy'Nut and impossibility to gain weight in 3 weeks of treatment were found to have a negative association with recovery rate (25).

Another study conducted in Southern Ethiopia conducted within OTC also treatment outcome and factors affecting time to recovery in children with SAM treated at outpatient therapeutic care program. Kaplan-Meier was used to estimate the time to recovery and Cox model to determine factors affecting time to recovery. Median times of recovery of 35 days and 49 days were reported for children with kwashiorkor and marasmus respectively. Results indicated that age, marasmus and weight gain are significant factors which could affect time to recovery of children with SAM

All these literatures did not assess the time-to-recovery of children with uncomplicated SAM treated by CHWs and factors affecting it.

# **CHAPTER THREE:**

## **3.0 MATERIALS AND METHODS**

## 3.1 Data source

This was a secondary data from a study entitled "Integrating SAM treatment into the iCCM package currently delivered by CHWs in Mali: a clinical cohort study with intervention" conducted by Action Against Hunger (Action Contre Ia Faim - ACF in French) and Ministry of Health (MOH) of Mali.

# 3.2 Study design and setting

It was a multicentre, randomised clinical cohort trial which prospectively followed up two groups of children between February 2015 and February 2016 in Kita. The intervention group was exposed to treatment delivered by CHWs and the control group was exposed to the treatment delivered in traditional health facilities.

## 3.3 Study population

All children under 5 years living in the study site who met the inclusion criteria.

## 3.3.1 Inclusion criteria

- Children between 6 and 59 months living in Kita were included.
- Children diagnosis with uncomplicated SAM with one of the criteria below:
  - Mid Upper Arm Circumference (MUAC) <115 mm</li>
  - o Bilateral oedema

- Weight/Height < -3 Z Score
- The capacity of the parents or the guard to give consent.

### 3.3.2 Exclusion criteria

Children living outside of Kita were not included.

#### 3.4 Variables

#### 3.4.1 The response variable

The dependent variable or the response is the time to recovery of the child (recovered: 1, censored: 0). Censored observations are units for which the event of interest has not yet occurred at the time data are analyzed.

#### 3.4.2 The explanatory variables

The explanatory variables or predictors which are called covariates, are those variables whose affect the time to recovery we would like to assess. For these children, the covariates we assumed to affecting time to recovery are age, gender, group of intervention, length/height, weight, MUAC on admission.

## 3.5 Sample size calculation

Assumptions made in the calculation included are type 1 error of 5%, power of 90%, median survival time of 30 days (4 weeks) for exposed and 37 days for non-exposed considering SPHERE standard (27).

The following formula was applied (28):

$$n = (z_{\alpha} + z_{\beta})^{2} [\Phi \mu_{E} + \Phi \mu_{C}] / (\mu_{E}^{-1} - \mu_{C}^{-1})^{2}$$
(1)

$$\Phi \mu_{i} = \frac{T}{\mu_{i}^{3}} / \left[ \frac{T}{\mu_{i}} - 1 + \exp\left( -\frac{T}{\mu_{i}} \right) \right], \ i = E, C$$
(2)

 $z_{\alpha/2}$  =1.96 at 95 % confidence interval (CI)

Power =1-  $\beta$  = 90 %,  $z_{\beta}$ = 1.28

E= Median time-to-recovery (survival time) in exposed group. We estimate 37 days (5 weeks) for exposed groups adding 1 week to the standard median time (27).

C= Median time-to-recovery (survival time) in non-exposed group. 30 days for control group which is the standard median time to recovery for children with uncomplicated SAM (27).

T= Total period of inclusion (365 days)

The minimal sample size n in each group was 58, adding 10 % for defaulters, then the sample size was 64 subjects in each group.

The minimal total sample size required for the two groups was 128 subjects.

#### 3.6 Sampling

Considering the geographical accessibility of the area, the population of children under 5, the competences of staff in charge of SAM in that area, the average income of the population, the stability of the population and the functionality of the communities' programs in that area, two groups of counties were preselected.

A good access to the road of certain villages, the quality of care available was considered for the selection of villages included in the study. Then two groups of primary health care (PHC) area with health facilities assumed to be comparable based on the above criteria was constituted. These were:

- Kita east group: Sebecoro, Kassaro, Guenikoro, Dafela
- Kita west group: Kobiri, Tambaga, Bougaribaya

Children were selected randomly from each group of PHC area for the follow up.

## 3.7 Data collection and management

Data collection was done using standardized questionnaires and tools:

- Questionnaire for the pilot study, the Semi Quantitative Evaluation of Access and Coverage (SQUEAC) study and self-administrated questionnaire of CHW
- Timetable journal of CHW for the estimation of time of follow up of CHW
- Check-list of case management for the quality of care
- Form of cases follow up at the entry and the exit from the nutritional program.

The data was collected by trained field workers. To ensure that each county of Kita's region participate in the study, a CHWs network was establish in the region. The training of these CHWs on the implementation of the iCCM included the management of SAM was done before the study.

Data were double-entered and verified using Microsoft Access database 2007 (Microsoft Inc., Redmond Washington), data entry errors were corrected, and data validated against the paper questionnaires to check for consistency and completeness.

## 3.8 Statistical Method used

The study focused on time to event (time-to-recovery), so the appropriate method of this study was survival analysis.

Kaplan Meier and Cox proportional hazard model were used for analysis and for model building.

## 3.8.1 Kaplan Meier estimator

Kaplan Meier estimator was used to study survival pattern and we used Log rank test to compare survival functions.

The survival pattern was presented as a Kaplan Meier plot which is a step function. It gives some indications about the shape of the survival distribution. In general, the figure shows different survivorship function depending on the number of groups compared and if one lies above another, its means that the group defined by the upper curve lived longer or have better survival experience (time-to-recovery) than the group define by the lower curve.

#### 3.8.2 Cox Proportional Hazards Model

For the multivariate analysis, we used Cox proportional hazard (PH) model to identify predictive factors of time-to-recovery. It was given by:

$$\lambda(t|z) = \lambda o e^{Z^T \beta} \qquad (3)$$

Where  $\mathbf{Z} = (Z_1, ..., Z_p)^T$  and  $\boldsymbol{\beta} = (\beta_1, ..., \beta_p)^T$ 

Z is a p x1 vector of covariate such as age, gender, weight, length/height, and other prognostic factors and  $\beta$  is p x 1 regression coefficient.

 $\lambda(t|z)$  is the expected hazard at time t,  $\lambda o$  is the baseline hazard and represent the hazard when all the predictors  $Z_1, \dots, Z_p$  are equal to zero.

Partial likelihood functions were used to estimate the parameter and partial likelihood ratio test was used to assess the significance of the coefficients.

The overall model goodness of fit was assessed with Likelihood ratio test.

#### 3.9 Data Analysis

All analysis was done using R statistical software (29).

In the first part of our analysis, we did an exploratory data analysis to have good insight in our database and check for any inconsistency and outliers. Every inconsistency, erroneous and outliers were managed, and the database was updated.

Categorical variables were generated as frequencies or percentages with their interquartile intervals and continuous variables as mean with their standard deviations. Graphs such as pie charts and/or tables were presented for percentage and frequencies and histogram and/or box plots and/or graphs for the means.

Kaplan Meier graphs were constructed to estimate time-to recovery in each group of children. These median times were compared using a log rank test.

Multivariate analysis was done using the standard Cox-model. Recovery was defined as a child with MUAC > 125 mm or with 15 % of weight gain (target weight) for two consecutive visits. Defaulters, death and transfer to impatient management was censored.

#### 3.10 Ethical consideration

The study was approved by the National Institute of Public Health Research called in french Institut National de Recherche en Santé Publique (INRSP) - Ethics and Research Committee (03/2015/CE-INRSP). Informed written consent was obtained from all parents of children included in the study. When they were not able to read, the benefits and the risks of the study before being included in the study was translated and explained to them in their local language.

## CHAPTER FOUR:

# 4.0 RESULTS

# 4.1 Characteristics of the sample

Out of 934 children followed up, 537 (57.50 %) were females and 397 (42.50 %) were males. The mean age (SD) was 14.45 ( $\pm$  8.18) months. Two hundred and thirty-five (25.16 %) children were in the control group (exposed to treatment delivered by health facility based staff) and 699 (74.84 %) were in the intervention group (exposed to treatment delivered CHWs and health facility based staff). Control and intervention groups were not statistically different in age (p-value = 0.187), and gender (p-value = 0.128) (Table 1).

**Table 1** Characteristics of children with uncomplicated SAM treated in rural area,Mali (N=934)

Characteristic	Control	Intervention	Total (N= 934)	Fisher
	(n=235)	(n=699)	Number (%)	P-value
	Number (%)	Number (%)		
Gender				
Female	125 (13.4)	412 (44.1)	537 (57.5)	0.128
Male	110 (11.8)	287 (30.7)	397 (42.5)	
Age group (months)				
[6,24]	219 (23.5)	628 (67.2)	847 (90.7)	0.187
(24,36]	15 (1.6)	58 (6.2)	73 (7.8)	
(36,59]	1 (0.1)	13 (1.4)	3 (1.5)	

#### 4.2 Anthropometric characteristic of children with uncomplicated SAM

The admission mean weight (SD) for control group was 6.48 ( $\pm$ 1.18) kg and for intervention group 6.50 ( $\pm$ 1.25) kg was not statistically different (p-value = 0.835). Also, admission mean length/height (SD) for control group 71.16 ( $\pm$  5.96) cm and for intervention group 71.16 ( $\pm$ 6.77) cm was not statistically different (p-value = 0.992). Children in the control group and intervention group were statistically different in mid upper arm circumferences (MUAC) (p-value = 0.003); with admission mean (SD) 113.71 ( $\pm$  7.16) cm for control group and 115.29 ( $\pm$  7.14) cm for intervention group (Table 2).

 Table 2 Admission anthropometric measurements of children with uncomplicated

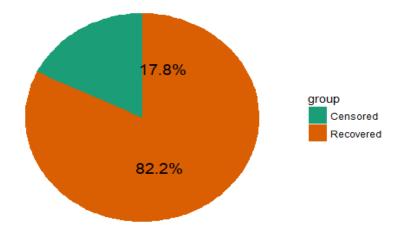
 SAM, Mali (N= 934)

Anthropometric	Control	Intervention	Total	T-test	P-
measurements	(n=235)	(n=699)	(N= 934)	value	value
(Mean (SD))					
Weight (kg)	6.48 (1.18)	6.50 (1.25)	6.50 (1.24)	-0.208	0.835
Length/Height(cm)	71.16(5.96)	71.16 (6.77)	71.16 (6.57)	-0.009	0.992
MUAC (cm)	113.71(7.16)	115.29 (7.14)	114.90(7.17)	-2.941	0.003

#### 4.3 Treatment outcome of children with uncomplicated SAM

Out of the 934 children treated, 768 (82.23 %) recovered, 7 (0.75 %) died, 51 (5.46 %) defaulted, 3 (0.32 %) non-respondent, 80 (8.56 %) transferred to inpatient center (IPC) and 20 (2.13%) transferred to other OPC.

After censoring deaths, defaulters, transfers and non-respondents, 768 (82.23 %) recovered and 166 (17.77 %) were censored (figure 1)



**Figure 1** Treatment outcomes of children with uncomplicated SAM in Mali's rural area, N= 934

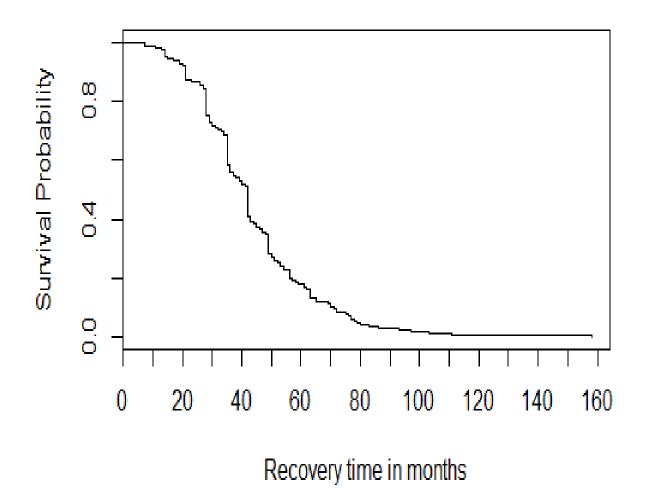
### 4.4 Recovery time of children with uncomplicated SAM

Using Kaplan Meier estimator, the median recovery time of the entire cohort was 42 days (95 % CI: 39–42) (Figure 2).

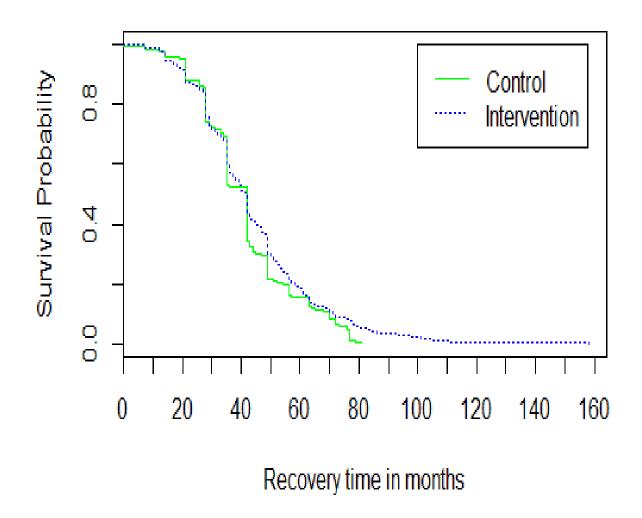
The entire cohort was stratified by group (control and intervention), gender, and age groups. The log rank test was used to compare median survival time. The analysis showed that there was no significant difference in median time recovery between control group and intervention group (p-value=0.124) (Figure 3). Time-to-recovery was also not significantly different for age groups (p-value=0.232) (Figure 4) but was significantly different for gender (p-value=0.017) (Table 3) (Figure 5).

Characteristic	Number (%)	Median recovery		Log rank	P-	
		time			value	
		Estimate	95%	6CI		
Groups						
Intervention	581 (75.65)	42	35	42	-1.54	0.123
Control	187 (24.35)	42	39	42		
Gender						
Female	440 (57.29)	42	40	42	2.40	0.015
Male	328 (42.71)	39	35	42		
Age group (months)						
[6,24]	707(92.06)	42	40	42	2.89	0.230
(24,36]	48(6.25)	35	35	42		
(36,59]	13(1.70)	29	27	50		

**Table 3** Recovery time of uncomplicated SAM children by intervention group, agegroup and gender, Mali



**Figure 2** Survival graph for overall recovery time of the entire cohort of children with uncomplicated SAM, median survival time =42 days



**Figure 3** Kaplan Meier estimate of recovery time in children with uncomplicated SAM by intervention group, Mali

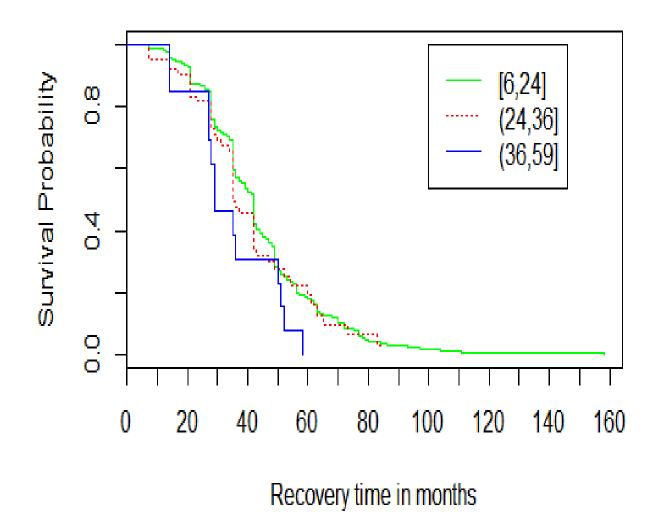


Figure 4 Kaplan Meier estimate of recovery time in children with uncomplicated SAM by age group, Mali

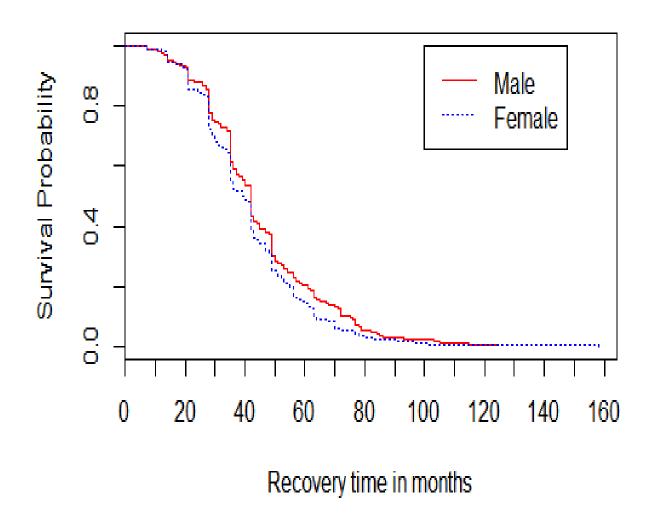


Figure 5 Kaplan Meier estimate of recovery time in children with uncomplicated SAM by gender, Mali

### 4.5 Regression using Cox Model

A Cox regression model was fitted with recovery time as outcome of interest and predictive variables were age, gender, weight, length/height, intervention group, MUAC.

After adjustment, independently significant predictive factors of time-to-recovery were weight and length/height on admission (Table 4). For every one kilogram (1 kg) of increase in weight, recovery rate increased by 76.7 % (AHR = 1.767, 95% CI: 1.47-2.12). Inversely, recovery rate decreased by 8.29 % (AHR = 0.917, 95% CI: 0.89-0.95) for every one cm of increased in length/height. The effect of group of intervention, gender, age and MUAC on the recovery rate were not statistically significant.

The overall model was highly significant (p<0.0001) (Table 4).

**Table 4** Predictive factors of time-to-recovery in children with uncomplicated SAM,Mali

Characteristic	Number (%)	Adjusted HR		P-value	
		Estimate	95%CI		
Groups					
Intervention	581 (75.65)	1			
Control	187 (24.35)	0.85	0.72 1.01	0.060	
Gender					
Male	440 (57.29)	1			
Female	328 (42.71)	1.12	0.97 1.29	0.126	
Age (months)	768(100)	1.01	1.00 1.02	0.076	
Weight (kg)	768(100)	1.76	1.47 2.12	<0.0001	
Length/Height(cm)	768(100)	0.92	0.89 0.95	<0.0001	
MUAC (cm)	768(100)	0.99	0.98 1.01	0.441	

Likelihood ratio test= 59.4 on 6 df, p<0.0001

#### CHAPTER FIVE:

#### 5.0 DISCUSSION

The results of this study inform about treatment outcome especially time to recovery of children with uncomplicated SAM treated in rural area in Mali by CHWs and in traditional health facility and factors affecting time to recovery.

The mean age of children with uncomplicated SAM was 14.45 months. Majority of children treated by CHWs and in health facility based staff were between 6-24 months.

This study revealed that recovery time of children with uncomplicated SAM treated by CHWs and health facility based staff and treated by health facility based staff was not statistically different. Recovery rate of children with uncomplicated SAM treated by CHW and health facility based staff was above the acceptable minimum standard of recovery rate 82.2 % > 75 % (27). Kabalo, M. Y. and C. N. Seifu conducted a cohort study in an African's outpatient management of SAM and found a recovery rate of 64.9% which is lower than our recovery rate (23). The length of stay of children in the same study was 6.8 weeks when our time to recovery was around 6 weeks even when children were treated by CHWs. These results were consistent with Yebyo, H. G., et al who found almost the same result in traditional OTP in a developing country (25).

This study showed that weight and length/Height were significantly affecting time to recovery of children with uncomplicated SAM. Our findings are similar to Melkamu Merid Mengesha et al. results who conducted a cohort study in OTC and used Kaplan-Meier to estimate the time to recovery and Cox models to determine predictors (26).

Thus, this study revealed that this model of care where CHWs treat uncomplicated SAM was not inferior to the traditional model of care of uncomplicated SAM.

#### STRENGTHS AND LIMITATIONS

This study is novel and original as there are very few publications about this topic. Most of the studies close to this one, were retrospective. This is a prospective study which controlled for bias and errors. We also had a very large sample size. The minimal sample size required for this analysis was 128 cases but a total of 934 participated in the study.

The fact that our study was interventional, we combined the CHWs with health facility based staff in the intervention for ethical issue because we were not 100 % sure of the capacity of the CHWs in management uncomplicated SAM at the time. This could be raised as a limitation.

#### CONCLUSION

This study showed that overall recovery rate and recovery time was above the minimum international standards. Children treated by CHWs and in traditional health facility did not have statistically different recovery rate or time to recovery. Statistically significant predictive factors were weight and length/height. The group of treatment was not significantly associated with the outcome. Therefore, we could improve access to care for children and reduced the death rate due to malnutrition in Africa by allowing CHWs to manage uncomplicated SAM.

#### RECOMMANDATIONS

The key finding of this study is that the model of care in which CHWs manage uncomplicated SAM was not inferior to the traditional model of care of uncomplicated SAM.

Therefore, heath systems in developing countries should include in the integrated community management package, the management of uncomplicated SAM.

Community health workers should be trained for that purpose.

#### REFERENCES

- 1. Malnutrition at Dorland's Medical Dictionary
- 2. Online Q&A. WHO 2017. http://www.who.int/features/qa/malnutrition/en/
- 3. UNICEF, WHO, World Bank Group joint malnutrition estimates, 2017 edit
- Leroy JL, Ruel M, Habicht JP, Frongillo EA. Linear growth deficit continues to accumulate beyond the first 1000 days in low-and middle-income countries: global evidence from 51 national surveys. The Journal of nutrition. 2014 Sep 1; 144(9):1460–6. pmid:24944283.
- ICF International, INFO-STAT (Mali), Ministry of Health (Mali), National Institute of Statistics (INSTAT) (Mali), Planning and Statistics Unit, Ministry of Health (Mali). Mali Demographic and Health Survey 2012-2013. Fairfax, United States: ICF International, 2014.
- Teferi E, Lera M, Sita S, Bogale Z, Datiko DG, Yassin MA. Treatment outcome of children with severe acute malnutrition admitted to therapeutic feeding centers in Southern Region of Ethiopia. Ethiop J Health Dev. 2010;24(3).
- Caulfield LE, de Onis M, Blössner M, Black RE. Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. Am J Clin Nutr. 2004;80(1):193–8.
- Jarso H, Workicho A, Alemseged F. Survival status and predictors of mortality in severely malnourished children admitted to Jimma University Specialized Hospital from 2010 to 2012. Jimma, Ethiopia: a retrospective longitudinal study. BMC Pediatrics.2015:15 (76).

- 9. Valid International (2006). CTC: Community based therapeutic care A field manual. www.ennonline.net/ctcfieldmanual
- 10. Community Based Management of Severe Acute Malnutirtion. Joint statement by World Health Organization/World Food Programme/United Nations System Standing Committee on Nutrition/The United Nations Children's Fund, 2007
- 11. Rogers E, Myatt M, Woodhead S, Guerrero S, Alvarez JL. Coverage of community-based management of severe acute malnutrition programmes in twenty-one countries. PloS One.2015;10(6) e0128666.
- 12. Bang AT, Bang RA, Stoll BJ, Baitule SB, Reddy HM, Deshmukh MD. Is homebased diagnosis and treatment of neonatal sepsis feasible and effective? Seven years of intervention in the Gadchiroli field trial (1996 to 2003). J Perinatol. 2005;25 Suppl 1:S62-71.
- 13. Baqui AH, Arifeen SE, Williams EK, Ahmed S, Mannan I, Rahman SM, et al. Effectiveness of home-based management of newborn infections by community health workers in rural Bangladesh. Pediatr Infect Dis J. 2009;28(4):304-10.
- 14. Darmstadt G. Validation of community health workers' assessment of neonatal illness in rural Bangladesh. Bulletin of the World Health Organization. 2009;87(1):12-9.
- 15. Linneman Z, Matilsky D, Ndekha M, Manary MJ, Maleta K, Manary MJ. A large-scale operational study of home-based therapy with ready-to-use

therapeutic food in childhood malnutrition in Malawi. Maternal & Child Nutrition. 2007;3(3):206-15.

- 16. E Amthor R, M Cole S, Manary M. The Use of Home-Based Therapy with Ready-to-Use Therapeutic Food to Treat Malnutrition in a Rural Area during a Food Crisis 2009. 464-7 p.
- 17. Alvarez Moran JL, Ale FG, Rogers E, Guerrero S. Quality of care for treatment of uncomplicated severe acute malnutrition delivered by community health workers in a rural area of Mali. Matern Child Nutr. 2017.
- 18. Puett C, Coates J, Alderman H, Sadler K. Quality of care for severe acute malnutrition delivered by community health workers in southern Bangladesh. Matern Child Nutr. 2013;9(1):130-42.
- 19. Alvarez JL, Dent N, Browne L, Myatt M, Briend A.Putting child kwashiorkor on the map.2016. Retrieved from http://www. cmamforum.org/Pool/Resources/Putting-Kwashiorkor-on-the-Map.pdf
- 20. Dawson P, Pradhan Y, Houston R, Karki S, Poudel D, Hodgins S. From research to national expansion: 20 years' experience of community-based management of childhood pneumonia in Nepal. Bulletin of the World Health Organization.2008;86(5), 339–343.
- 21. Ghebreyesus TA, Witten KH, Getachew A, O'Neill K, Bosman A, Teklehaimanot A. Community?based malaria control in Tigray, northern Ethiopia. Parassitologia.1999;41(1-3), 367-371.

- 22. de Sousa A, Tiedje KE, Recht J, Bjelic I, Hamer DH. Community case management of childhood illnesses: policy and implementation in Countdown to 2015 countries. Bull World Health Organ. 2012;90(3):183-90.
- 23. Kabalo MY, Seifu CN. Treatment outcomes of severe acute malnutrition in children treated within Outpatient Therapeutic Program (OTP) at Wolaita Zone, Southern Ethiopia: retrospective cross-sectional study. J Health Popul Nutr. 2017;36(1):7
- 24. Saaka M, Osman SM, Amponsem A, Ziem JB, Abdul-Mumin A, Akanbong P. Treatment Outcome of Severe Acute Malnutrition Cases at the Tamale Teaching Hospital. J Nutr Metab. 2015;641784.
- 25. Yebyo HG, Kendall C, Nigusse D, Lemma W. Outpatient therapeutic feeding program outcomes and determinants in treatment of severe acute malnutrition in tigray, northern ethiopia: a retrospective cohort study. PLoS One. 2013;8(6):e65840.
- 26. Merid M, Mengesha N, Balewgizie D, Sileshi T, Dessie Y. Treatment outcome and factors affecting time to recovery in children with severe acute malnutrition treated at outpatient therapeutic care program. Global Health Action. 2016;9.
- 27. SPHERE. The SPHERE humanitarian charter and minimum standards in disaster response. 3rd ed. Rugby, United Kingdom: The SPHERE Project, 2011.
- 28. Gross AJ, Clark VA. Survival distributions: reliability applications in the biomedical science. New York: Wiley; 1975.

29.R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2016. URL https://www.R-project.org/.