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Noma in northwest Nigeria: a neglected disease in neglected populations

by

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Abstract

Background

Noma, also known as cancrum oris, is a gangrenous infection of the oral cavity, which causes widespread orofacial destruction. If untreated, noma has a reported 90% mortality rate within weeks after the onset of first symptoms. Noma progresses through distinct stages defined by the World Health Organisation (WHO); Stage 0: simple gingivitis; Stage 1: acute necrotizing gingivitis; Stage 2: oedema; Stage 3: gangrene; Stage 4: scarring. Stage 5: sequelae. It is unclear how many patients with the early stages of noma will progress to the later stages of disease. Treatment in the early reversible stages with antibiotics, wound debridement and nutritional support greatly reduces morbidity and mortality. Acute noma is most often reported in children aged between two and five years. Many patients who survive the acute stages of the disease suffer into adulthood with disfigurement and disability of varying degrees. Noma is thought to be most prevalent in developing countries in Africa and Asia. Estimates for noma prevalence and incidence vary. In 1998, the WHO estimated an annual incidence of 140,000 cases of acute noma and 770,000 noma survivors living with sequelae. Two Nigerian studies estimated the burden of disease ranged from seven cases per 1,000 children aged between one and 16 years (2003) to 6.4 per 1,000 children (2003). A study from 2019 estimated the period prevalence of noma from 2010 to 2018 was 1.6 per 100,000 population at risk in Nigeria. These estimates are based on expert opinion, number of hospital admissions and retrospectively collected hospital-based data and it is unclear which stages of noma were included. Risk factors for the disease include poor oral hygiene, malnutrition, co-morbidities and low socioeconomic status. Despite its ancient history (reported by Hippocrates (460 - 370 BC)), noma-related literature remains mainly confined to case reports and case series.

By employing both qualitative and quantitative methods, we sought to examine the biopsychosocial features of noma, its epidemiology and treatment in northwest Nigeria in order to inform advocacy

and prevention efforts. The three overarching objectives to fulfil this aim were to assess the distribution of noma among children in northwest Nigeria; identify factors associated with noma (including factors influencing health-seeking behaviour and risk factors for the development of noma) and gain an understanding of the biomedical and non-biomedical care provided to noma patients in this setting. The knowledge gained through this thesis will support the assessment of the need for advocacy around noma, effective resource allocation and the planning of intervention strategies.

Methods

We conducted a scoping literature review, three quantitative studies (risk factors, outcomes, prevalence) and two qualitative studies (language and beliefs and traditional healing practices) in northwest Nigeria. Data were collected from patient caretakers at the Noma Children's Hospital, hospital staff, children and traditional healers in villages within Sokoto and Kebbi States. Data collection methods included quantitative surveys, oral screenings, anthropometric measurements, quality of life questionnaires, qualitative in-depth interviews and focus group discussions. Consenting adult respondents answered questionnaires and participated in interviews, and where applicable, data was collected from assenting children. Quantitative analyses included descriptive statistics as well as univariable and multivariable risk factor analyses. Qualitative data was manually coded and analysed thematically.

Findings

We included 74 cases (noma patients presenting at the hospital in the year preceding data collection) and 222 controls (both median age of five years (inter-quartile range 3, 15 years)) in the risk factor study. Vaccination coverage for polio and measles was below 7% in both cases and controls. The multivariable analysis identified the child being fed pap every day (adjusted odds ratio (aOR) 9.8;

95% confidence interval (CI 1.5, 62.7) as a risk factor. The mother being the primary caretaker (aOR 0.08; CI 0.01, 0.5) and the caretaker being married (aOR 0.006; CI 0.0006, 0.5) were protective factors.

Of the 37 patients with noma sequelae included in the outcomes study, 21 (56.8%) were male and 22 (62.9%) were aged six years or older. Fifteen patients (40.5%) had two to three surgeries. The most frequently used surgical procedure was a deltopectoral flap (n=16 patients; 43.2%). Trismus was released in 12 patients (32.4%), of these; none had a normal mouth opening at the follow-up visit. Despite this finding, all respondents reported that the surgery had improved their quality of life.

In the cross-sectional study assessing the prevalence of all stages of noma, we included 3,499 households and 7,122 children aged <15 years; 4,239 (59.8%) were aged 0 to 5 years. Simple gingivitis was identified in 3.1% (n=181; CI 2.6-3.8), acute necrotizing gingivitis in 0.1% (n=10; CI 0.1-0.3), and oedema in 0.05% (n=3; CI 0.02-0.2). No cases of late-stage noma were detected.

Naming of the disease differed between caretakers and healthcare workers in the language and beliefs study. Beliefs about the causes of noma were varied (spirits, animals, insects, previous infections). Noma patient caretakers spoke of the mental health strain due to stigmatization as a key issue. Difficulty in accessing care was evident. A lack of trust in the health system was mentioned as a barrier to care.

Traditional healers offered specialised forms of care for specific conditions and referral guidance. They viewed the stages of noma as different conditions with individualised remedies and were willing to refer noma patients. Caretakers trusted traditional healers.

Conclusion

Social conditions and childhood feeding practices are associated with the occurrence of noma in northwest Nigeria. This thesis has shown that following their last surgical intervention, noma patients do experience some improvements in their quality of life, but continue to face functional challenges that inhibit their daily life. We found many, widely distributed, early-stage noma cases in northwest Nigeria indicating a large population at risk of progressing to the later stages of disease. Caretaker and practitioner perspectives may enlighten efforts to improve case finding, and to understand barriers to accessing health care. Differences in disease naming illustrated the difference in beliefs about the disease. Traditional healers could play a crucial role in the early detection of noma and the health-seeking decision-making process of patients. Intervention programmes should include traditional healers through training and referral partnerships.

In conclusion, this thesis provides a unique view of the biopsychosocial features, epidemiology and treatment options for noma in northwest Nigeria. Noma is a disease, which is indicative of a weak health system and socio-economic environments of extreme deprivation. Intervention programmes should include widespread health system improvements that could address a host of risk factors for noma, and simultaneously other childhood diseases. These include increasing access to quality health care (including vaccinations), ensuring effective referral mechanisms, predominantly in rural areas, and the creation of a robust surveillance network. Health financing initiatives would need to be paired with these improvements. Nutritional programs aimed at caretakers of young children and community-based oral health initiatives could be effective mechanisms to curb the number of noma cases. Awareness-building initiatives targeting healthcare workers and community members are necessary to improve the detection and timely management of noma in endemic settings.

The combined findings of this thesis highlight the neglected nature of noma and make a strong case for placing noma on the WHO neglected tropical diseases list. This initiative could foster awareness among policy-makers and governments and direct much needed funding to facilitate further research, surveillance and targeted health interventions that would contribute to the eradication of noma.

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Thank you to my mentor Annick who took me under her wing from thousands of kilometres away, and since that one e-mail exchange in 2016, has completely transformed my life. This thesis is as much yours as it is mine. You have taught me to be patient, resilient and hardworking. I will forever be grateful for the opportunities you have granted to me. Thank you for showing me compassion during the difficult times, and for always demanding the best from me. I will always look up to you and will cherish the lessons you have taught me.

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This thesis is dedicated to my family. Thank you to my husband Paul for always being interested in my work and for understanding my long absences, thank you for making me smile each day. Thank you to my mum who has, throughout my life, been a strong source of support, who taught me to be compassionate and to always have a dream to work towards. To the baby we lost during this process, you are with me each day. To my dad who would have so enjoyed being a part of this journey, I miss you dearly.

Preface

This thesis is presented in fulfilment of the requirements for the degree of Doctor of Philosophy in the Division of Public Health Medicine, School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town. The work included in this thesis is original research and has not, in whole or in part, been submitted for another degree at this or any other university. The contents of this thesis are entirely the work of the candidate, or, in the case of multi-authored published papers, constitutes work for which the candidate was the lead author. This thesis includes published manuscripts, as per general provision 6.7 in the General Rules for the Degree of Doctor of Philosophy of the University of Cape Town.

I confirm that I have been granted permission by the University of Cape Town's Doctoral Degrees Board to include the following publications in my PhD thesis, and where co-authorships are involved, my co-authors have agreed that I may include the publications. The following manuscripts are included in the thesis and are presented as self-contained chapters in the following order:

1. Language and beliefs in relation to noma: a qualitative study, northwest Nigeria. Farley E, Lenglet A, Abubakar A, Bil K, Fotso A, Oluyide B, Tirima S, Mehta U, Stringer B.
   Published in PLoS Neglected Tropical Diseases in 2020.
   https://doi.org/10.1371/journal.pntd.00067972

2. Risk factors for diagnosed noma in northwest Nigeria: A case-control study, 2017. Farley E, Lenglet A, Ariti C, Jiya NM, Adetunji AS, van der Kam S, Bil K.
   Published in PLoS Neglected Tropical Diseases in 2018.
   https://doi.org/10.1371/journal.pntd.0006631

3. ‘I treat it but I don’t know what this disease is’: a qualitative study on noma (cancrum oris) and traditional healing in northwest Nigeria. Farley E, Bala HM, Lenglet A, Mehta U, Abubakar N, Samuel J, de Jong A, Bil K, Oluyide B, Fotso A, Stringer B, Cuesta JG, Venables E.
   Published in International Health in 2019. https://doi.org/10.1093/inthealth/ihz066

4. Outcomes at 18 months of 37 noma (cancrum oris) cases surgically treated at the Noma Children’s Hospital, Sokoto, Nigeria. Farley E, Amirtharajah M, Winters R, Taiwo A, Oyemakinde M, Fotso A, Torhee L, Mehta U, Bil K, Lenglet A.
   Published in Transactions of the Royal Society of Tropical Medicine and Hygiene in 2020. https://doi:10.1093/trstmh/traa061

5. Prevalence of noma in northwest Nigeria: cross -sectional study. Farley E, Juliana O, Schuurmans J, Ariti C, Saleh F, Uzoigwe G, Bil K, Oluyide B, Fotso A, Amirtharajah M, Vynke J, Brechard R, Adetunji A, Ritmeijer K, van der Kam S, Baratti-Mayer D, Mehta U, Isah S, Ihekweazu C, Lenglet A.
   Published in BMJ Global Health in 2020. https://doi:10.1136/bmjgh-2019-002141

All analyses are based on data collected as part of ongoing MSF operational research on noma. The candidate was employed as an epidemiologist with MSF working on this project from 2017 (and is still working in this role for the organisation). The PhD candidate, in consultation with her supervisors, developed the independent concepts for the projects presented in this PhD theses. The candidate was the lead author on all protocols, led data collection teams in Nigeria, prepared the datasets for analysis, conducted all analyses, and was the lead author of the manuscripts. Co-authors reviewed and approved the manuscripts and the PhD candidate reviewed co-author

comments and integrated them into the manuscripts prior to submission. The contribution of the candidate to each manuscript is outlined at the start of each chapter.

The candidate had three supervisors, two from UCT (primary UCT supervisor Dr Ushma Mehta, UCT co-supervisor Associate Professor Mary-Ann Davies) and an MSF supervisor (Annick Lenglet). Dr Mehta provided oversight of the UCT PhD process and critical input on the overall design of the thesis. Dr Mehta worked closely with the candidate and provided critical review on the introductory, literature review, risk factors and concluding chapters. Dr Mehta is a co-author for the language and beliefs, outcomes, traditional healing and prevalence manuscripts. Associate Professor Davies provided oversight of the UCT PhD process, critical input on the overall design of the thesis and on the introductory, literature review and concluding chapters as well as critical review of all the manuscripts with a particular focus on the prevalence and outcomes chapters. Ms Lenglet played a critical role in all aspects of the thesis, from the protocol development for the individual MSF studies, through the implementation phase (with in the field support), and provided continual input on the analysis and write-up of each of the chapters. Ms Lenglet provided critical review on the introductory, literature review and concluding chapters and is a co-author on all publications.

The candidate's primary supervisor has confirmed to the University of Cape Town Doctoral Degrees Board that the included papers all overwhelmingly reflect the candidate's own scientific work.

Student name: Elise Sarah Farley Student number: FRLELI001

Signed: Signed by candidate

List of Abbreviations

aOR	Adjusted odds ratio
ASA	American society of anaesthesiologists
BMI	Body mass index
C	Caretaker
CI	95% confidence interval
cm	Centimetre
DEFF	Design effect
ERB	Ethical review board
FGD	Focus group discussions
GAM	Global acute malnutrition
Hb	Haemoglobin
HIV	Human immunodeficiency virus
IDI	In-depth interviews
IQR	Interquartile ranges
Kg	Kilogram
MSF	Médecins Sans Frontières
MUAC	Mid-upper arm circumference
mm	Millimetre
MAM	Moderate acute malnutrition
NA	Not applicable
NTD	Neglected tropical disease
NCH	Noma Children's Hospital

NOITULP	Nose, outer lining, inner lining, trismus, upper lip, lower lip, particularities
OR	Odds ratio
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
SAM	Severe acute malnutrition
SD	Standard deviation
SMART	Standardized monitoring and assessment of relief and transition
TH	Traditional healer
UCT	University of Cape Town
UDUTH	Usmanu Danfodiyo University Teaching Hospital
USD	United States dollars
WHZ	Weight-for-height Z score
WHO	World Health Organisation

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Chapter 1 Introduction

1.1 Background

Noma, also known as cancrum oris is a gangrenous infection of the oral cavity which causes rapid, widespread orofacial destruction [1]. If untreated, death usually occurs within weeks after the onset of first symptoms [1, 2]. Treatment with antibiotics, wound debridement, and nutritional support in the early reversible stages of the disease greatly reduces mortality and morbidity [2]. Noma occurs mainly in children aged between two and five years [1]. Those who survive often have severe facial disfigurements and multiple functional impairments including difficulties eating, seeing, and breathing, contributing towards stigmatization [2]. For those who survive the acute stages of infection, the defect heals with contractures, resulting in various degrees of disfigurement that change with time as the child grows and teeth erupt. Extensive reconstructive surgery can provide substantial cosmetic improvement and assist with regaining functionality, although long-term functional benefits may be limited [3–6].

Noma is a biological indicator of extreme poverty, severe malnutrition, unsafe drinking water, poor sanitation, poor oral hygiene practices, high infant mortality, limited access to quality health care, low childhood vaccination rates [2] and comorbidities such as measles [7, 8] and human immunodeficiency virus (HIV) [9–18].

In 1998, the World Health Organisation (WHO) estimated that 140,000 new cases of noma occur each year globally and that 770,000 patients were living with noma sequelae at that time [19]. Noma is most prevalent in low socioeconomic settings [2]. The majority of cases are currently reported in Africa [3, 7, 16, 18, 20–23] and Asia [21, 24–32]. However, over the past

15 years, there have been sporadic reports of cases originating and being treated in Turkey [33], Afghanistan [34], Italy [35], the United Kingdom [36] and the United States [11].

Many of the noma cases reported in the 1900's and 2000's were from Nigeria [7, 23, 25, 37–43]. The Noma Children's Hospital (NCH) in Sokoto, northwest Nigeria (Figure 1.1) is run by the Nigerian Ministry of Health and has been providing treatment for noma patients for many years. Since 2014, Médecins Sans Frontières (MSF) has supported noma initiatives at the hospital. Conditions other than noma (cleft lip and palate, burns and a range of ophthalmological conditions) are treated at the NCH by Nigerian Ministry of Health teams. Programmes offered specifically for noma patients include: clinical treatment for acute cases, nutritional support, counselling for patients and family members, surgical interventions performed four times a year, outreach training for health workers and community members and active case finding. Since 2014, 476 noma patients have been admitted and treated at the NCH. Four times a year, an MSF volunteer team comprising of approximately six health professionals including plastic and maxillofacial surgeons, anaesthetists and nurses, travel to Sokoto to participate in surgical interventions. Approximately 20 patients are operated on over a period of two weeks. During the intervening periods, patients are cared for by two Ministry of Health doctors, a team of nurses (Ministry of Health and MSF staff), mental health professionals (MSF staff) a nutrition team (Ministry of Health and MSF staff) and a physiotherapist (MSF staff). Spending time at the hospital allows patients and caretakers to meet and interact with one another, and the mental health team facilitate group discussions that provide a further layer of peer based support. There is no cost to noma patients for in-hospital medical care, surgery, medications or food during the duration of stay. Transport costs for noma patients are reimbursed once they arrive at the hospital. An adult caretaker stays with paediatric patients. This would incur additional direct costs for the caretaker (time

Figure 1. 1 Insert map of Africa indicating Nigeria (green). Larger map of Nigeria showing Sokoto and Kebbi States northwest Nigeria (orange) and NCH (red circle).

away from other children, home and/or job) which are not covered by the MSF and Ministry of Health partnership. On top of these direct costs, there are indirect costs that can affect the whole family such as stigma, discrimination and mental health difficulties. The MSF team offer mental health support for patients and caretakers at the hospital and attempt to decrease stigma and discrimination at a community level through the awareness raising initiatives run by the outreach team. The combined Ministry of Health and MSF outreach team operate in Sokoto and Kebbi States and visit approximately 30 villages each month where they conduct active noma case finding, awareness raising (with community members, leaders and health care workers), defaulter tracing (those who have missed their most recent appointment at the hospital) and follow-up with previously operated noma patients. Patients are referred to the NCH via contacts made by the outreach team, and by other health facilities in northwest Nigeria. The studies that form a part of this thesis were run by MSF study teams based at the NCH.

1.2 Rationale

As a neglected disease, little is known or understood about noma despite the fact that it has catastrophic outcomes including high mortality rates and is debilitating and disfiguring in a vulnerable paediatric population. The knowledge gained through this thesis will support the:

- Assessment of the need for advocacy around noma and to support such advocacy efforts if needed,
- Effective and efficient resource allocation by policy-makers towards eradicating this neglected disease and;
- The planning of intervention strategies aimed at improving both prevention and management of noma.

As the thesis was carried out with the full support and collaboration of key role-players including MSF, the network of noma organisations and the Nigerian Ministry of Health, it is anticipated to have a meaningful impact on the prevention and management programmes of this devastating condition.

1.3 Aims and objectives

1.3.1 Aim

By employing both qualitative and quantitative methods, we sought to examine biopsychosocial features of noma, its epidemiology and treatment in northwest Nigeria in order to inform advocacy and prevention efforts.

1.3.2 Specific objectives

1. To assess the distribution of noma among children in Sokoto and Kebbi States, northwest Nigeria.
2. To identify factors associated with noma in this setting, including factors influencing health-seeking behaviour and risk factors for the development of noma.
3. To gain an understanding of the biomedical and non-biomedical care provided to noma patients in this setting.

1.4 Conceptual framework

This thesis is based on a socioecological framework of factors associated with noma. The risk of acquisition, clinical progression and health outcomes of noma are shaped by a web of inter-related factors. This is perhaps more relevant in the case of diseases that disproportionately affect the world's poorest children. Health decisions made by individuals are influenced by circumstances, local beliefs, cultural norms as well as political and economic conditions [44].

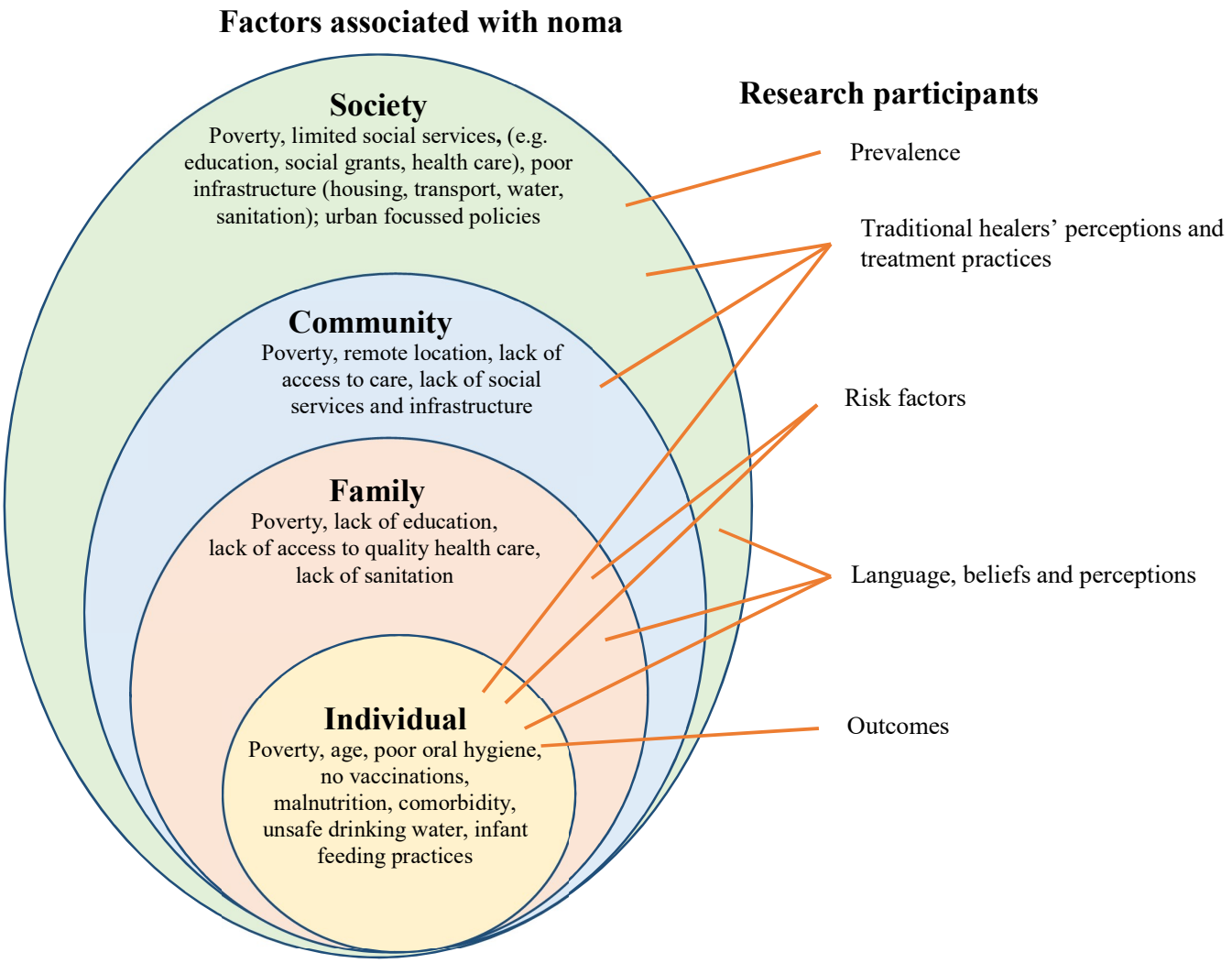
Socioecological frameworks have been utilised in other public health studies [44–48] to illustrate the complexities and the webs within which these individuals live. Socioecological frameworks are illustrated with overlapping concentric circles to show how the individuals' behaviours, decisions and health outcomes are nested in different layers of social organisation [44].

The noma socioecological framework (Figure 1.2), developed for the thesis, was based on frameworks used in previous public health studies [45, 47, 48]. This framework illustrates how this thesis will explore the interplay between individual, family, community and societal factors. Noma has been associated with factors within each layer of this framework as illustrated in the Figure 1.2. This framework was utilised during the planning of the thesis and as a result, participants in each layer of the framework including the individual (case control, outcomes, qualitative studies), the family (case control, language and beliefs study), community (traditional healer study) and society (qualitative and prevalence studies) were included. By utilising this socioecological framework, we have been able to better understand the complex interplay between individual, familial, community and societal factors that influence the causes and consequences of noma.

1.5 Overall structure of the thesis

The dissertation includes this introductory chapter that contextualises the dissertation; a review of the available literature on noma up to January 2019; five chapters based on manuscripts from studies that involve the collection and analysis of primary data (two qualitative and three quantitative – one descriptive and two analytical) and a concluding chapter which synthesises and highlights the major findings across the thesis, and outlines the recommendations that stem from the findings of the thesis. Due to the paucity in noma

Figure 1. 2 Conceptual framework.



literature, the studies included in this thesis are necessarily diverse and some are descriptive in nature.

Chapter 2 presents a scoping review of the literature on noma and provides information on noma's pathology, clinical progression, the history and epidemiology of the disease, the known risk factors for the development of noma, aetiology, therapeutic management and outcomes including mortality.

Chapter 3 describes an exploratory qualitative study aimed at improving our understanding of the local concepts (language and beliefs) of noma amongst health care workers at the NCH and caretakers of noma patients. The development of the question guides for this chapter were based on the findings from the scoping literature review.

Chapter 4 presents an analysis of risk factors for diagnosed noma in northwest Nigeria. The need to assess risk factors for noma and the development of the questionnaire for this chapter were based on the findings from the scoping literature review. The language around disease naming used in the questionnaire was based on the findings from Chapter 3.

Chapter 5 describes the demographic characteristics, surgeries performed, complications seen and the longer-term follow-up status of a cohort of patients from the NCH. The need to assess noma patient outcomes and the development of the questionnaire for this chapter were based on the findings from the scoping literature review. The language around disease naming used in the questionnaire was based on the findings from Chapter 3.

Chapter 6 explores traditional healers' perceptions of noma. This manuscript offered insight into the pluralistic nature of the Nigerian health system, with a specific focus on the role of traditional healers' in the pathway to care for noma patients. The topic for this chapter was derived from the findings of the scoping literature review which showed there was no research on the role of traditional healers in noma care as well as Chapter 3 and Chapter 4 in which patients mentioned visiting traditional healers or taking traditional treatments. The language around disease naming used in the questionnaire was based on the findings from Chapter 3.

Chapter 7 enumerates the burden of disease in Sokoto and Kebbi States by conducting a point prevalence study among children. The findings of the scoping literature review indicated the need for further enumeration of the burden of disease, which was the foundational idea of this chapter. The language around disease naming used in the questionnaire was based on the findings from Chapter 3. The risk factors identified in Chapter 4 were included in this questionnaire.

Objective 1 was fulfilled in Chapters 2 and 7. Objective 2 was achieved in Chapters 2, 3, 4, 6 and 7. Objective 3 was addressed in Chapters 2, 5, and 6 (Table 1.1).

1.6 Data source

All data for the thesis was collected as part of continuing operational research that MSF is conducting to support its noma programmes. Noma is a challenging disease to study due to the remote location of patients, the stigma and isolation of the patients, a lack of robust surveillance, difficulties accessing healthcare and healthcare workers lack of knowledge about the disease [2, 49]. These issues place MSF in a unique position to study noma due to

Table 1. 1 Objectives met in each chapter of the thesis.

Objective	Ch	Manuscript title and publication status	Data source/ MSF study
Objective 1: To assess the distribution of noma among children in Sokoto and Kebbi States, northwest Nigeria	Ch 2	**Title:** Scoping literature review **Status:** Not for publication	NA
	Ch 7	**Title:** Prevalence of noma in northwest Nigeria: cross-sectional study **Status:** Published in BMJ Global Health	MSF study 4
Objective 2: To identify factors associated with noma in this setting, including factors influencing health-seeking behaviour and risk factors for the development of noma.	Ch 2	**Title:** Scoping literature review **Status:** Not for publication	NA
	Ch 3	**Title:** Language and beliefs in relation to noma: a qualitative study, northwest Nigeria. **Status:** Published in PLoS Neglected Tropical Diseases	MSF study 1
	Ch 4	**Title:** Risk factors for diagnosed noma in northwest Nigeria: A case-control study, 2017 **Status:** Published in PLoS Neglected Tropical Diseases	MSF study 1
	Ch 6	**Title:** 'I treat it but I don't know what this disease is': a qualitative study on noma (cancrum oris) and traditional healing in northwest Nigeria **Status:** Published in Transactions of the Royal Society of Tropical Medicine and Hygiene	MSF study 2
	Ch 7	**Title:** Prevalence of noma in northwest Nigeria: cross-sectional study **Status:** Published in BMJ Global Health	MSF study 4
Objective 3: To gain an understanding of the biomedical and non-biomedical care provided to noma patients in this setting.	Ch 2	**Title:** Scoping literature review **Status:** Not for publication	NA
	Ch 5	**Title:** Outcomes at 18 months of 37 noma (cancrum oris) cases surgically treated at the Noma Children's Hospital, Sokoto, Nigeria. **Status:** Published in Transactions of the Royal Society of Tropical Medicine and Hygiene	MSF study 3
	Ch 6	**Title:** 'I treat it but I don't know what this disease is': a qualitative study on noma (cancrum oris) and traditional healing in northwest Nigeria **Status:** Published in International Health	MSF study 2

continual access to noma patients through its support to the NCH. MSF believe that research is essential to improve the effectiveness of humanitarian aid programmes, and that publishing research forms a vital part of advocacy on behalf of the populations that the organisation assists. As such, the organization is committed to conducting operational research, endeavouring to add to the scant body of knowledge around noma.

The aims of the operational research studies were to guide evidence-based policy and practices with local and international stakeholders. The operational research studies were structured around the main gaps in knowledge and the MSF noma project needs, to enable evidence-based decision-making.

The data included in this thesis were drawn from four operational research studies. The titles of these studies are as follows:

MSF study 1: Risk factors for diagnosed noma and language and beliefs about the disease in northwest Nigeria, 2017.

MSF study 2: Long-term follow-up of noma patients after surgical, nutritional and mental health interventions at the Noma Children's Hospital in northwest Nigeria, 2018 to 2020.

MSF study 3: Noma and traditional healing in northwest Nigeria. A qualitative study with caretakers of noma patients and traditional healers, 2018.

MSF study 4: Determining the prevalence of all stages of noma in northwest Nigeria, 2018.

MSF study 1 was the first study conducted, followed by MSF study 2 and MSF study 3 which were begun in parallel. MSF study 4 was the final project. The PhD candidate has permission and support from MSF to use the data from these studies towards a PhD (Appendix 1.1 and 1.2). MSF study 1 was a mixed methods study that incorporated an initial qualitative part assessing the language and beliefs around noma, and a subsequent case control study assessing the risk factors for noma. This study is the basis for two of the PhD chapters, Chapter 3 (Language and Beliefs) and Chapter 4 (Risk Factors). MSF study 2 was a dual-phased study. The data collected during the first phase of this study was included in the thesis in Chapter 5. Only surgical interventions with patients who survived the acute stage of infection (i.e. not nutritional and mental health interventions) are described in this thesis. The second phase is a prospective cohort study; data collection for this phase is still ongoing and has not been included in this thesis. All of the data from MSF study 3 and 4 were included in thesis Chapter 6 and Chapter 7 respectively (Table 1.1). The role of the PhD candidate during these studies is described in the preface of the thesis, and the contributions of the candidate to each specific chapter is noted on the first page of each chapter.

1.7 Ethics

All data gathered as part of the dissertation gained approval from the University of Cape Town (UCT) Human Research Ethics Committee, MSF Ethical Review Board (ERB), Usmanu Danfodiyo University Teaching Hospital (UDUTH) ERB in Nigeria and the Sokoto and Kebbi States Ministry of Health ERB (the states in which the data collection occurred). All approvals are in Appendix 2. Written informed consent from research participants and, where applicable, primary caretakers was gained for data collection in all chapters. Where applicable, assent was requested from child respondents aged between eight and 17 years. A confidentiality and conflict of interest certificate was signed by all research staff. All electronic recordings were

deleted off any recording devices and data collection tablets once uploaded to the secure MSF cloud server. All paper copies are locked in a secure cupboard at the program site and will be destroyed after five years. All data was collected using a unique participant identification number and did not include names or other identifying data. Where necessary, a separate data collection form containing identifying data linked to the participant's unique identifying number was kept. This information was only accessible to the PhD candidate and a limited number of other research team members directly involved in data collection. No names or identifying data of research participants were mentioned in reports, publications or abstracts. Individuals participating in the project were treated equitably and fairly. No photographs were taken for the purpose of this thesis.

Chapter 2 Scoping literature review

There is a paucity of literature on noma (cancrum oris) due to the neglected nature of this disease in general and in the scientific community [25]. The rapid progression and reported high mortality rate [1], the remote location of patients, under-reporting and misdiagnosis of cases [21] contribute to limited literature being available and a poor understanding of the disease. There has however, been ongoing reporting of noma cases from around the world for many centuries and a few scientists have, for decades, been researching noma. These include Dr Enwonwu [10, 43, 50–53], Dr Marck [10, 43, 50–53], Dr Baratti-Mayer [25, 54–56], Dr Chidzonga [18, 20], Dr Srour [32, 57, 58] and Dr Feller [9, 59, 60]. Using empirical evidence, the thesis aims to fill some of the gaps in knowledge around noma with the hope of adding valuable insight into the disease while contributing to the existing body of research.

2.1 Methods

We conducted a scoping review of the literature on noma to consolidate the information available and to understand the size and scope of available research on the disease. The main topics of interest included: the history and epidemiology of the disease, noma's clinical progression and aetiology, treatment regimens, mortality rates and the risk factors for the development of noma. The scoping review methodology was chosen as it uses rigorous and transparent methods, allowing for the collation of a large and diverse body of literature while incorporating findings from multiple study designs [61, 62]. This scoping review was conducted in line with Preferred Reporting Items for Systemic review and Meta-Analyses (PRISMA) requirements (Appendix 3.1).

2.1.1 Databases searched

The following databases were searched for articles to include in this literature review: PubMed; PsycINFO via Ebsco Host; Science Direct; Social Science Citation Index via Web of Science; MEDLINE via PubMed; Cumulative Index to Nursing and Allied Health Literature via Ebsco Host; Cochrane Library; Population Information Online; LILACS; SciELO and Scopus.

2.1.2 Searching methods utilized

An initial search of each database was done online via the UCT Health Sciences Library platform by the PhD candidate. All articles identified were listed and if full text articles were available, they were downloaded. For articles where full text was not initially available, the individual journals were searched and, where available, articles were downloaded. For any full text articles not found, the UCT Health Sciences Librarian was requested to source some of the outstanding articles. The corresponding authors of outstanding articles were contacted where possible for copies of their manuscripts.

2.1.3 Eligibility criteria

The databases and journals were searched using the following eligibility criteria: 1) noma, cancrum oris related; 2) peer reviewed; 3) primary study; 4) addressed a main theme of interest; 5) any publication date; 6) all study designs; and 7) all languages.

2.1.4 Search Terms

Databases were searched with the following terms: "cancrum oris" OR “noma” OR "cancrum oris cases" OR "cancrum oris defects" OR "cancrum oris like lesions" OR "cancrum oris noma" OR "cancrum oris, noma".

2.1.5 Data extraction

Data from the eligible studies were extracted using a standardized data extraction tool (Appendix 3.2). Data extracted included: title; author; journal; year of publication; geographic location of first author; geographic location of study; number of cases/individuals in study; research question/aim; methodology; analysis; results; area of interest; conclusions; implications for future research and practice; gaps in knowledge and any other noteworthy comments.

All non-English papers were translated into English using Google translate, anything unclear was checked with a language expert. The PhD candidate performed the standardized data extraction and eligibility evaluations on each study and evaluated if the study addressed one of the research topics of interest.

2.1.6 Analysis

An analysis was conducted by grouping individual factors into themes within the topics of interest (the history and epidemiology of the disease, noma's clinical progression and aetiology, treatment regimens, mortality rates and the risk factors for the development of noma). These topics of interest were explored in-depth and findings on each of these topics are concisely reported.

2.1.7 Included articles

Our initial search identified 171 manuscripts for review, of which 125 were included in the literature review. The oldest manuscript was from 1843 and the most recently published manuscript was from January 2019. The other 46 manuscripts were excluded as they either

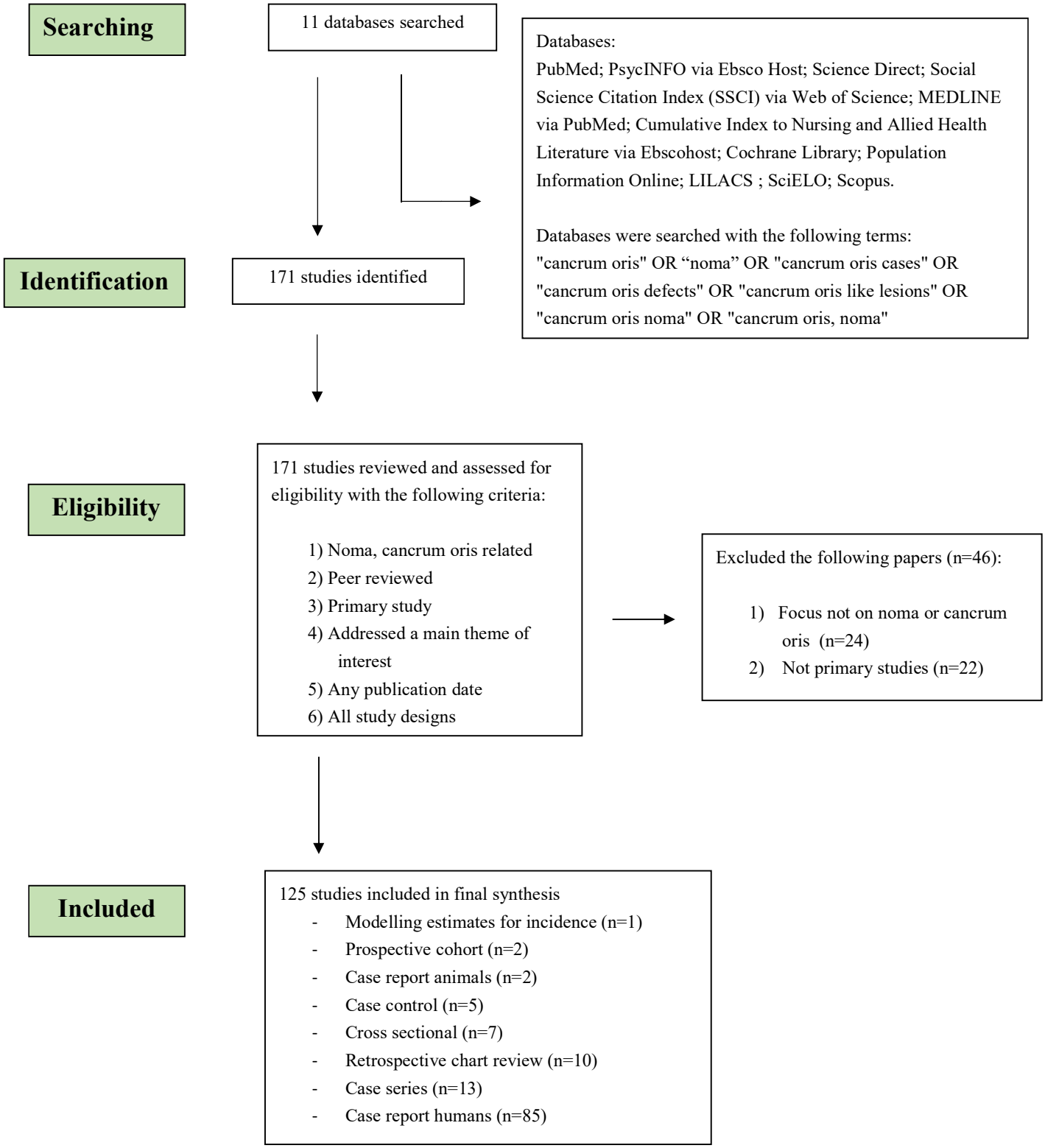
did not directly relate to noma, did not meet the inclusion criteria, or they were not considered to be primary research. The majority of the studies (n=85, 68%) were case reports (Figure 2.1).

2.2 History of noma

There are reports of noma by physicians such as Hippocrates (460-370 BC) and Galen (129-200 AD) [22]. However; others believe that these referred to general ulceration of the body and not noma as the disease is currently understood [63]. The first clinical description of the disease we now call noma, was written by Battus in 1620, who labelled it 'water canker' [63, 64]. The word 'noma' is derived from a Greek word which, loosely translated, means 'to devour' [65] and was first used by Dutch surgeon Cornelis van de Voorde in 1680, for a rapidly-spreading ulceration originating in wet soft tissues in children, 'typical of the mouth' [64].

The term 'noma' and 'cancrum oris' are currently used interchangeably [10, 12, 33, 39]. In the 1800's, there were ongoing discussions about the usage of the terms with some viewing them as two separate diseases [66]. In a publication from 1862, 'noma' referred to ulcerative stomatitis (lesion on the skin or an internal mucous surface of the mouth) and 'cancrum oris' referred to gangrenous stomatitis (death of the tissue of the mouth) [66]. In contrast, in 1848, Tourdes defined the disease of 'noma' as it is currently understood today as "a gangrenous disease affecting the mouth and face of children living in bad hygiene conditions and suffering from debilitating diseases, especially eruptive fever, beginning with an ulcer on the oral mucosa rapidly spreading outside and destroying the soft and hard tissues of the face and almost always fatal" [25].

Figure 2.1 Flow diagram of databases searched and articles included in the noma scoping review.



Our literature review revealed many illustrations by physicians. Below are a select few showing a range of impressions from these physicians. Each sketch shows the severity of the facial destruction (Figures 2.2-2.5).

There have been some inconsistencies in the literature, with infections not likely to be noma, being labelled as noma. In one study the lesions were not isolated in the oral region but were also on the perineum [53], but a diagnosis of noma was still given. Noma neonatorum was first described in 1977 [67], and is a necrotizing infection seen in neonates in which gangrenous lesions involve the mucocutaneous junctions of oral, nasal, and anal area, and, occasionally, the eyelids and the scrotum [10, 53, 67–69]. This infection resembles noma, and is sometimes incorrectly reported as noma, but this infection is not noma, and needs to be differentiated as such [53, 70]. The main differentiating factors being that noma neonatorum is caused by *Pseudomonas aeruginosa* while with noma numerous other pathogens are implicated; and noma neonatorum affects neonates while noma mostly affects children aged between two and five years [53, 67, 68, 71].

In Laos, the name commonly used for noma is 'Pagnad Pak Poue' meaning 'disease of mouth rotting' [32]. In Zambia, tribes in a specific area have labelled the disease as 'aka popo', meaning the child has been fed a stillborn fetus, and the flesh is 'coming out' (describing the sloughing of the cheek) [3]. In Hausa, the most widely spoken language in northwest Nigeria, the term 'ciwon iska' and 'bakin kare' are reportedly used for noma [64]. Both of these words are generalized terms (disease of the wind and mouth of the dog) which have reportedly caused confusion in patient recruitment drives for surgical interventions, as patients with ailments such as cleft lip and palate also respond to the calls [64].

Figure 2. 2 Sketch of noma patient (4 years old), 1892 [63].

Figure 2. 3 Postmortem sketch of noma patient, 1872 [65].

Figure 2. 4 Noma patient, 3 years old, admitted 16th May, died 20th May 1885 [72].

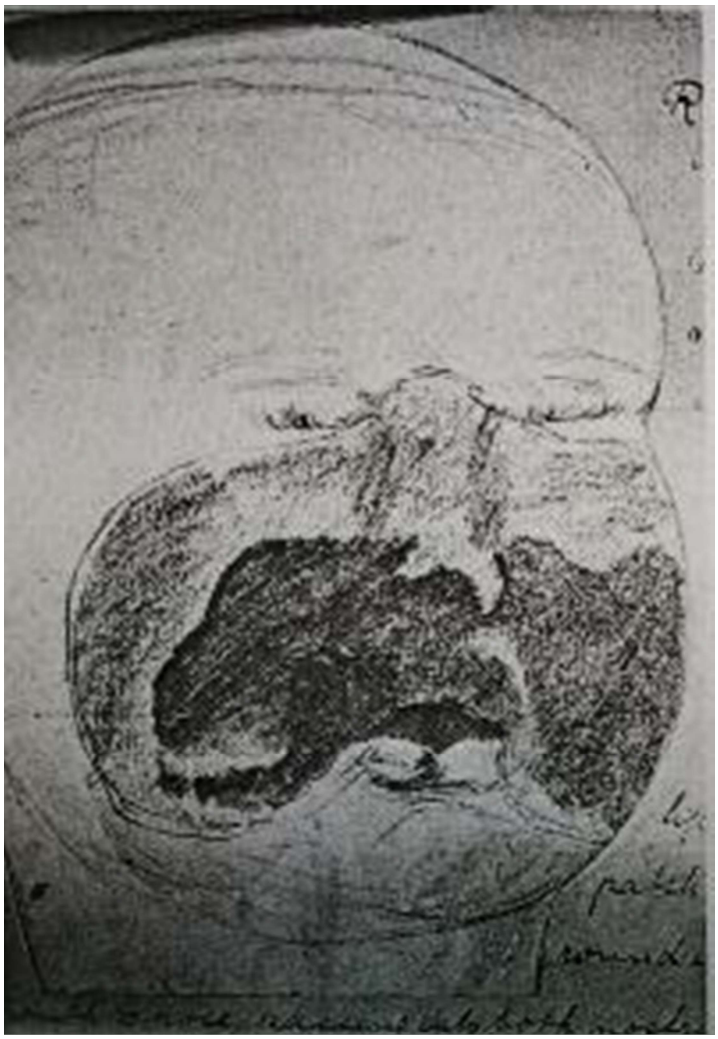
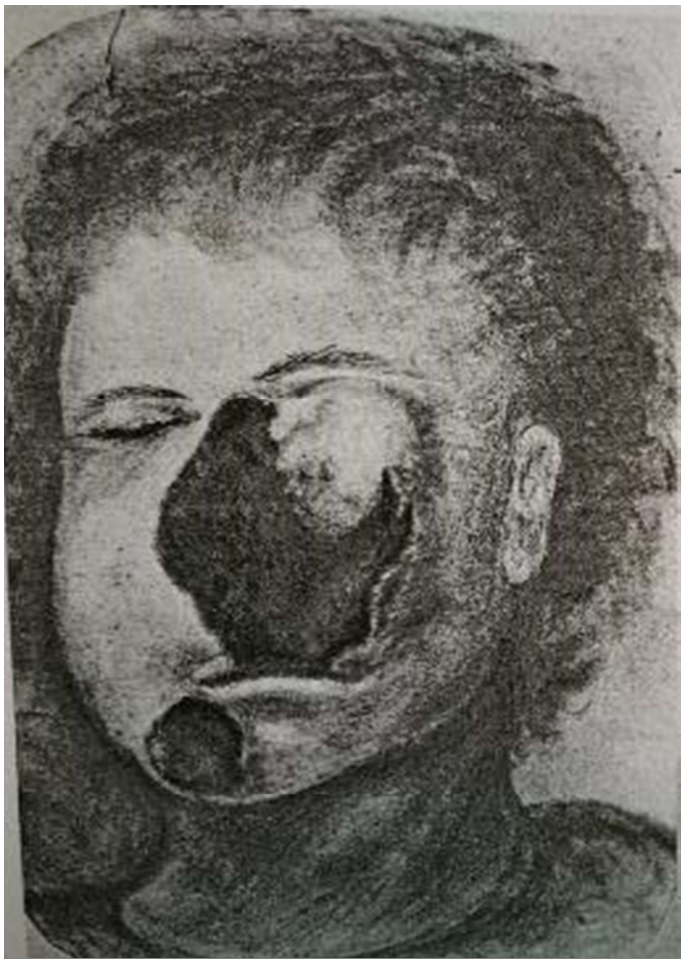


Figure 2. 5 Noma patient, lived for only six days after admission to hospital, 1887 [72].



Other reported Hausa names include ‘gaude’ and ‘sadde’, translated as ‘the disease of cattle rearers’ [8]. This name is indicative of the beliefs in the Hausa community that the disease is transmitted from animals to children [8].

2.3 Clinical progression

Noma is a rapidly progressing infection of the oral cavity, associated with a reported 90% mortality rate within weeks after the onset of noma, if left untreated [1]. Noma most commonly affects children between two and five years of age [2]; however, reports of acute noma cases in adults, mostly in conjunction with other infections have been reported [15, 27, 51, 73]. While the clinical manifestation and sequelae of noma in each case is unique, the infection invariably starts as an inflammation of the gums, which then leads to ulceration and the rapid destruction (within weeks [1]) of the cheek and in some cases the jaw, lip, nose and/or the eye [3, 4]. Deaths are primarily due to starvation, aspiration pneumonia, respiratory insufficiency or sepsis [25, 74]. Treatment with antibiotics, wound debridement and nutritional support in the early reversible stages of the disease can reduce the duration and severity of the acute phase of noma and the extent of tissue damage, thus reducing mortality and morbidity of noma (discussed in detail below) [2]. The infection can become inactive (with or to a lesser extent without antibiotic treatment), after which, patients often need complex surgical reconstruction to restore form and function [4]. Patients who survive often have severe facial disfigurements [2] and multiple physical impairments such as difficulty eating, seeing and breathing [1]. Noma can cause stigmatization due to these impairments [2].

For the purposes of case detection in the field, the WHO has classified noma into stages, the first stages (Stage 0 to 4) are the active or acute stages of noma lasting only a couple of weeks; Stage 0: simple gingivitis; Stage 1: acute necrotizing gingivitis; Stage 2: oedema; Stage 3:

gangrene. Stage 4: scarring is accompanied by contractures, which develop as the child grows and Stage 5: sequelae is the final stage and is also known as the inactive or chronic stage of noma and refers to the condition of patients who survive the acute stages of infection with varying degrees of physical and/or functional deformities [1] (Appendix 4). There were no reports of noma reoccurring once reaching Stage 5 [59]. None of the literature included in this review reported that noma was contagious [59]. There was also no evidence on the triggers which would cause a progression to the later gangrenous stages of the disease.

2.4 Aetiology

The pathogenesis of noma is poorly understood and the microbiology is debated. Strikingly, this quote from a paper written in 1893 still partly reflects the current debated nature of the pathogenesis of noma "There must surely be a specific organism and a combination of predisposing causes, not poverty alone, but poverty plus a sickly habit of body" [63].

A range of organisms have been identified in the oral flora of noma patients [8, 50, 52, 56], such as *Fusobacterium necrophorum* [8, 50, 52]. The causal association with noma, however has been debated as it has not consistently featured in oral microbial studies [10, 56, 75]. Other studies have noted that noma incorporates the characteristics of an opportunistic infection, implicating a change in the equilibrium of commensal bacteria due to a derailment of host defences [20, 22, 75, 76]. There is a strong likelihood this may be true as most cases have concurrent infections or immunodeficiency states (these comorbidities are discussed in detail below).

Table 2.1 below offers a summary of the etiologic studies included in this review and the organisms identified, the details of each study and limitations of the study methods. One of these limitations is delayed acquisition of a culture [50] which may result in identification of super infectious agents rather than the causative agent(s). The acute phase of noma is relatively short and delayed treatment-seeking may pose challenges in acquiring samples in the early acute phase. Non-probability sampling methodologies, that do not choose the study participants at random, are a further limitation [77, 78] which mean the findings have restrictions in terms of generalizability as the findings are only relevant to the group enrolled in the study and not the population as a whole [79]. Some of the studies included in the review and detailed in Table 2.1 have no comparison group [20, 50]. This makes it impossible to identify causal links between the organisms and noma infection as there is no control group to compare the results to [78]. Other studies included that utilize case control study designs [10, 54, 56] do not provide evidence of causal links but do provide information on which to base future research hypotheses to be tested. The case control study design has the potential for introducing biases, including measurement bias (due to the retrospective nature of collecting data about predictor variables) and selection bias (can occur during the identification of case-patients and control-patients if their inclusion depends on the exposure of interest) [77], affecting associations seen. These limitations will impact on the generalizability of the findings of these studies and the inferences that can be made.

Table 2. 1 Microorganisms found in the oral flora of noma patients by year.

Study	Study details	Organism	Limitations
Falkler, 1999 [50]	Study type: Cross-sectional study Location: Nigeria n: Eight cases Additional details: Cancrum oris lesions (present for six weeks to two years) were cultured for anaerobic microorganisms.	*Fusobacter iumnecrophorum* and *Prevotella intermedia* were isolated from seven and six of the eight lesions, respectively.	Long duration of infection before testing (up to two years), small sample size, no healthy matched comparison group.
Phillips, 2005 [10]	Study type: Case control study Location: Nigeria n: 68 acute noma cases, 63 village and 45 urban controls Additional details: Cases were found over four years through house visits. Controls were matched by age and were children attending out-patient clinics and primary health care centres for routine checks, and had no recent history of any disease, fever and diarrhoea. Oral bacteria were studied by polymerase chain reaction on six cases. Excluded those treated with antibiotics or traditional medicine in last 48hrs. Excluded measles, HIV and malaria comorbid patients.	Bacteria observed at the highest frequencies in noma lesions were *Prevotella intermedia* (83%), *Tannerella for sythensis* (83%), *Porphyromonas gingivalis* (50%), *Campylobacter rectus* (50%) and *Treponema denticola* (50%).	Control selection (children attending health care facility) could have biased results as these children were already accessing care. It is unknown how long each patient had noma for. The sample size for bacterial testing was small (n=6).
Chidzonga, 2008 [20]	Study type: Retrospective chart review Location: Zimbabwe n: 48 acute noma cases, five cases had microbiologic investigations Additional details: All cases presented one to two weeks after onset of symptoms	*Staphylococcus aureus, Klebsiella species, group D Streptococcus, and group B hemolytic Streptococcus*.	Small sample size, retrospective chart review, no control group.

Baratti-Mayer, 2013 [56]	Study type: Prospective matched, case-control study Location: Niger n: 82 acute noma cases, 327 matched controls Additional details: Study took place over six years. Exact stage of noma cases not defined. Controls matched on age and home village. Extracted total genomic deoxyribonucleic acid. Cases who received antibiotics or whose specimens deteriorated were excluded (n=20), 117 microbial samples were processed from noma cases and 235 from controls. Multivariable model showed organisms associated with noma.	A reduced proportion of *Spirochaeta, Fusobacterium, Capnocytophaga*, and *Neisseria* in the oral microbiota, but an increased proportion of *Prevotella* associated with noma. Controls had higher *Fusobacterium* genus levels raising doubts about previous findings.	Controls were significantly older than cases. 28% of observations in the analysis were excluded because of missing data for microbiological variables due to problems collecting data due to poor health.
Huyghe, 2013 [54]	Study type: Case control study Location: Niger n: 84 acute noma cases, 37 acute necrotizing gingivitis cases and 343 controls Additional details: Cases had no antibiotics, no dental cleaning and did not receive fortified food during the 3 previous months. Subjects with lesions older than 4 weeks were excluded.	Compared to the healthy controls, a lower bacterial diversity was found in noma samples. Less *Porphyromonadaceae, Tannerella spp.*, *Capnocytophaga spp., Fusobacteria and Cetobacterium spp.* were found in noma samples. Raises doubts about *Fusobacterium necrophorum*.	Authors state need for time series data and the utilization of high-throughput sequencing capacity to elucidate the aetiology of noma.

2.5 Treatment

There are recommended treatments, which are reported to be effective in the differing stages of noma.

2.5.1 Acute phase treatment (Stages 0 to 4)

Historically (1800's and early 1900's), noma cases presenting at biomedical institutions were managed with nutritional support with high protein foods (fruit, eggs, milk, meat [63, 80, 81]) alcohol (wine, brandy and whisky [63, 66, 80, 82, 83]) and wound cleaning using bicarbonate of soda [80, 84], leeches [84] and nitric acid [66, 85, 86]. It is difficult to know whether these methods were beneficial as all evidence was derived from case series and case reports.

More recently (later 1900's and 2000's), timely administration of broad-spectrum antibiotics have shown to be effective in reducing the severity and sequelae of noma by arresting the acute phase of the infection in some patients [9, 20, 21, 31, 32]. A range of antibiotics were reported in the included studies such as amoxicillin [9, 87–89], metronidazole [11, 33, 39, 50, 87], lincomycin [35] and cefotaxime [33, 90]. No studies comparing the relative efficacy of these antibiotics were identified.

Wound cleaning and debridement was shown to be important including daily irrigation with saline [8, 9, 39, 87–89, 91] and antiseptic dressings [37, 92]. Wound debridement involves the removal of necrotic tissue to promote healing and reduce the risk of secondary infection [20, 22, 25, 32, 37, 92]. Nutritional support, either orally or via a nasogastric tube, is another cornerstone of noma treatment as it builds the patients' immune systems, which enables their body to fight off infection [20, 21, 25, 93]. This nutritional support has not been reported to

be effective in isolation, but only when accompanied by wound debridement and antibiotic treatment [2].

Therefore, the current WHO guidelines for the management of the active stages of noma in clinical settings includes [1]: oral hygiene (mouth wash Chlorhexidine 0,2%, 10 ml), antibiotic treatment (Amoxicillin), nutritional support (high protein), wound cleaning (compresses soaked in hydrogen peroxide) and dressing (honey for local dressing and for antibacterial action and regeneration) [1].

2.5.2 Chronic phase treatment (Stage 5)

Once noma becomes inactive, patients can survive into adulthood but often require extensive reconstructive surgery and physiotherapy to correct the resulting structural and functional defects [94]. Physical sequelae include displacement of the teeth and intense scarring and bony fusion between the maxilla and mandible [2, 4, 92, 94–96]. Sequelae around daily functioning may include difficulty eating, seeing, talking and breathing [57, 94, 96]. Trismus (a restriction in mouth opening) is one of the most disabling sequelae [6] and can lead to complications such as aspiration, malnutrition, poor oral hygiene, speech deficits, a compromised airway and pain [97].

The clinical manifestation of each noma case is unique, and as such, the surgical procedures used to treat each noma case differ [3, 5, 38, 55, 98–101]. Reported surgical techniques include pedicled supraclavicular flaps for the treatment of large unilateral facial defects [100]; myocutaneous submental artery flaps, bony and/or soft tissue trismus releases [92], forehead flaps for nasal reconstructions [92] and lower lid ectropion release [92]. In one study, extra-articular ankylosis due to noma was treated using soft tissue reconstruction with large free flaps

[55]. Mouth opening was performed by bone-bridge excision, sometimes associated with contralateral coronoidectomy [55]. In a further study, the reconstruction of an upper lip defect was conducted using Gillies fan flaps [102]. A 2006 book on noma surgical techniques includes information on the reconstruction of the lips and corner of the mouth using Abbe, Estlander and fan flaps; and the reconstruction of the cheek using temporo-parietal fascia and deltopectoral flaps; and the reconstruction of central defects using radial forearm and local turnover flaps [4].

Physiotherapy is an essential part of noma treatment, especially to prevent or minimise trismus [98] and can lead to improvements in eating, chewing and speaking [103].

Noma can often lead to stigmatization and resultant social isolation of the patients and their family members from the communities [2]. The management of noma patients invariably requires social and psychological support. There are no publications exploring or examining the effectiveness of these mental health interventions.

Outcomes of noma treatment are difficult to ascertain due to inconsistent patient follow-up [6]. This is mostly due to the remote locations of the home villages of patients and difficulties in accessing health care facilities [24, 25, 32]. The extent of long-term sequelae and their impact on quality of life depends on the severity of the disease at initial presentation, efficacy of antibiotic treatment, wound debridement and the facial structures affected [6, 9, 20, 21]. No reports of traditional or non-biomedical treatments were found during this review.

2.6 Mortality

There is limited evidence around the pathogenesis of noma leading to death. Deaths have primarily been reported due to starvation, aspiration pneumonia, respiratory insufficiency or

sepsis [25, 74]. Factors that favour survival (apart from antibiotic treatment and wound debridement) are unknown. The mortality rate of noma depends on multiple factors and is poorly enumerated. The WHO (based on expert opinion and retrospective chart analyses) states that noma has a mortality rate of 90% within weeks after the onset of noma if left untreated [1]. The speed with which death occurs is also debated, some state death occurs in as little as two weeks from the onset of first symptoms [1] but it is unclear about which symptoms these are. The clearest reported estimate is that death can occur in a matter of days after the onset of oedema [25]. What is certain is that when noma is identified and treated timeously, mortality greatly decreases [58].

Table 2.2 explores the mortality rates reported in various studies included in this review. These estimates highlight the differences in mortality rates in groups who received no antibiotic treatment (49-94%) in comparison to those who had received drug therapies such as antibiotics (0-38%) (Table 2.2). It should be noted that these estimates are derived from case series and retrospective chart reviews, no standardized reporting of noma stage was used and the studies do not all have the same follow-up periods, thus the evidence should be evaluated with these study design restrictions in mind as they could over- or under-estimate the mortality rates of noma patients.

2.7 Epidemiology

In recent years, noma has been reported in many countries around the world but primarily in low and middle income countries in Africa and Asia [3, 7, 16, 18, 20–32]. In 2007, the WHO carried out a survey in African member states, which found that 39 of the 46 countries surveyed had reported noma cases in the year prior to data collection [104].

Table 2. 2 Mortality reported in included studies.

Study	Location	Study design	Cases	Mortality (%)	Treatment
Tourdes, 1848 [105]	Europe	Case series	239	73%	No drug therapy
Barthez, 1855 [105]	Europe	Case series	29	89%	No drug therapy
Ritchie, 1872 [65]	Europe	Case series	8	63%	Iron with citric-acid, nutritional support
Springer, 1904 [105]	Europe	Case series	88	94%	Wound debridement
Gupta, 1945 [28]	India	Case series	79	49%	Pentavalent antimony (treatment of leishmaniasis), nutritional support, vitamins, blood transfusions, local antiseptic treatment
Jelliffe, 1952 [81]	Nigeria	Case series	53	30%	Penicillin
Mehrotra, 1966 [30]	India	Case series	20	15%	Antibiotics, multivitamins, high protein diet, sequestrectomy, plastic reconstructive surgeries
Adekeye and Ord, 1978–1982 [25]	Nigeria	Case series	13	0%	Antibiotics
Bourgeois, 1981-93 [25]	Senegal	Case series	73	10%	Drug therapy, kind not specified
Oginni, 1982-96 [25]	Nigeria	Case series	133	0%	Drug therapy, kind not specified
Nath, 1998 [3]	Zambia	Retrospective chart review	117	20%	Nutrition, wound care
Chidzonga, 1996 [106]	Zimbabwe	Case series	8	38%	Antibiotics, wound debridement, removed mobile teeth, irrigated wounds
Millogo, 2012 [17]	Burkina Faso	Retrospective chart review	212	HIV co-infected patients 38%; non-HIV patients 6%	Antibiotics, anti-retroviral therapy
Konsem, 2014 [107]	Burkina Faso	Retrospective chart review	55	15%	Antibiotics

Those with the highest number of reported cases were Burkina Faso, Ethiopia, Mali, Niger, Nigeria and Senegal which led to these countries being labelled the 'noma-belt' [104]. This term is commonly used when reporting the epidemiology of noma. However; the information gathered that led to this term was not standardized and not based on robust prevalence or incidence estimates [104]. In the last 15 years, cases have also been reported to occur and be treated in southern Africa [3, 16, 18, 21], Turkey [33], Afghanistan [34], South Korea [108], India [24, 31, 109, 110], Laos [32], Italy [35] the United Kingdom [36] and the United States [11, 74], indicating a much wider distribution than the usually reported 'noma-belt' [104].

The oldest estimate we found of the burden of disease, based on hospital admissions, indicated that, noma was diagnosed once out of every 5,000 cases of children admitted to hospital with an illness, between 1860 to 1871 in Edinburgh [65]. In 1997, Barnes *et al*. estimated that, based on records from three referral centres, the prevalence of noma was 1 case per 1,250 children aged two to six years per year in Nigeria [53]. In 1998, the World Health Organisation (WHO) estimated that 140,000 new cases of noma occur each year globally and that 770,000 patients were living with noma sequelae at that time [19], the origin of this estimate is unclear [111]. In 1999, it was estimated that there was an annual incidence of 4.2 acute noma cases per million Senegalese children aged 1–4 years [112]. This estimate was calculated using a WHO recommended formulae, based on a 5-20% presentation rate of both acute and chronic noma, and an 80-90% mortality rate in the acute stages of the disease [112]:

$$\text{Total number of survivors (S)} = \frac{\text{No of survivors who reach care (R) x 100}}{\text{\% of survivors estimated to seek care (X)}}$$

$$\text{Incidence (I)} = \frac{\text{Total number of survivors (S) x 100}}{\text{\% case survival rate (y)}}$$

Through a retrospective chart review (n=6,390) in 2003, Denloye *et al.* estimated seven cases per 1,000 children aged between one and 16 years had noma between 1986 and 2000 in Nigeria [42]. In that same year, a northwest Nigerian study by Fieger *et al.* modelling noma incidence based on the number of clefts, concluded that the incidence of noma is estimated to be 6.4 per 1,000 children from 1996 to 2001 [7]. These estimates may not accurately reflect the present incidence of acute noma or the prevalence of patients with noma sequelae as they are based on expert opinion or data collected many years ago. It is also unclear which stages of noma are included in these estimates [49].

Figures 2.6, 2.7 and 2.8 explore the changing geographical distribution of noma case reports and case series from the 1800's to 2019. There is a shift in case reporting from primarily in Europe and India in the 1800's, to parts of Africa and North America in the 1900's to South America and Asia in the 2000's. Noma cases were reported in war-time soldiers in the 1880's [80, 85]; in Belsen and Auschwitz concentration camps during World War II [7, 8, 32, 39, 113–115] and the general population in war-time Netherlands where the population suffered through famine in the winter of 1944/1945 [7]. Since these war-time reports in Europe, the occurrence of noma dramatically decreased and is only sporadically reported in the region today [36].

The maps in Figures 2.6 to 2.8 do not necessarily indicate increasing prevalence of noma, as the quality of evidence is low (based on cases reports and case series [116]). Without robust prevalence and estimates across countries at various times, it is not possible to accurately describe the changing geographical distribution of the disease.

Figure 2. 6 Number and geographical distribution of case reports and case series in the 1800's included in the literature review.

Figure 2. 7 Number and geographical distribution of case reports and case series in the 1900's included in the literature review.

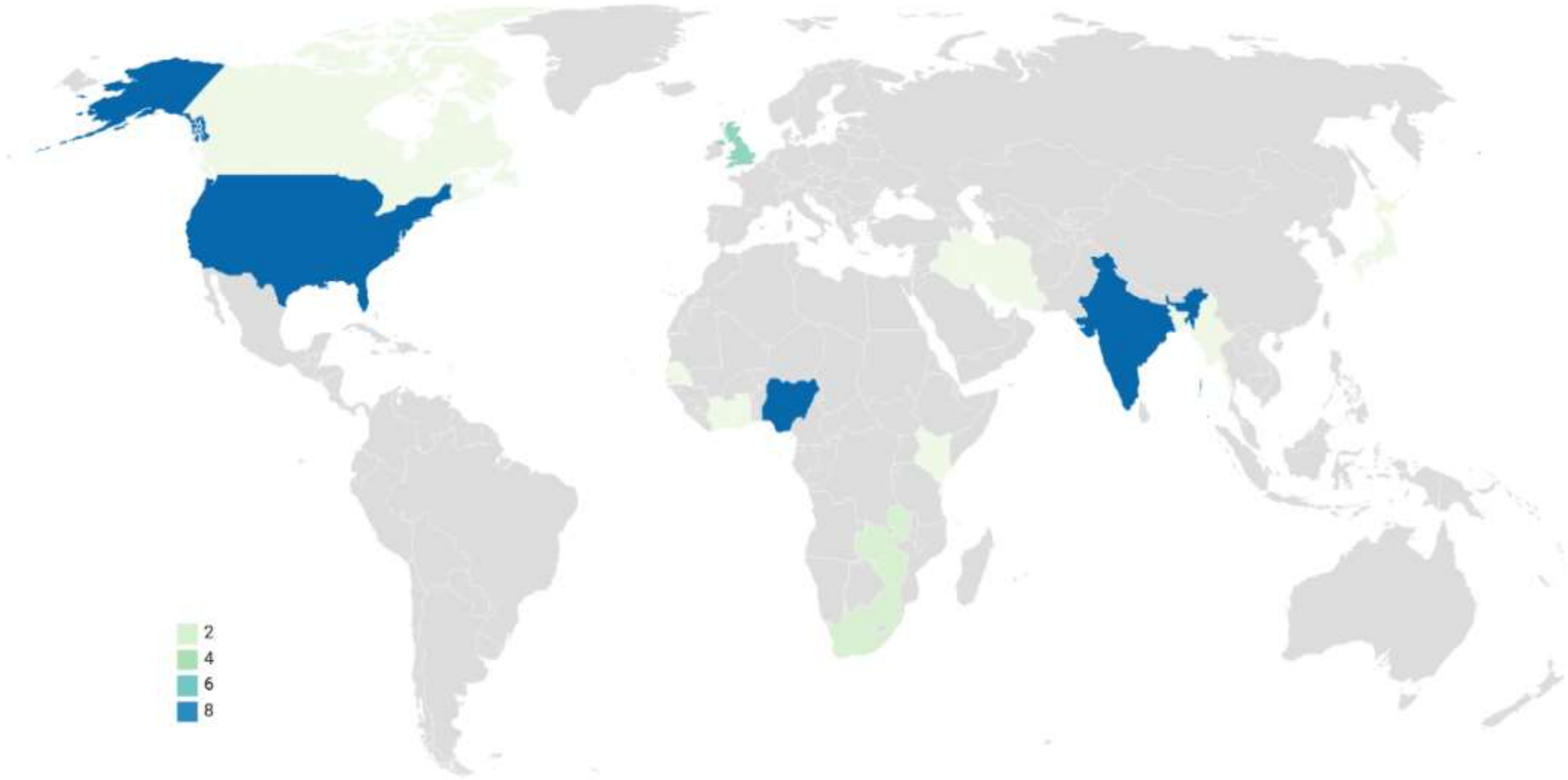


Figure 2. 8 Number and geographical distribution of case reports and case series in the 2000's included in the literature review.

2.8 Risk factors

There is limited primary evidence on the risk factors for the development of noma. The table below explores the risk factors noted in the primary studies included in this review (Table 2.3). Reported risk factors for the development of noma in these primary studies include being aged between two and five years [3, 20, 22, 23, 40–42, 117], not being breastfed [43], comorbidities either at the time of noma diagnosis or in the three months leading up to diagnosis [3, 8, 17, 22, 23, 40–43, 56, 107, 117], lack of access to quality health care [117] including childhood vaccinations [34], low vitamin A and vitamin C levels [10], poor oral hygiene practices leading to gingivitis (Stage 0 noma) [34], low socioeconomic status of the family [107], a high number of previous pregnancies in the mother [56] and the absence of chickens at home [56].

Other studies have hypothesized further risk factors for noma development including household variables such as proximity of livestock to living areas and poor sanitation [34], which is thought to lead to possible contamination of water and food sources and consequently increasing the risk of infections [118, 119]. However; caution is needed when interpreting these findings as they are based on the proportions of cases vs controls having these risk factors without any clear statistical testing.

Table 2.3 Risk factors for noma identified in primary research.

Study	Study details	Risk factors identified	Limitations
Osuji, 1990 [40]	Study type: Cross-sectional Location: Nigeria n: 58 cases of acute necrotizing gingivitis (Stage 1 noma as categorized under the WHO system [1]), 5 noma cases (diagnosed as advanced acute necrotizing gingivitis with sequestrum formation)	• Respondents aged between 2-7 years (n=49, 85% acute necrotizing gingivitis cases, n=3, 60% noma cases) • Rainy season (n= 42, 67%) • History of recent febrile illness (n=55, 87%)	Data collected retrospectively. 18 children examined by authors, the remaining charts were reviewed- could provide inconsistent data. Limited standardization of data collection. No robust analysis of risk factors.
Lazarus, 1997 [22]	Study type: Retrospective chart review, reviewing charts of cancrum oris patients from the previous 35 years Location: South Africa n: 26 respondents	• Respondents mean age 4 years 4 months (range 1-15 years) • Malnutrition (n=7/ 11 (whose records had comorbidity information), 64%) • Gastroenteritis (n=4/11, 36%) • Measles (n=3/11, 27%)	Data collected retrospectively, no standardization, no control group
Nath, 1998 [3]	Study type: Retrospective chart review over 15 years n: 81 respondents	• Respondents aged between 1 and 4 years (n=67, 83%), • Diarrhoea (n=13, 28.9%) • HIV (n=26/45 (children admitted between 1989-93), 60.5%), • Malnutrition (n=15/ 45 (no. children assessed for malnutrition), 33.3%) • Rainy season (n=60, 74.1%),	Data collected retrospectively, no standardization, no control group
Ndiaye, 1999 [117]	Study type: Prospective cohort Location: Senegal n: 25 later stage noma cases, 1058 acute necrotizing gingivitis cases	• Noma respondents mostly aged >15 years (n=13, 52%), acute necrotizing gingivitis respondents mostly aged between 1-4 years (n=465, 44%) • No access to quality care (n=20/25 (noma only), 80%)	The definitions of a noma case were not clear, results were not always separated into noma stages. Descriptive, uncontrolled case series, risk factors not clearly laid out or examined, and no clarity on which risk factors were present for each stage of noma. Most of the children aged between 0-4 years were acute but the remaining respondents were chronic noma patients, this could introduce recall bias and skew associations seen due to the long length of time between the acute phase and the study (most cases aged over 15 years).

Enwonwu, 1999 [8]	Study type: Case control study Location: Nigeria n: 86 noma cases	• Respondents mean age 5.9 years (Standard Deviation) (SD) 2.6 years • Malnutrition (Weight-for-height Z score (WHZ) ≤ -2.0 SD) (n=9, 10.2% controls, n= 17, 19.4% cases)	Risk factor analysis confined to prevalence of factor in cases vs controls. Some risk factors are not clearly examined with statistical methods and results are not clearly laid out.
Oginni, 1999 [23]	Study type: Retrospective chart review of noma patients from 1982 to 1996 Location: Nigeria n: 146 noma patients, 133 acute, 13 chronic (which was 1.7% of all patients admitted to the hospital during this time).	• Respondents mean age 4.7 years (SD 2.6 years) • Malnutrition (n=146, 100 %) • Poor oral hygiene (n=122, 83.6%)	Missing/incomplete clinical data; no standardization in diagnosis. Risk factors identified by descriptive analysis. Percentages do not correlate with patient numbers.
Denloye, 2003 [42]	Study type: Retrospective chart review 1986 to 2000 Location: Nigeria n: 45 noma cases	• Respondents mean age 4.2 years (SD 2.7 years) • Malnutrition (n= 45, 100%) • Malaria (n= 14, 31%) • Measles (n=14, 31%)	Missing/incomplete clinical data including vaccination history.
Enwonwu, 2005 [43]	Study type: Case control Location: Nigeria n: 91 noma cases	• Respondents mean age 2.6 years (SD 1.0) • Malnutrition (median height for age z-score noma group -3.74, control group 1 -1.41, control group 2 0.85)	Children with comorbidities excluded.
Phillips, 2005 [10]	Study type: Case control Location: Nigeria n: 68 noma acute cases	• Biological markers suggestive of malnutrition (lower plasma levels of vitamin A ($p<0.001$), vitamin C ($p<0.05$) and zinc ($p<0.001$)) • Marked reductions ($p<0.001$) in albumin and blood haemoglobin.	Healthy controls matched by age and village not included. Respondents' ages not clear from the manuscript.
Chidzonga, 2008 [20]	Study type: Retrospective chart review of charts between 2002 and 2006 Location: Zimbabwe n: 48 acute noma cases, all HIV positive (by design)	• Respondents aged <16 years (n=11, 64.7%) • Gender (female n= 31, 64.6%)	No control group, limited information and analysis on risk factors

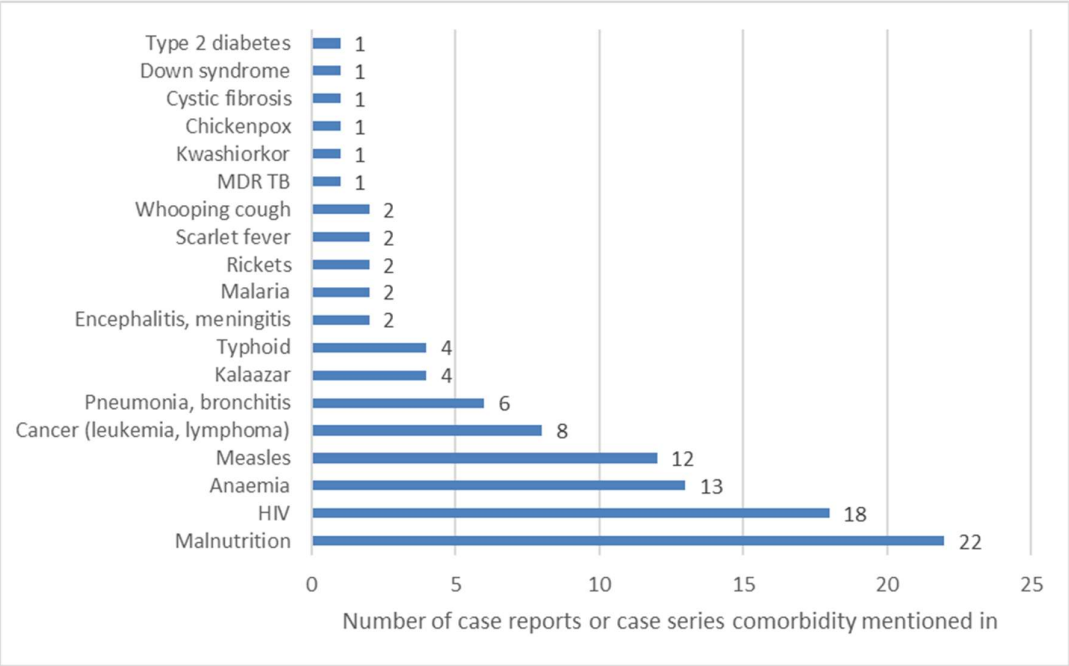
Millogo, 2012 [17]	Study type: Retrospective chart review from 1988 to 2007 Location: Burkina Faso n: 212 patients (n=14, 6.6% had HIV)	• Respondents mean age 15.3 years for HIV group, 4.7 years for non-HIV infected group • Concurrently HIV-infected patients had higher mortality (38% vs 6%)	Data collected retrospectively
Baratti-Mayer, 2013 [56]	Study type: Case control Location: Niger n: 82 cases and 327 controls	• Respondents aged 0-12 years • Severe stunting (Height-for-age Z score ≤3 SD) (Odds Ratio) (OR) 4.87, 95% Confidence Interval (CI) 2.35–10.09) • Wasting (WHZ ≤3 SD) (OR 2.45, CI 1.25–4.83), • High number of previous pregnancies in the mother (OR 1.16, CI 1.04–1.31) • Presence of respiratory disease, diarrhoea or fever in the 3 months prior to data collection (OR 2.70, CI 1.35–5.40) • Absence of chickens at home (OR 1.90, CI 0.93–3.88)	Age matching of cases not strictly followed, recall bias due to study design
Konsem, 2014 [107]	Study type: Chart review 2003 to 2012 Location: Burkina Faso n: 55 acute noma cases	• Respondents mean age 7.64 years • Concomitant Bronchopneumonitis (n=20, 36.4%) • Malaria (n=14, 25.4%) • HIV (n=11, 20.0%) • Low standard of living (n=21, 38.2%) • Anaemia (n=14, 25.4%)	Data collected retrospectively.
Adeniyi, 2019 [41]	Study type: Retrospective chart review from 1999 to 2011 Location: Nigeria n: 159 acute noma cases	• Respondents aged between 1–5 years (n= 139, 87.4%) • Concurrent disease at presentation or in the 3 months preceding their presentation at the hospital (n=148, 93.1%) • Measles (n=75, 47.2%)	Data collected retrospectively, lack of standardization of information collected.

		• Protein-energy malnutrition (n=67, 42.1%)	
WHZ- weight-for-height Z score OR = Odds Ratio SD = Standard Deviation CI = Confidence Interval WHO = World Health Organisation HIV = human immunodeficiency virus			

Reported comorbidities in the primary studies (case control, cohort, retrospective chart reviews) include malnutrition [22, 23, 41–43, 56], respiratory disease [56, 107], diarrhoea [22, 56], HIV [17, 20, 107], malaria [42, 107] and vaccine preventable diseases, specifically measles [22, 41, 42]. Most of the case reports and case series (n=68, 72%) listed at least one comorbidity. The most widely reported comorbidities in the case reports and case series included in this review were malnutrition [11, 28, 29, 32, 34, 81, 85, 88, 89, 120–122], HIV [13, 15, 18, 73, 121, 123], anaemia [20, 33, 89, 103] and measles [30, 65, 86, 101] (Figure 2.9). As this information is based solely on case reports and case series, primarily reported from health care centres, no causal link or strength of association can be measured. Infections are usually the product of a compromised host and a single offending agent or multiple offending agents. Due to challenges with conducting scientifically robust risk factor analysis for noma, it is difficult to separate comorbidities from predisposing conditions and true causative factors.

One theory for the higher incidence of noma in the two to five year age group, is that this is the teething age when deciduous teeth are formed, this tooth formation slows down the circulatory flow to the gums due to compression, leaving the oral cavity more susceptible to infections [117]. A Zambian study postulated that during the weaning period, children eat more solid food, which was less nutritious and less sterile than breast milk, and this placed them at potential risk for noma development [3]. Another study showed that if weaning foods are prepared under unhygienic conditions, they are frequently contaminated with pathogens and are a major factor in the cause of diarrhoeal diseases [124], a further reported risk factor for noma [59].

Figure 2. 9 Number of case reports and case series each comorbidity is reported in.



Studies that attempted to identify risk factors for noma were hampered by the retrospective nature of case ascertainment limiting the kinds and standardization of risk factor data collected [3, 17, 20, 22, 23, 41, 42, 107]. The absence of a suitable control group precluded the ability to find associations between noma and potential risk factors [3, 20, 22, 78, 117]. In other studies there was no statistically robust examination of risk factors using proven statistical methods such as multivariable regression (which would adjust for confounders), limiting the validity and reliability of results [8, 23, 40, 117]. More robust studies, in the form of either prospective cohorts, cross-sectional studies or case control studies are needed to understand the risk factors for the disease.

2.9 Gaps in the literature

There is a dearth of literature on noma. The date of the first study included in this review was 1843, and since this time, an average of one publication has been written on the disease per year (calculated based on the studies included in this review). Despite significant progress in scientific methods since the first study, the literature remains predominantly populated with case reports and case series of noma. Ideally, more scientifically robust studies are needed to better characterize the aetiology, risk factors and effective treatment and prevention measures of this neglected disease. The reasons behind this neglect include the lack of knowledge about the disease by healthcare workers [21, 125], the hypothesized low prevalence of the disease [1], which may, in part, be due to assumed inconsistent surveillance and reporting on the disease [41], the relative inaccessibility of the affected communities and the rapid progression of the disease. This inaccessibility is characterized by difficulties faced by these communities in accessing formal health care. As evidenced by this review, the changing patterns of noma mostly follow the changing global patterns of wealth and development. As countries have developed, access to health care and living conditions have improved and noma prevalence has

declined (besides the few continuing sporadic case reports). Currently, noma cases continue to be reported in the most underserved, remote and disenfranchised areas of Africa and Asia in particular [3, 7, 16, 18, 20–32]. In the absence of sound evidence-based public health measures, noma is likely to persist for the foreseeable future.

Based on this literature review, some of the main gaps in knowledge are enumerating the burden of disease (both incidence and prevalence); describing the true mortality rate and pathogenic cause(s) of noma and the role of different comorbidities (specifically measles and HIV) and social structures in the development of noma. Factors that influence prognosis and the long-term outcomes after care (surgical and non-surgical) [37] including the most effective antibiotic treatment protocols [6] need to be assessed. The knowledge of health care workers (biomedical and traditional) about noma in high risk areas, the number of medical school and tropical medicine curriculums that include noma; and the role the varying healthcare actors could play in prevention [126] also need to be explored. An additional area for future studies would be to compare prevention methods and messaging [21] to identify the most effective mechanisms.

2.10 Contextualizing the thesis

2.10.1 Nigeria overview

Nigeria, situated in West Africa (Figure 1.1) is home to more than 202 million people and is Africa's most populous country [127]. Nigeria is comprised of an overarching federal government, and then subdivided into 36 autonomous states with 774 local government areas [127–129]. There are 250 ethnic groups in Nigeria with three dominant tribes – the Ibo, Hausa-Fulani and Yorubu [130]. Over 500 languages are spoken across the country, Hausa is the

most commonly spoken language (spoken by 63 million people, predominantly in the north), English and Pidgin English are the most commonly spoken communal languages (spoken by 60 million people) [131]. The two main religions in Nigeria are Christianity and Islam which are roughly equally practiced by the country's population along a north-south divide, Christianity in the south and Islam in the north [130]. 1999 marked the year of return to democracy for Nigeria, and since then six democratic elections have taken place [128]. Prior to this Nigeria had a range of political systems in place. 1804 saw the creation of the caliphate in Sokoto, Nigeria which still exists today with the area being overseen by the Sultan [132]. The colonial takeover of Nigeria by Britain occurred in the 1800s [132]. The 1900s marked the rise in nationalism leading to independence in 1960 followed shortly thereafter in 1966 by the first of many coups [132]. Several secession attempts of various parts of the country were met with brutal suppression [132], the most notorious of these being the 1967 - 1970 Biafran war which led to the death of an estimated three million people, the majority of these were civilians who died due to starvation [133]. This conflict had many underlying causes but was largely linked to the economic value of the crude oil found in the Niger Delta, the region ear-marked for secession [133].

Nigeria is Africa's largest crude oil supplier [130] and has the largest natural gas reserves on the continent [128]. Fluctuating oil prices have seen the GDP growth drop from an average of 7% between 2000 and 2014 to the first recession in Nigeria in 25 years in 2016, when the economy contracted by 1.6% [128]. There is great inequality in Nigeria (Gini coefficient 43.0 (0 represents perfect equality, while an index of 100 implies perfect inequality)) [134]. Economic growth is too slow to lift the bottom half of the population out of poverty and growth projections remain dire indicating living conditions will worsen [128]. The core reason for the high levels of poverty in Nigeria are the high unemployment rates (23%) [128] paired with

widespread corruption and political instability [132]. Large sections of the population are unable to access basic services [128]. These issues are magnified in the north due to regional insecurity (discussed below) and non-inclusive development policies [128], 74% of the population in the north live below the poverty line vs 54% in the south [135].

Women are at increased risk of suffering from the effects of poverty as they are frequently excluded from many aspects of life including the economy, social society, politics and intellectual endeavours [130]. Violence against women is rife, 23% of women have reported being victims of physical or sexual violence [130]. Nigeria has reported more than 23 million girls married as children [130]. Higher rates of illiteracy are reported amongst females nationwide but this gender divide is magnified in the north where only 20% of women are literate and have attended school [130]. In many traditional Hausa speaking communities in the north (including the areas where data collection for this thesis occurred) many females are confined to their compounds after marriage where they are reliant on their husbands to provide all necessary goods (clothes, food, firewood etc.), non-family males are not permitted entry to these compounds [136, 137].

Several security challenges currently plague Nigeria. The most notorious is the Boko Haram insurgency in the northeast of the country which has resulted in 30,000 deaths and the displacement of over two million people [138]. The group is most well-known for their 2011 bombing of the United Nations headquarters in Abuja and the 2014 kidnapping of 276 school girls from Chibok which caused global outrange and bought the group much desired attention which has spurred it on to further kidnappings and mass casualty bombings [138, 139]. A less well publicised but even more deadly conflict is occurring in the northwest where rising levels of farmer-herder conflict have led to the death of thousands of people and the displacement of

hundreds of thousands [130, 140]. There has also been a rise of banditry and kidnappings for ransom in Nigeria [140–142], further increasing the levels of insecurity in the country.

2.10.2 Nigerian health system

The structure of the health system in Nigeria is complex. The three tiers of the Nigerian political system are responsible for the three tiers of the health system: the local government areas provide primary health care; the state governments provide secondary health care and the federal government provide tertiary healthcare [129]. Access to quality health care is a challenge in Nigeria, a lack of resources and differing allocations between these tiers have led to poor health outcomes in general in the country [129].

Health care is mostly reliant on patient service fees [129]. As of 2005, the WHO estimate that one night in a tertiary level hospital would cost United States Dollars (USD) 22, an outpatient visit to a secondary hospital would cost USD 5 and a 20 minute health centre visit would cost USD 7 [143]. These costs are catastrophic for households that earn a median household income of USD 2 per day [143].

Nigeria has one of the highest number of health care workers in Africa; however, at 1.95 health care workers per 1,000 population members [144], the number is still too low to effectively deliver essential health services with distribution of the health care workers largely confined to urban settings. Access to oral health services is also limited. There are an estimated 1.2 dentists per 100,000 population members [145]. In one Nigerian study, 94% of respondents (n=154, mean age 33.44 years (SD 2.34 years) living in rural areas) had never visited the dentist [146]. The violence and displacement mentioned above leads to further challenges in accessing health care for citizens as travelling is dangerous, and it also means a decrease in services reaching

these communities. This lack of access leads to significant poor health status and outcomes in this population [129, 147].

There is variation of the services offered and the coverage of the health system in the different states of Nigeria with northern states, where data collection for this thesis took place, being less well served than the southern states [129, 147]. Per capita government spending on health is greater in the south than in the north, and private companies employing people and contributing to their staffs health care is more common in the south than in the north [129]. This leads to more catastrophic health expenditure in the north than the south [129].

2.10.3 Noma in Nigeria

Nigeria stands out as a country with a high number of cases reported in the 1900's and 2000's [6–8, 23, 37–39, 41–43, 50, 64, 71, 81, 89, 99, 100, 102, 148]. This could be due to the presence of a dedicated noma hospital in Sokoto which is closely linked to an international network of researchers rather than as a result of the true distribution of this condition. The NCH staff [5, 6, 41] and members of international non-governmental organizations including the Dutch Noma Foundation who have supported programmes at the hospital [7, 21, 37, 38, 64, 99, 149] have frequently published on noma. The presence of a dedicated facility to support noma care has also likely improved detection and referral of noma cases in the region. There is also a culture of academic publishing in the country, Nigeria publishes the second most publications in Africa, second only to South Africa [150]. This could elevate the number of publications on noma, skewing assumptions on distribution. Only robust prevalence estimates derived from systematic surveillance efforts in settings where noma has been reported are likely to improve our understanding of the global burden of noma in other countries.

In terms of the comorbidities listed in this review, in 2011, 71% of children in Nigeria aged under five years were classified as anaemic (Haemoglobin (Hb) <110 g/L) [151]. The WHO reported that in Nigeria in 2017, there were 11,190 measles cases reported [152]. Immunization coverage in Nigeria for measles is estimated at 42%; much lower than the 70% average for Africa [152]. The fertility rate in Nigeria between 2010 and 2013 was 5.5 births per women (rural 6.2, urban 4.7), the median age at first birth is 20.2 years [153].

Given the national interest in noma, the unique health facility dedicated to treating noma and high prevalence of known risk factors for noma, this setting was identified as a unique setting for answering some of the outstanding questions around noma. The gaps in knowledge identified in this review have informed the goals and objectives of this thesis. By consolidating and expanding our knowledge on the prevalence, risk factors, beliefs, perceptions and traditional healing practices around noma, we hypothesise that we will be able to improve our ability to recommend interventions and approaches aimed at reducing the impact of this debilitating disease on children in northwest Nigeria.

2.11 Limitations

Given the inclusion time period of the review (from the 1800's to present) it is likely that some manuscripts (especially in the earlier years) were not available on current indexing systems and hence not included in this review. The candidate used Google Translate to translate non-English papers, which could have led to some misinterpretation as it is not an official academic translating service. The inclusion of published manuscripts only and not grey literature could have limited the amount of information identified.

2.12 Conclusion

Noma is a disease that affects young children in the most disenfranchised communities. It is a devastating, disfiguring and often fatal condition that requires urgent and intensive clinical and surgical care, often difficult to access in these settings. Noma has been reported in the literature for many hundreds of years. Given the assumed rarity of the disease and limited accessibility of the communities at greatest risk, there are limited primary epidemiological studies on the disease, with the majority of the literature being case reports. Little is understood about the offending organism(s) and preventable risk factors. The clinical presentation of each noma case is unique and depending on the stage of presentation, and extent of physical damage could require a variety of surgical, clinical and social interventions to manage. What is clear from the literature is the wide geographical spread of noma, the need for better controlled studies to identify the offending pathogens, understand and prioritise the risk factors in order to develop effective targeted interventions to reduce the burden of this condition in the most affected populations.

Chapter 3 Language and beliefs

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Additional resources

Question guides and informed consent forms used in this chapter can be found in Appendix 6.1 and Appendix 7.1.

Relevance of this paper to the thesis

There is limited literature on the names and beliefs about noma and the explanatory models around the disease in this setting. This manuscript explored the language used to describe noma along with the beliefs about the causes of the disease. The findings from this manuscript will be utilized in prevention programming and messaging in outreach activities at the NCH in Sokoto, Nigeria.

Contribution of the student and co-authors

EF, AL, EF, AF, KB and BS conceptualised the project. EF developed the protocol with input from all authors. EF and AA conducted the data collection. EF conducted the data analysis with guidance from BS. EF, AL and BS interpreted of data. EF wrote the first draft of the manuscript. All authors critically reviewed the manuscript and provided final approval.

3.1 Abstract

3.1.1 Background

Noma is an orofacial gangrene that rapidly disintegrates the tissues of the face. Little is known about noma, as most patients live in underserved and inaccessible regions. We aimed to assess the descriptive language used and beliefs around noma, at the NCH in Sokoto, Nigeria. Findings will be used to inform prevention programmes.

3.1.2 Methods

Five focus group discussions (FGD) were held with caretakers of patients with noma who were admitted to the hospital at the time of interview, and 12 in-depth interviews (IDI) were held with staff at the hospital. Topic guides used for interviews were adapted to encourage the natural flow of conversation. Emergent codes, patterns and themes were deciphered from the data derived from IDIs and FGDs.

3.1.3 Results

Our study uncovered two main themes: names; descriptions and explanations for the disease, and risks and consequences of noma. Naming of the disease differed between caretakers and heath care workers. The general names used for noma illustrate the beliefs and social system used to explain the disease. Beliefs were varied; participant responses demonstrate a wide range of understanding of the disease and its causes. Difficulty in accessing care for patients with noma was evident and the findings suggest a variety of actions taking place before reaching a health centre or health worker. Patient caretakers mentioned that barriers to care included a lack of knowledge regarding this disease, as well as a lack of trust in seeking medical care. Participants in our study spoke of the mental health strain the disease placed on them, particularly due to the stigma that is associated with noma.

3.1.4 Conclusion

Caretaker and practitioner perspectives may enhance our understanding of the disease in this setting and can be used to improve treatment and prevention programmes, and to understand barriers to accessing health care. Differences in disease naming illustrate the difference in beliefs about the disease. This has an impact on health-seeking behaviours, which for noma patients has important ramifications on outcomes, due to the rapid progression of the disease.

3.2 Introduction

Noma, also known as cancrum oris, is a neglected disease of extreme poverty. It presents as a rapidly progressing gangrenous infection of the oral cavity, and is associated with a high mortality rate [96]. Noma mostly affects children under the age of five years [94]; if untreated, it has been estimated that up to 90% of patients with noma die within weeks after the onset of noma [1, 154], and those who survive have severe facial disfigurements [94]. Due to the widespread destruction of the facial structures including the cheek, nose, lips and eyes, patients with noma also have multiple physical impairments such as difficulty eating, seeing and breathing, and many suffer from stigmatization in their communities [2]. Noma is thought to be most prevalent in low socioeconomic regions in Africa and Asia [2]. The WHO estimate that 140,000 new cases of noma occur annually [1], however this figure is debated due to a lack of robust evidence on the epidemiology of the disease.

Since 2014, MSF has collaborated with the Nigerian Ministry of Health to treat noma patients identified across the northwest of Nigeria, at the NCH in Sokoto. This program provides nutritional, psychosocial, and surgical interventions for patients with noma. Identification of patients with noma relies on active case detection within villages through extensive outreach

activities and widespread communication campaigns to raise awareness of the existence of the NCH.

There is still much to learn about noma, as most patients live in difficult to reach areas, and the disease often goes undiagnosed and is under-reported. Given that many cases occur in underserved areas, few studies have aimed to explore and describe societal and community perceptions of this medical condition. One study in the medical literature examined the language used to describe noma in Hausa (the predominant language in northwest Nigeria). The term most commonly used was "ciwon iska", which translates to 'the disease of the wind' [64]. Language used to describe diseases carry culturally determined associative meanings [155] and have been reported to affect people's conceptions of disease and the health care options they choose [156].

Understanding and using appropriate language is one of the cornerstones of ensuring an effective communication strategy with patients, as well as their families and communities. We conducted this qualitative study to gain an understanding of the locally used descriptive language and concepts of noma. Specifically, we aimed to understand the perspectives of family members of patients with noma and treating practitioners. We anticipated that our findings would inform future interventions and prevention programmes.

3.3 Methods

3.3.1 Setting

The NCH in Sokoto, northwest Nigeria, has provided treatment for patients with noma for many years, and, since 2014, MSF has supported noma initiatives at the hospital.

3.3.2 Study Design

A descriptive qualitative research design was used in which data was gathered from caretakers of patients with noma and staff at the hospital using FGDs and IDIs guided by topic-led questions. Both IDIs and FGDs were carried out using themes relevant to the study aims, adhering to the open-ended, qualitative interview procedure. The choice of methods was used to gain a rich understanding of the topic specifically the patient and practitioner perspectives of the disease [157].

3.3.3 Recruitment and Sampling

Five FGDs with adult caretakers were conducted between June and July 2017 (predominantly the mothers, grandmothers or fathers of the patient with noma) who were looking after the patients at the hospital as were 12 IDIs with healthcare staff. Convenience sampling was paired with multivariate sampling (the selection of a wide range of participants from both urban and rural areas and a mix of male and females) to ensure a wide variety of participants for the five FGDs. The research assistant (AA) selected men and women for the groups separately, due to the social norms of this region, respecting any cultural sensitivities. There were three female groups and two male groups as the majority of caretakers were female. FGDs were composed of not more than eight participants at a time. Vignettes were used to encourage participant reflections [158] on relevant life memories, and current experiences related to noma were explored. Purposeful multivariate sampling (participants selected who would offer the widest variety of information) [159] was used to recruit healthcare staff members for in-depth interviews in order to ensure rich descriptive data from a diverse group. Twelve staff members were actively selected at the NCH, by which time data saturation occurred [160]. Three male program management staff, one male and four female medical team members and three male and one female paramedical staff members were selected (laboratory, mental health, pharmacy,

nutrition staff).

3.3.4 Data Collection

Interviews were audio-recorded in quiet, private, locations that were familiar to participants. All FGDs were conducted by AA in Hausa; the Principal Investigator (EF) conducted the IDIs in English as all respondents were fluent in English. AA translated transcriptions of recorded interviews verbatim from Hausa to English. Confidentiality was enabled for all participants by replacing the names of the respondents and all data referring to them with numerical codes indicating the type of sample (IDI for in-depth interview; FGD for focus group). During the FGD, participants agreed to keep confidential what was discussed during the group session. Both FGD and IDI respondents were reassured that data that could potentially identify a person or location was anonymized using pseudonyms that could not be traced back to them. Electronic data were password-protected.

3.3.5 Data Validation and Analysis

Data validation was conducted through continual checking throughout the IDIs and FGDs; by repeating an understanding of what participants were saying throughout the interview, to ensure a correct and clear interpretation.

Data analysis started from the moment data were gathered. Data were initially managed through reading and re-reading all transcriptions of recorded conversations allowing for familiarisation and initial coding of data. EF and BS manually analysed the data by highlighting words, phrases or paragraphs, which then emerged into codes that were constantly compared. Participant responses from IDIs were compared with FGD findings. Common

patterns and themes were identified. Points of agreement and divergent themes were established through this process.

3.3.6 Ethics

Ethical approval was obtained from the MSF, UDUTH and the Sokoto and Kebbi States Ministry of Health ERBs. Informed consent for interviews and audio-recordings were sought using an information sheet translated into Hausa stating the purpose of the study and the voluntary nature of participation. All interviewees were over the age of 18 and each participant provided written informed consent (for participants who were illiterate, the consent form was read aloud to them and a thumbprint was then requested). All participants were assured that there was limited risk of harm from participation in this study, and that they were free to withdraw at any point.

3.4 Results

We present two themes that emerged during analysis: naming and explanations for noma (Table 3.1 and 3.2) and risks and consequences of noma (Table 3.3). We illustrate our findings through quotes from participants.

Table 3.1 Names used by caretakers and staff to describe noma.

	Caretakers	Staff
Danhurawa	X	
Tuareg	X	
Akin	X	
Ciwon iska	X	X
Ciwon daji	X	X
Ciwon/maci dan wawa	X	X
Zaizayar baki		X
Noma		X
Sakiya		X

Table 3.2 Naming and explanations of noma with illustrative quotes.

Names	
Caretakers	
"Danhurawa" that is the name we called it. Danhurawa that is the name we called our own. Everyone that comes to see it will say yes it is the one. They will say that she is suffering from it.	FGD 1, female
They called "iska" and another name is "maci dan wawa" which eats the gums that is the names I know iska and maci dan wawa. maci dan wawa eats the teeth and eats the mouth and make a hole just like this one	FGD2, male
They called the disease "disease of Tuareg" and another name is like Akin	FGD 2, Male
They were saying it was ciwon daji (cancer)	FGD 3, Female
Health care staff	
The word noma itself in the local language it means farming. So often they mixed it up with farming.	IDI 3, Male, Paramedical
The only name they given to the disease either they say ciwon daji locally which is example like is disease from the bush.	IDI 7, Male, Paramedical
Ciwon daji!	IDI 9, Female, Medical
They always call it noma	IDI 11, Female, Medical
Beliefs and explanations	
Caretakers	
This disease is caused by insect, even the measles they did is caused by an insect, insect from the bush. This insect of these Jinn is also an insect. The measles they called is also an insect from the bush.	FGD 1, Female
(I) am sure it is one of the traps of iska (Jinn).	FGD 2, Male
Measles is the cause of the disease.	FGD 3, Female
Some will say it is (caused by) a bird. We told you that if someone get the disease they will say that the bird has catch him, it will make your mouth to swell up until they poke it and it will burst out and destroy the mouth by falling off. It is all happening.	FGD 3, Female
It is God that brings the disease; God gave you the disease	FGD 3, Female
It was henna that is the cause. It was henna that my mother applied on me (henna beautifully designed) then she put me on her back then a witch saw me but then nobody knew that she was a witch. She then said this henna that you put on her? Is so beautiful! That is all she said! Then people said that my mother should quickly cover my legs. The next day an abscess came out that is the first thing that people saw. After a week then I changed and transformed to what I am today.	FGD 3, Female

Health care staff	
The patients believe that it is because of evil cast or evil eye.	IDI 1, Male, Non- medical program staff
I think I have heard someone saying it's like witchcraft.	IDI 3, Male, Paramedical
They (patients and caretakers) have a strong belief that whatever happened is from God.	IDI 3, Male, Paramedical
It is just evil spirit that is responsible for it. They don't believe that it is medical problem.	IDI 6, Female, Paramedical
They always believe it is iska that is the belief; iska they believe is just like a wind or let us say Jinns. This Jinn are something that are in between us but we cannot see them, Jinn can appear in trees and in wind in something, or that is they believe that the Jinns are the ones that came in and cause such kind of problem.	IDI 7, Male, Paramedical
FGD- focus group discussion, IDI- in-depth interview	

Table 3.3 Risks and consequences of noma with illustrative quotes.

Access to Health Care	
Caretakers	
After some few days we heard the news of this hospital. They said that they can treat this type of case. Then they prayed and wish us well and success. Then we were told to hurry and go there so that we can confirm that they can really treat the disease. When we arrived, there was a test being carried out and we told that it is possible. Then they show us. All praise be to Almighty Allah he is much better now. We are optimistic that it will be successful.	FGD 4, Male
But if it is the village, they will be given a treatment that is different from the disease. You will be struggling to get the medicines while the sickness will be spreading. You will be running up and down looking for treatment while disease will be expanding.	FGC 4, Male
Health care staff	
I can say that noma is not widely known, and this is the only hospital which is exclusively dedicated for the noma children disease. The one of its kind and then more than 300 patients have benefited from the plastic surgeries, re-constructive surgeries.	IDI 1, Male Non- medical program staff
We go to all the LGAs in Sokoto, Kebbi and Niger State. We do active case findings that mean trying to find new patients. Also, we do health promotion along the way.	IDI 1, Male, Non- medical program staff
Impact of the Disease	
Caretakers	
People run away from whatever you use, just because someone's mouth has cut they will say they will not eat with him.	FGD 2, Male
When you get this disease some people will be discriminating you, some will be running away from you. But you will not be very happy in life.	FGD 3, Female
After some time it will form water then they will poke it (using the traditional hot iron) after that then the mouth will burst out and fall off.	FGD 3, Female
We were collecting traditional medicines. We were given it to him. We were using Traditional medicines. Woods, powder and so many different types was given to him.	FGD 4, Male
The issue is that it destroys and eats the gums, destroys someone's mouth, that people is destroyed also; there is no destruction that is more than this.	FGD 2, Male
After some days before a week she changes and transform to this.	FGD 3, Female
What scared us more and makes us to quickly rushed here was that it was itching him and he was scratching it the suddenly I saw his fingers going inside the mouth area where the disease has affected it cut and falls off.	FGD 4, Male

Health care staff	
The success story I would like to share is from a patient that had noma for a long time and she was operated in Lagos without success, she was operated in Ibadan without success. Until somebody saw her (a doctor who has worked at NCH before). The doctor saw her covering her face and she wrote a letter for her to come down to Sokoto. So she got surgery about two, three surgeries, she is fine and she is even an employee of this hospital. So is a good story.	IDI 4, Female, Medical
He is always afraid of people because he stays in the bush. So I have to tell him that these people you are seeing they are just like your friends and your colleagues we are here to help you we will not do anything to harm you. Before he was discharge he has plenty friends in the ward he will go to this bed he will gist (talk with) he will go to that bed jumping from one ward to the other.	IDI 9, Female Medical
FGD- focus group discussion, IDI- in-depth interview	

3.4.1 Naming noma

The most commonly used name among the health care workers was noma. One important finding was that:

> *"The word noma itself in the local language means farming. The word noma, the same spelling, the same pronouncement, so often they (patients) refer to it in the context of farming"* (IDI 3).

Several names for the disease were given by the FGD participants:

> *"In our place we called it ciwon daji"* (FGD 4).

Naming of the disease differed between caretakers and heath care workers. Table 3.1 explores these differences, and suggests only a few overlapping terms; ciwon iska, ciwon daji and ciwon/maci dan wawa.

3.4.2 Beliefs and explanations

Names form a part of the understanding of the disease in this setting; the broad names used for noma such as ciwon daji are described in association with the beliefs and social system used to explain the disease. Caretakers shared several terms for the disease as well as beliefs about why and how the disease is caused. The three causative categories that were identified were spirits, living creatures (insects and animals), and connections with previous illness.

Spirits including Jinn and God were frequently reported:

> *"(I) am sure it is one of the traps of Jinn"* (FGD2),
>
> *"They always believe this thing happens (because) God allow it to be"* (IDI7).

Jinn was described as the world of other creatures that we cannot see. The world of Jinn is a spiritual realm all around us filled with normal people leading normal lives. There are good Jinn and bad Jinn, and Jinn can enter human bodies and cause harm:

> *"Jinn are something that are between us but we cannot see them. Jinn can appear in trees and in wind in something, Jinns are the ones that came in and cause such kind of problem (referring to noma)"* (IDI 7).

Some respondents linked the disease to evil spirits or people:

> *"One of the patients believed that it is because of evil cast or evil eye"* (IDI 1),
>
> *"It is just evil spirit that is responsible for it"* (IDI6).

Various animals and insects were also mentioned as the potential cause behind noma:

> *"This disease is caused by insect; even the measles they did is caused by an insect. Insect from the bush"* (FGD 1).

Previous infections were also noted as a potential cause:

> *"Measles is the cause of the disease"* (FGD 3).

Whilst beliefs are varied, the participant responses demonstrated a broad range of understandings about the disease and as such, it is thought to exist for multiple reasons.

3.4.3 Risks and consequences: access to health care

Caretakers in our study stated they had taken patients to other health centres before being advised to go to the NCH:

"We took him (to) Binji Town, Binji Hospital, they diagnose him and checked him, then they said go to Noma Hospital, that is the only place you can get treatment for this and that is why we came here" (FGD 2).

Other first points of care were traditional healers, community health centres and private doctors. Treatment options were varied, some attempted to treat the initial oedema phase of noma:

"After some time it will form water (swelling) then they (traditional healer) will poke it (using the traditional hot iron/knife) after that then the mouth will burst out and fall off" (FGD 3).

Others struggled to find suitable treatment:

"You will be struggling to get the medicines while the sickness will be spreading. You will be running up and down looking for treatment while disease will be expanding" (FGD 4).

This suggests a combination of actions taking place before reaching a health centre or official health worker. Some participants mentioned barriers to care including a lack of knowledge about the disease and a lack of trust in the health system as well as distance from care:

"People are coming from very far distance; they said that some people are even coming as far as Kaduna they are coming here" (FGD 1).

Limited access to prescribed medication was also reported:

"You will be struggling to get the medicines while the sickness will be spreading" (FGD 4).

"As we want to come to the hospital, everyone is saying not to go as we will just be wasting our time. Then some people said how can we see this situation of life and death and just give up we have to try and save a life by seeking for treatment?" (FGD 1).

"Back home they will only be trying this and that because they don't know what it is and they don't know anything about it" (FGD 4).

3.4.4 Impact of the disease

The impact of noma is not just limited to physical presentation; participants in our study spoke of the strain on their mental health that the disease placed on them as caretakers, with stigmatization highlighted as a key difficulty:

"It cannot allow you to enjoy your life when you are in the company of people. You will not be happy when you are mingling with people. They will not include you in their important discussions. They will not like to sit with you. They will not eat food with you. The only thing is that you will be hiding yourself" (FGD 4).

Caretakers spoke of the physical impact of the disease and its rapid progression along with concomitant infections:

"From the time (the patient had) measles to the time that she started this disease (noma), it was just two weeks" (FGD 1).

The stages of noma were reported as moving rapidly from a swelling of the mouth, to the disintegration of the cheek:

"Her own started with the swelling, then the swelling will go down and again it will swell, after some time then the mouth was destroyed on the lower lip. Then the flesh

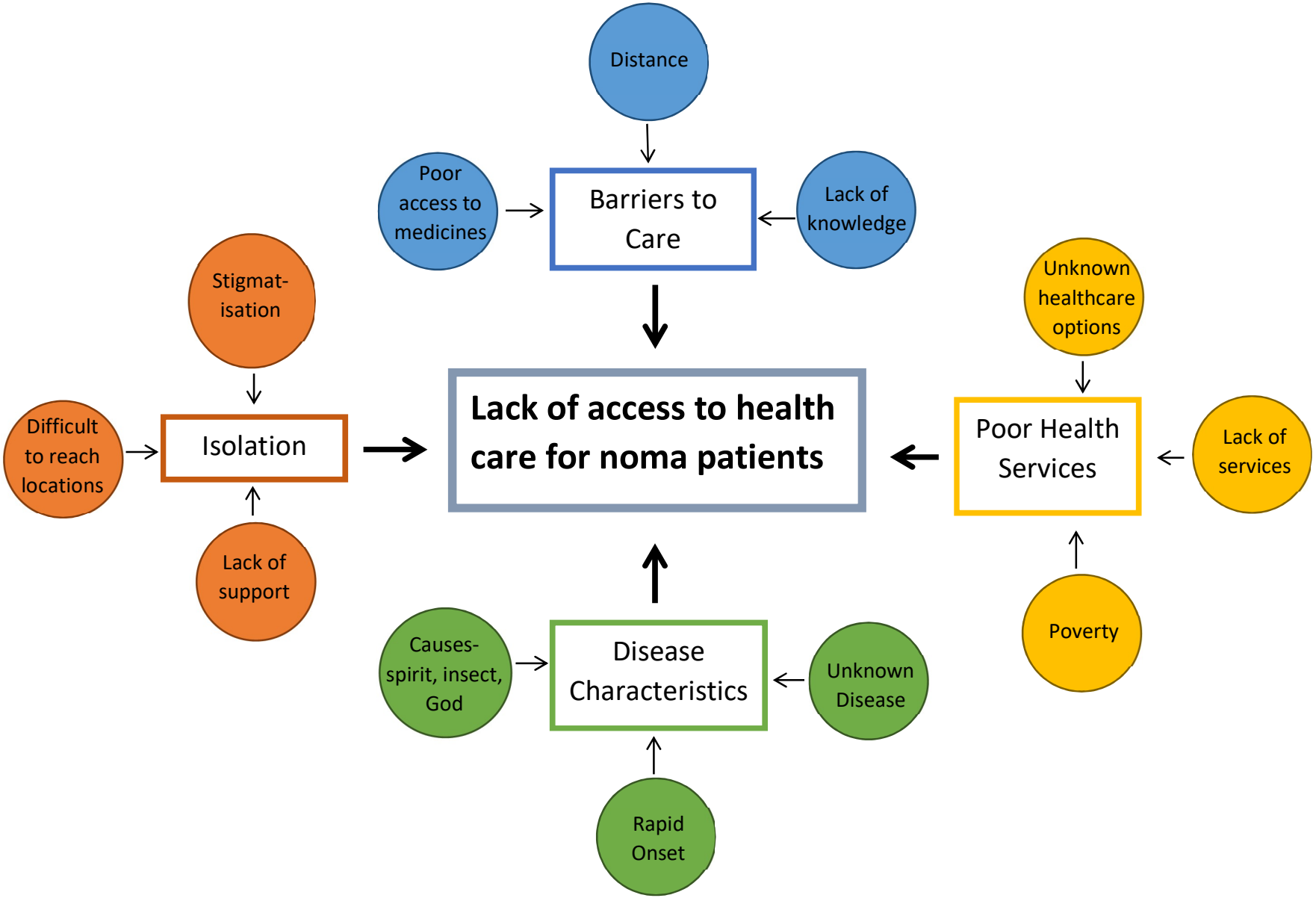
was coming out and falling off that is all. One day the mouth cut off, it was infected and destroyed, in just a day" (FGD 1).

Health workers spoke of destructive patient interactions and stories were mentioned which indicated the impact stigmatization and social isolation have on the mental and physical health of patients and caretakers (also highlighted in [161–164]):

"He (patient) is always afraid of people because he stays in the bush. So, I have to tell him that these people (other patients) you are seeing they are just like your friends and your colleagues we are here to help you we will not do anything to harm you. Before he was discharged he has plenty friends in the ward he will go to this bed he will gist (talk with) he will go to that bed jumping from one ward to the other" (IDI 9).

The isolation that caretakers and healthcare professionals reported may influence the ability patients have to access health care and for outreach messaging to reach them. The lack of access to care for patients with noma is explored further in Figure 3.1.

Figure 3.1 Analytical framework, lack of access to care.



3.5 Discussion

3.5.1 What's in a name?

Our primary emergent theme, naming of noma, shows this to have multiple attributes in northwest Nigeria. Diseases often have multiple names, and frequently the most common name is only one of multiple reported for a single disease. Naming of diseases can originate from visible symptoms; work on lymphatic filariasis in Nigeria has reported that local names for the disease include "elephant legs" and "swollen legs", which appropriately describe the visible manifestation of the disease [165]. Other naming options come from expected causes or, quite commonly in biomedicine, diseases are named after the individuals involved in historical descriptions, such as Alzheimer's or Parkinson's [166].

Noma is a Latinised form of a common Greek word, and is a metaphor for the continuing process of a wildfire [64]. This metaphor links conceptually with the rapid progression of the disease, as does the Hausa word ciwon iska, which loosely translates to 'the disease of the wind' [64], this could also refer to the understanding of disease transmission (spirits or animals travelling by the wind). The naming of noma as ciwon daji which loosely translates to 'cancer' in English is also of interest, as this is similar to a biomedical name for the disease which is frequently used, cancrum oris, meaning mouth cancer [64]. Some of the other names for noma used by staff in our study were different to those used by patients. Health care workers in our study most commonly reported using the word noma when discussing the disease; this is expected, as it is the name used most commonly in the biomedical community. Noma, however is not the only name used in this community to describe this disease; other terms include necrotizing ulcerative stomatitis and cancrum oris [64]. Our results suggest that the name most commonly used by patients to describe noma was ciwon daji. The use of names such as ciwon

iska by caretakers shows a naming system more linked to a spiritual conceptualisation of the disease, and limited biomedical understanding of the disease process.

A further novel finding from this work is that the word noma in Hausa means farming. This has the potential to cause confusion during awareness campaigns and should be taken into consideration during the planning phase. The commonly used names for identifying noma should be incorporated into all messaging used in noma prevention and treatment programmes. This will create clearer communication between project staff, the community, patients and their caretakers and allow for an incorporation of more comprehensive language around this disease to ensure messaging is clear and effective.

3.5.2 Explanations for noma

The way diseases are described and understood can differ between people and groups due to a wide range of perceptions and shared social understanding of the illness, differences in language used [156], understanding of the clinical diagnosis itself [167], and the value judgements placed on these concepts [168]. Producing an explanatory model of disease [169] can provide a significant contribution to effective treatment programmes and therefore positive program outcomes. An explanatory model for noma was formed as the names used for noma were seen to be associated with a social understanding about the disease, which can be shown to impact upon what care is sought or followed by patients.

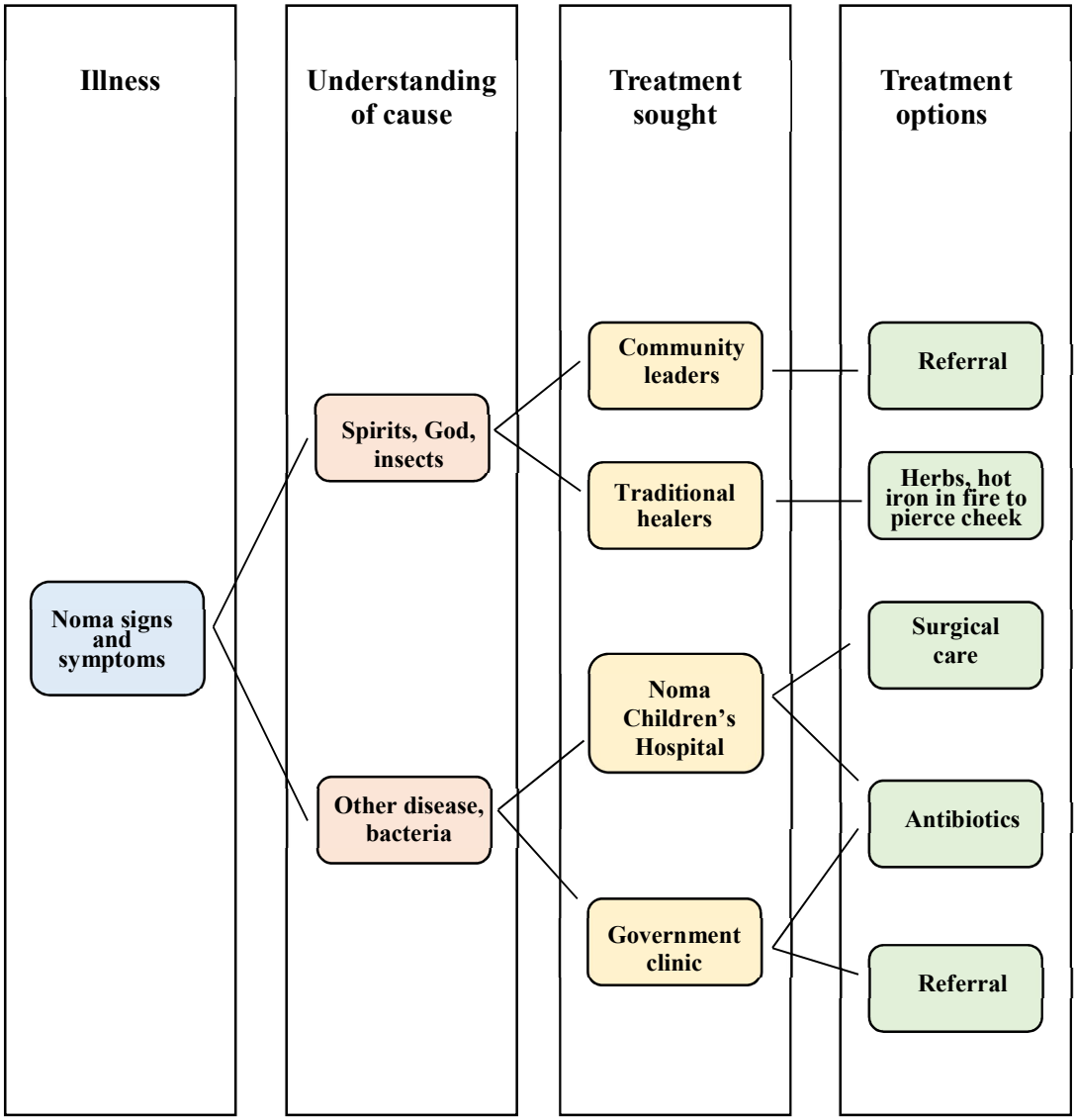
There is limited literature on the explanatory models around noma in this setting. However, a study on models for health-seeking behaviour for leprosy patients in Adamawa State, central Nigeria has shown that the majority of respondents explained the illness in terms of traditional beliefs and as 'God's wish'[170], as did patients in a further Nigerian study on orofacial clefts

[171]. The leprosy and cleft participants in these studies reported seeking help from alternate health sources, for example traditional healers [170, 171], as did a study assessing health-seeking behaviours for hypertension in Nigeria [172]. Patients were all able to identify what disease they had by name in both the leprosy [170] and hypertension [172] studies, which indicates that these diseases are better understood in the Nigeria context than noma.

From our findings, the notion that noma is linked to the spirit world, is reiterated in a study from northern Nigeria. In that work, it was reported that not much was known about noma in those communities, and as such, broad names such as 'ciwon iska' (disease of the wind) were used [64]. During our interviews, the caretakers explained iska as being sent by 'Jinn', the spirit world. This name links noma to the spirit world and offers insight into the potential explanation for noma in this community. If caretakers believe noma has a spiritual cause, this could explain why many caretakers seek care from traditional healers. Traditional healers typically offer treatment strategies which probe deeply into the psychological, spiritual, and social contexts of illness [173], as well as physical treatment including piercing the cheek with a sharp object and/or offering herb mixtures to place on the wound or ingest.

Our findings suggest there is no primary explanation within this community for the disease; biomedical beliefs are less dominant, thus suggesting a pluralistic understanding of the disease. The neglected nature of this disease could contribute to and exacerbate this. As so little is known about the disease globally, there is limited knowledge to share on prevention. This has an impact on the care that is sought with consequences such as poor linkage to treatment, under-reporting and poor outcomes for patients. Our findings suggest that a caretaker's knowledge and explanations for the disease may affect health-seeking treatment decisions (Figure 3.2). The beliefs people hold about disease have been shown in other studies to impact health-

Figure 3.2 Explanatory model for noma.



seeking behaviours [155, 156, 174–176]. Figure 3.2 illustrates how beliefs can result in certain actions. We do however, note that decisions are very unlikely to be as simplistic as illustrated in the diagram, and that several different actions could take place due to a certain set of beliefs.

3.5.3 Risk and consequences of noma

Access to health care in this part of Nigeria is difficult, health care is expensive and poor infrastructure makes transportation to health facilities challenging [177]. A lack of access to healthcare has been widely reported as a risk factor for noma development [7, 32, 75, 94], and our results add weight to these assertions in that caretakers mention the difficulties they experienced accessing care for this disease. The rapid progression of noma, lack of access to care, and the delays caused by caretakers having to progress through several facilities (clinics or traditional healers), means that resulting morbidity and mortality can be severe.

The impact of noma is multifactorial; both caretakers and health workers in our study spoke of the mental health strain the disease placed on both patients and caretakers. The social isolation caused from stigmatization of diseases is well documented [161–164]. Mental strain caused by social isolation has a wide ranging impact and can negatively affect both the mental and physical health of patients and their families [161–163]. Caretakers described the physical impact of the disease and its rapid progression along with associated links with concomitant diseases. The stages of noma were reported as moving from a swelling of the mouth, to the disintegration of the cheek skin, which follows clinical descriptions in the literature [1].

Names, beliefs, access to health care and the impact of noma are all interlinked, and form a web of issues that compound the ruthlessness of the disease. The strength of this study is that it explored the topic from two perspectives; that of the caretakers of patients, and the healthcare

staff at the NCH. There were several limitations to the study, the caretakers being interviewed were already at the hospital, and had likely had education on the disease from hospital staff prior to our interviews, and the beliefs they reported could have been different from caretakers in the population who did not reach the hospital. This bias could be mitigated by conducting a similar project with community members who do not have a family member affected by the disease. Further research needs to focus on the link with traditional healing, understanding the true burden of the disease and the pathogenic cause. This would enable efficient prevention programmes to be formulated.

This chapter has offered an overview of the naming, explanatory models for and risks and consequences of noma in northwest Nigeria. Caretaker and practitioner perspectives enhance a better understanding to support case finding, referral and knowledge on barriers to care. The impact of the differences noted between the names used between health workers and patients is apparent. Different naming of diseases illustrates the difference in beliefs and has an impact on health-seeking behaviour, which for noma patients, has severe ramifications due to the rapid progression of the disease. Other areas where noma is endemic would benefit from similar assessments that include patient caretaker and practitioner perspectives to ensure a comprehensive understanding of the contextual issues and explanatory models of the disease. The commonly used names for identifying noma should be incorporated into all messaging used in the noma prevention and treatment programmes.

Chapter 4 Risk factors

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Additional resources

The questionnaire and informed consent forms used in this chapter can be found in Appendix 6.2 and Appendix 7.2.

Relevance of this paper to the thesis

Noma is a preventable disease, however there is limited knowledge on what the risk and protective factors are for noma. This chapter presents an analysis of risk factors for diagnosed noma in northwest Nigeria. The findings from this manuscript will be utilized in prevention programming and messaging in outreach activities at the NCH in Sokoto, Nigeria.

Contribution of the student and co-authors

EF, AL, NMJ, ASA, SvdK and KP conceptualised the project. EF developed the protocol with input from all authors. EF conducted the data collection. EF conducted the data analysis with guidance from AL and CA. EF, AL and CA interpreted of data. EF wrote the first draft of the manuscript. All authors critically reviewed the manuscript and provided final approval.

4.1 Abstract

4.1.1 Background

Noma (cancrum oris), a neglected disease, rapidly disintegrates the hard and soft tissue of the face and leads to severe disfiguration and high mortality. The disease is poorly understood. We aimed to estimate risk factors for diagnosed noma to better guide existing prevention and treatment strategies using a case-control study design.

4.1.2 Methods

Cases were patients admitted between May 2015 and June 2016, who were under 15 years of age at reported onset of the disease. Community controls were individuals matched to cases by village, age and sex (three per case). Caretakers answered the questionnaires. Risk factors for diagnosed noma were estimated by calculating univariable and multivariable ORs and adjusted odds ratios (aOR) and respective CI's using conditional logistic regression.

4.1.3 Results

We included 74 cases and 222 controls (both median age five (interquartile range 3, 15) years). Five cases (6.5%) and 36 (16.2%) controls had a vaccination card (p=0.03). Vaccination coverage for polio and measles was below 7% in both groups. The two main reported water sources were a bore hole in the village (cases n=27, 35.1%; controls n=63, 28.4%; p=0.08), and a well in the compound (cases n=24, 31.2%; controls n=102, 45.9%; p=0.08). The multivariable analysis identified potential risk and protective factors for diagnosed noma which need further exploration. These include the potential risk factor of the child being fed pap (type of porridge staple made from maize, sorghum, or millet), every day (aOR 9.8; CI 1.5, 62.7); and potential protective factors including the mother being the primary caretaker (aOR 0.08; CI 0.01, 0.5) and the caretaker being married (aOR 0.006; CI 0.0006, 0.5).

4.1.4 Conclusion

This study suggests that social conditions and infant feeding practices are potentially associated with being a diagnosed noma case in northwest Nigeria; the findings warrant further investigation into these factors.

4.2 Introduction

Noma or cancrum oris, is a poorly understood, rapidly progressing gangrenous infection of the oral cavity, associated with a high mortality rate [1]. It mostly affects children under the age of five years [1]. It is estimated that if left untreated, up to 90% of noma cases die within weeks after the onset of noma [1, 154], and those who survive have severe facial disfigurements [94]. These can result in multiple physical impairments such as difficulty speaking, swallowing, eating, seeing and breathing which can lead to stigmatization in their communities [2]. The majority of cases are currently reported in Africa [3, 7, 16, 18, 20–23] and Asia [21, 24–32]. However, over the past 15 years, there have been sporadic reports of cases originating and being treated in Turkey [33], Afghanistan [34], Italy [35], the United Kingdom [36] and the United States [11]. A northwest Nigerian-based study concluded that the incidence of noma is estimated to be 6.4 per 1,000 children from 1996 to 2001 [7], and the WHO estimates that 140,000 children contract noma each year globally [19].

Little is understood about noma as most cases live in underserved, difficult to reach locations, many cases go undiagnosed and the mortality rate is so high. Previous observational studies have suggested that risk factors for the development of noma include malnutrition, low birthweight, absence of breastfeeding, poor oral hygiene, comorbidities, proximity of livestock to area of residence, large family size, access to unsafe drinking water and living in a village

with a high prevalence of acute necrotizing gingivitis [1, 2, 34, 43, 56]. Recently, an increased incidence of noma has been reported in higher resource settings in patients with immunosuppressive diseases such as HIV [17, 20, 107].

Since 2014, MSF has collaborated with the Nigerian Ministry of Health to treat noma patients identified across the northwest of Nigeria, in Sokoto. The program provides nutritional, psychosocial (for the patient and their families) and medical care to prepare noma patients for the required surgical interventions at the NCH. These are conducted by Nigerian Ministry of Health and MSF surgical teams on a routine basis; since August 2015, the program has treated 227 noma patients. We conducted a case-control study to identify risk factors for diagnosed noma in terms of demographic characteristics, medical history, socioeconomic-behavioural aspects and access to health care in order to better guide existing prevention and treatment strategies for this neglected disease.

4.3 Methods

4.3.1 Setting

The study was conducted in Sokoto and Kebbi States, which are located in northwest Nigeria.

4.3.2 Study population

Cases were defined as patients with diagnosed noma admitted to the NCH between May 2015 and June 2016 who were under 15 years of age at self-reported onset of the disease. Controls were individuals matched to cases by village of residence, current age (±2 years) and sex.

4.3.3 Sample size

Our aim was to include all cases enrolled at the NCH in the year before data collection, and we calculated that with a sample size of 67 cases and 200 controls (three controls per case), we would be able to estimate an OR of 2.5 for suspected risk factors with a power of 80% and 60% of controls being exposed to that risk factor. Controls were selected from houses neighbouring those in which the cases and their families live.

4.3.4 Data collection

Parents or caretakers of cases and controls were asked questions, topics covered included sociodemographic characteristics (age, gender, education, employment, total household members), their current living conditions (water source, proximity to livestock, material of houses) and their vaccination history (read on vaccination card if available). Additionally, parents and/or caretakers were asked to respond to questions pertaining to the duration of breastfeeding after the cases and controls were born and other nutrition-related practices during the neonatal period and current practices. The health status, access to health care and health care seeking behaviour for the case or control in the previous 12 months were also assessed. Finally, all cases and controls aged less than five years at the time of interview had a mid-upper arm circumference (MUAC) measurement taken at the time of the interview.

The questionnaire was formatted in KoBoCollect (KoboToolBox ©) and uploaded to tablets for mobile data collection purposes. Completed questionnaires were uploaded daily to a secure MSF server through an internet connection. The study co-ordinator verified all completed questionnaires on a daily basis for data consistency and quality.

4.3.5 Data analysis

We calculated the frequencies and respective proportions for all categorical variables and used chi-square tests for comparison of these variables between cases and controls. For continuous variables, we calculated means with SD or medians and interquartile ranges (IQR) (depending if approximately normally distributed) for cases and controls separately, and used t-tests to compare normally distributed variables, and Kruskal Wallis tests for non-normally distributed variables.

Food variables for current feeding practices were categorised as animal products (meat, milk, egg), grains (fura, mashed rice, millet, corn, bread) and vegetables (sweet potato, beans, bean cake, moringa leaf, ground nut cake, cassava). Respondents could answer with 'Yes', 'No' and 'Don't know'. We grouped all responses for 'No' and 'Don't know' into a single category. To investigate the impact of this grouping, we conducted a sensitivity analysis for each of these variables. As the results showed that the direction of association remained the same, we retained this grouping as the reference category.

We estimated risk factors for being a diagnosed noma patient by comparing odds of exposure in cases and controls using univariable and multivariable conditional logistic regression to calculate OR and their respective CIs and p-values. The multivariable conditional logistic regression model was constructed using all risk factors that had a p-value of <0.2 in the univariable analysis and sufficient outcomes in each category. Variables were eliminated from the multivariable model using a manual backwards stepwise approach [178], and multivariable models were compared using the likelihood ratio test, any variable with a p-value under 0.2 was kept in the model. All data analyses were conducted with Stata 14 (StataCorp, College Station, TX, USA).

4.3.6 Ethics

Ethical approval was obtained from the MSF, UDUTH and the Sokoto and Kebbi States Ministry of Health ERBs. All interviewees were over the age of 18 years and written informed consent was provided by each participant (for participants who were illiterate, the consent form was read aloud to them and a thumbprint was then requested). Caretakers were defined as the primary caretaker of the child in question. All participants were assured that there was limited risk of harm from participation in this study, and that they were free to withdraw at any point.

4.4 Results

4.4.1 General findings

Out of the 112 noma patients who had sought care in the program between May 2015 and June 2016, we identified 87 who lived in Kebbi and Sokoto States and were eligible for inclusion in the study. Of these, ten could not be located, and we managed to interview 77 cases (88.5%). We were unable to reach the village of three identified cases for logistical reasons. Thus, the final analysis included 74 noma cases and 222 controls. Six of the cases had died in the time between discharge and the interview; the interviews were still conducted with their caretakers. At the time of first admission to the hospital, 17 of these cases had acute noma, 57 had inactive noma, two had trismus and one had no diagnosis noted at time of admission to the hospital. Twenty-one cases were hospitalized at the time of interview and the remaining 56 were interviewed in their home villages.

As expected, there were no significant differences in matching variables (sex and age of child) between cases and controls. The control group differed from the case group in that caretakers were younger, their family sizes were smaller (and houses in the compound fewer) and most of their houses were made of mud, wood or bamboo (which might be a proxy for higher

socioeconomic status) (Table 4.1). Also, the respondents for the control group were more frequently the mother of the child. The self-reported median age of onset of noma amongst cases was 2.0 (IQR 2.0, 3.0) years.

Cases between six months and five years old had lower mean MUAC measurements (mean 134; SD 20) than controls (mean 142; SD 11; p=0.002). Six percent of cases (n=5) had a vaccination card available at the time of interview, compared with 16% (n=36; p=0.03) of controls. The vaccination coverage (based on the vaccination card) for polio (cases n=3, 3.9%; controls n=13, 5.9%; p=0.7) and measles (cases n=2, 2.6%; controls n=15, 6.8%; p=0.1) was very low for both cases and controls. Parents and caretakers reported that most cases (n= 63, 81.8%) and controls (n= 158, 71.2%; p=0.22) had been breastfed for between one to two years after birth. With respect to the main source of drinking water, parents reported that the two main water sources were a borehole in the village (cases n=27, 35.1%; controls n=63, 28.4%; p=0.08) and a well in the family compound (cases n=24, 31.2%; controls n=102, 46.0%; p=0.08). In terms of animal ownership, the proportion of case and control families reporting owning donkeys, dogs, sheep, goats and chickens were similar. Case families, however, were less likely to have cows in their compound compared with controls (cases n=36, 46.8%; controls n=128, 57.7%; p=0.09).

4.4.2 Risk factor analysis

The univariable analysis suggested that the likelihood of being a diagnosed noma case increased when the household was large (>10 people), the child had a higher birth weight (self-reported weight), breastfeeding occurred for >1 year, first solid food was given after the

Table 4.1 Sociodemographic characteristics of cases and controls (p-values from chi-squared, t-test or kwallis).

Sociodemographic characteristic		Controls n=222 (%)	Cases n=77 (%)	P-value
Child age (years) at time of interview, Median (IQR)		5.0 (3.0, 15.0)	5.0 (3.0, 15.0)	0.94
Child sex (female)		113 (50.9%)	37 (48.1%)	0.67
Caretaker age (years)	18-34	147 (68.7%)	37 (48.7%)	0.002
	35-90	67 (31.3%)	39 (51.3%)	
	Missing	8	1	
Child first born (yes)		33 (14.9%)	13 (16.9%)	0.4
Family size (number of children sleeping in 1 hut), Mean (SD)		11.5 (8.8)	15.8 (13.8)	0.0016
Number of wives, Mean (SD)		2.0 (7.6)	1.6 (0.7)	0.64
Main caretaker	Mother	132 (59.5%)	25 (32.5%)	<0.001
	Other	36 (16.2%)	28 (36.4%)	
	Relationship not specified	54 (24.3%)	24 (31.2%)	
Caretaker employed	No	76 (45.2%)	33 (51.6%)	0.39
	Yes	92 (54.8%)	31 (48.4%)	
	Missing/NA	54	13	
Caretaker education	None	66 (29.7%)	28 (43.8%)	0.34
	Some education (Arabic, primary, secondary school)	102 (46.0%)	36 (56.3%)	
Number of houses in compound, Mean (SD)		3.5 (2.8)	4.5 (3.5)	0.008
Main materials of house wall	Wood, mud, bamboo	175 (78.8%)	41 (53.3%)	<0.001
	Stone, brick, cement	45 (20.3%)	12 (15.6%)	
	Other	2 (0.9%)	24 (31.2%)	
IQR-:interquartile range, SD: standard deviation, NA: not applicable				

age of 12 months, the child ate pap (type of porridge staple made from maize, sorghum, or millet), and grains each day. Protective factors against acquiring noma included: the mother being the primary caretaker, the caretaker being married, having a well in the compound, colostrum being given to the child, child first given water over the age of seven months, all children in the household being alive and the child having taken medication (traditional or biomedicine) in the year preceding the interview (Table 4.2).

Due to collinearity, the following variables were not included in the multivariable analysis: the food group variable "Grains" (fura, mashed rice, millet, corn, bread), material the walls of the house was made out of, wealth score, measles, polio, one or more vaccination being reported on a vaccination card. In the multivariable analysis, eating pap every day remained strongly associated with diagnosed noma (OR 9.8; CI 1.5, 62.7; p=0.02) as did a later age of first solid food (>12 months) (OR 5.07; CI 0.9, 26.08; p=0.07). Variables that were protective against being a case included the mother being the primary caretaker (OR 0.08; CI 0.01, 0.5; p=0.007), the caretaker being married (OR 0.006; CI 0.0006, 0.5; p=<0.001) and colostrum being given to the baby (OR 0.4; CI 0.09, 2.09; p=0.07) (Table 4.2).

4.5 Discussion

This study has highlighted potential risk and protective factors associated with being a diagnosed noma case in northwest Nigeria, including caretaker demographics and infant feeding practices. This identification aims to shed light on potential useful areas for further investigation. Similar risk factors have been suggested including the absence of breastfeeding [56], dietary habits [3], unsafe drinking water, limited access to high quality health care, high infant mortality [2], and food security [57]. A 2017 review noted that

Table 4.2 Univariable and multivariable risk factors for being a noma case from conditional logistic regression.

		Controls (n=222)	Cases (n=77)	Univariable			Multivariable		
		n (%)	n (%)	OR	CI	P-Value	aOR	CI	P-Value
Primary caretaker is mother	Yes	132 (60%)	25 (32%)	0.2	0.1, 0.5	<0.001	0.08	0.01, 0.5	0.007
Caretaker married	Yes	158 (71%)	14 (18%)	0.03	0.01,0.09	<0.001	0.006	0.0006, 0.5	<0.001
Child first born	Yes	33 (15%)	13 (17%)	1.2	0.6, 2.5	0.6			
Caretaker educated	Yes	102 (46%)	36 (47%)	1	0.6, 1.8	1			
Caretaker employed	Yes	92 (41%)	31 (40%)	0.9	0.5, 1.7	0.9			
Total household members	1-9	113 (51%)	29 (38%)	Reference					
	10 or above	109 (49%)	48 (62%)	1.8	1.006, 3.09	0.05	2.06	0.8, 5.3	0.1
Compound life									
Water source	Other	120 (54%)	53 (69%)	Reference					
	Well	102 (46%)	24 (31%)	0.5	0.2, 0.9	0.04			
Water treated	Yes	73 (33%)	24 (31%)	0.9	0.5, 1.6	0.8			
Electricity	Yes	77 (35%)	25 (32%)	0.5	0.2, 1.4	0.2	0.2	0.04, 1.5	0.1
Number of livestock species in compound	1-3	100 (45%)	40 (52%)	Reference					
	4 or more	122 (55%)	37 (48%)	0.8	0.4, 1.4	0.4			
Nutrition									
Colostrum	No	19 (9%)	19 (25%)	Reference			Reference		
	Yes	149 (67%)	44 (57%)	0.3	0.2, 0.7	0.002	0.4	0.09, 2.09	0.07
	Don’t know	54 (24%)	14 (18%)	0.05	0.005, 0.4		0.001	<0.001, 0.5	

Breast fed duration	7-12 months, other	64 (29%)	14 (18%)	Reference					
	>1 year and <2 years	158 (71%)	63 (82%)	16.9	2.1, 134.5	0.008			
Age (months) child first given water	0.6	126 (57%)	53 (69%)	Reference					
	7 or above months	26 (12%)	6 (8%)	0.4	0.2, 1.2	0.03			
	Don't know	70 (32%)	18 (23%)	0.2	0.07, 0.8				
Age (months) first given solid food	0-11	112 (51%)	44 (57%)	Reference			Reference		
	12 months or after	38 (17%)	16 (21%)	1.2	0.6, 2.3	0.03	5.07	0.9, 26.08	0.07
	Don't know	72 (33%)	17 (22%)	0.2	0.05, 0.7		0.2	0.01, 2.9	
Pap every day	Yes	124 (56%)	55 (71%)	3.5	1.5, 8.2	0.004	9.8	1.5, 62.7	0.02
Food eaten at least once a day (ref = no/don't know)									
- Animal products	Yes	28 (13%)	10 (13%)	0.9	0.4, 2.1	0.9			
- Grains	Yes	165 (74%)	62 (81%)	5.9	1.2, 29.7	0.03			
- Vegetables	Yes	57 (26%)	21 (27%)	1	0.5, 1.9	1			
- Drinks	Yes	94 (42%)	36 (47%)	1.2	0.7, 2.2	0.6			
- Child, family eat same meals	Yes	165 (74%)	61 (79%)	3.4	0.8, 13.6	0.09			
Health									
Births in total (mother of child)	0-5	99 (46%)	30 (39%)	Reference					
	6 or more	69 (31%)	34 (44%)	1.4	0.8, 2.6	0.5			
	Don't know	54 (24%)	13 (17%)	<0.001	0, -	0.5			
Births alive	Some died	64 (29%)	43 (56%)	Reference					
	All still alive	103 (46%)	20 (26%)	0.4	0.2, 0.6	0.003			
	Don't know	55 (25%)	14 (18%)	<0.001	0, -				

Birth weight	Low/normal	27 (12%)	9 (12%)	Reference					
	High	78 (35%)	39 (51%)	1.6	0.7, 3.7	0.03			
	Don't know	117 (53%)	29 (38%)	0.7	0.3, 1.7				
Medication in previous year	Yes	127 (57%)	32 (42%)	0.4	0.2, 0.7	0.006	0.3	0.07, 1.6	0.2
OR = odds ratio; aOR=adjusted odds ratio; CI = 95% confidence interval; P = p value from logistic regression model									

measles vaccination was a protective factor for noma [57], but we were unable to corroborate this as the estimated vaccination coverage in both cases and controls was too low for a relevant comparison to be conducted. Our multivariable analysis did not identify an association between noma and household size or water source as reported elsewhere [75, 179], however, the univariable analysis suggested a possible association between these exposures and diagnosed noma and therefore warrants further investigation. We were also unable to confirm other reported risk factors for noma including high numbers of previous pregnancies in the mother [56] pre-existing illness, malnutrition [41], poor oral hygiene practices [34] and proximity of livestock to the area of residence [34].

One novel observation of the study was some weak evidence for the possible protective nature of colostrum. There are inherent health benefits associated with colostrum as it is rich in antibodies that confer passive immunity and growth factors which have been shown in recent studies to assist in the treatment of autoimmune disorders and gastrointestinal conditions [180]. Recent case reports have highlighted the global problem of noma and in some cases a relationship to concomitant infections including HIV positive patients in London [36] and the United States [11], and a Korean child with Crohn's disease [108]. These reports offer insight into the disease and strongly suggest that immunosuppression plays a role in the causal pathway of noma development which supports the finding of the protective nature of colostrum. However, it should be noted that these are clinical case reports and not analytical epidemiological studies. It is also possible that mothers who give their children colostrum are also more likely to follow other health messaging. Both aspects would have a favourable impact on the overall health status of an infant and therefore render the child to be at a lower risk of noma development. Our findings on this point were not definitive but this could be a useful point for future research.

The finding in the univariable analysis that having taken medication in the year prior to the study was a protective factor could indicate that having access to health care plays a role in noma development. This could be due to health care proximity or possibly due to improved socioeconomic status which would allow the families to pay for transport to get to health care and/or health care provision. Those who develop noma would conceivably have fewer possibilities to seek care for other diseases or the beginning stages of noma, and as such are at higher risk of developing the disease.

The finding that eating pap every day is a risk factor for diagnosed noma development, could be due to the fact that pap is the food usually used for weaning in Nigeria, it has a low nutrient density and has been reported to be at risk of unhygienic handling [181]. Two microbiological analyses of foods commonly used in weaning (including pap) in Nigeria, showed bacterial contamination at higher levels than international guidelines recommend [182, 183]. All of these factors mean that during the weaning period, the use of pap can predispose infants to infections and subsequently high mortality rates [181]. Possible solutions to reduce this exposure, would be to strengthen education about hygienic food preparation [182], the benefits of alternate practices such as fermentation which enhances nutritive value of the food [181] or encouraging variety in the diet. Improving feeding during the weaning time is crucial to decrease child malnutrition, mortality rates and to enhance development [183].

The findings showed that in both the case and control groups there was a high proportion of child morbidity and that families where the majority of infants born to the same mother survived, were less likely to have a noma case. This finding suggests that sociodemographic characteristics of families and households play a role in the disease dynamics of diagnosed noma. Our study suggests that more children die in households where noma cases are detected.

This could indicate that children in these households are also more exposed to unsafe water, poorer standards of living and reduced access to care, as all of these exposures are known to be associated with higher infant mortality [184–189].

Vaccination coverage in the study population is well below the standards recommended by the Nigerian Ministry of Health [190] and WHO [191]. There is evidence that the occurrence of vaccine preventable diseases and malnutrition precede the onset of noma [2, 11, 20, 32, 192]. The low coverage of vaccination not only increases the risk of morbidity and mortality from vaccine preventable diseases, but is a contributing factor in immunosuppression which is thought to play a key role in the sequence of events for noma development.

Our study is unique because available evidence around noma manifestation and risk factors for the development of the disease is based on a handful of primary studies [56, 75, 179], case reports [32, 34, 36, 108] and reviews [2, 20, 94]. These studies were methodologically different from ours which could offer reasons for the differing findings. A case control study conducted in Niger came closest to the current study design, although this study was conducted over six years and the controls were not matched on sex [56]. Our results also differ from those of a further Niger-based study [179], which included four villages in the study population and focused on the link between noma and acute necrotizing gingivitis. In comparison, our study was conducted over a relatively short time period and was retrospective in nature. Furthermore, our cases and controls were matched on sex in addition to village of residence and age, which might have eliminated some bias that could have been present in the previously mentioned studies. Finally, our study included diagnosed noma cases who were resident across 80 villages in two States of northwest Nigeria, so they represent a much wider geographical area than the

previous studies, which might have contributed to the differences in risk factors identified [179].

We attempted to interview all patients cared for at the hospital in the year before data collection, however this was not possible due to several constraints. Even though we managed to exceed our minimum sample size, we identified strong associations between only a minority of the explored risk factors and diagnosed noma. It is likely that the risks associated with individual exposures for noma are weaker than we assumed in the original sample size calculation.

A further limitation is that our risk factor analysis only represents those cases who sought care at the NCH in Sokoto. Due to the reported 90% mortality rate within weeks after the onset of noma [1] if untreated and rapid progression of noma, this likely means that the results of the current study are only applicable to the subset of noma cases who experienced the least severe complications from the disease.

The measurement of malnutrition using only the MUAC was a limitation as this tool is useful to diagnose severe acute malnutrition but noma is reported to be associated with chronic malnutrition or stunting. Finally, we included all cases who were under the age of 15 at the time of self-reported disease onset. Therefore some cases (and thus controls) were under 15 years at the age of onset but were currently ≥18 years (13 cases) thus we interviewed them personally and not their caretaker. This might have introduced some bias into the study as certain questions around infant feeding practices etc. would only have been possible to be answered by their caretakers, leading to missing information on these questions. We tried to mitigate this by conducting sensitivity analyses for these variables which resulted in similar findings.

In conclusion, our case control study suggests that infant and current feeding behaviours as well as caretaker demographics may affect the risk of developing noma. Malnutrition and low vaccination coverage, high morbidity of infectious diseases along with limited access to health care are all likely contributing factors. We recommend that prospective studies are implemented to better understand the sequence of events contributing to the development of noma. Only with these sets of indicators will it be possible to better formulate and target prevention programmes.

Chapter 5 Outcomes at 18 months after surgery of patients treated at NCH

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Additional resources

The questionnaire and informed consent and assent forms used in this chapter can be found in Appendix 6.3 and Appendix 7.3.

Relevance of this paper to the thesis

Noma cases are each unique and require a broad range of treatments including pharmacological, surgical, physiotherapy and psychosocial interventions. This manuscript describes the characteristics of a cohort of patients surgically treated at the NCH, their clinical treatment at the hospital including the procedures they underwent and their quality of life and clinical status after surgery. The findings from this manuscript will be utilized in program planning and for the formulation of a robust follow-up system at the NCH in Sokoto, Nigeria.

Contribution of the student and co-authors

EF, MA, AL and KB, conceptualised the project. EF developed the protocol with input from all authors. LT conducted the retrospective chart review with assistance from EF and MJO. EF and MJO collected the remaining data. EF conducted the data analysis with guidance from AL and MO. EF, MA, RW, AOT and AL interpreted the findings. EF wrote the first draft of the manuscript. All authors critically reviewed the manuscript and provided final approval.

5.1 Abstract

5.1.1 Background

Noma is a rapidly progressing infection of the oral cavity often resulting in severe facial disfigurement. We present a case series of noma patients treated surgically at the NCH, northwest Nigeria.

5.1.2 Methods

A retrospective descriptive analysis of routinely collected data was undertaken (demographics, diagnosis and surgical procedures undergone) and follow-up assessments (anthropometry, mouth opening and quality of life measurements) were conducted. Patients living in Sokoto or Kebbi States who had noma surgery more than six months prior to data collection were included.

5.1.3 Results

Of the 37 patients included, 21 (56.8%) were male and 22 (62.9%) were aged six years or older. The median time between last surgery and follow-up was 18 months (IQR 13, 25 months). At admission, the most severely affected anatomical area was the outer cheek (n=9; 36% of patient's had lost between 26% and 50%). Twelve patients (32.4%) had one surgery and 15 patients (40.5%) had two to three surgeries. The most frequently used surgical procedures were the deltopectoral flap (n=16 patients; 43.2%) and trismus release (n=12, 32.4%). For the eight trismus release patients where mouth opening was documented at admission, all had a mouth opening of between 0-20 millimetres (mm) at follow-up visit. All of the patients reported that the surgery had improved their quality of life.

5.1.4 Conclusion

Our findings show that at follow-up, surgically treated noma patients report improvements in their quality of life despite limited increases in mouth opening. Although reconstructive surgery in noma patients can improve aesthetics and function, it did not restore patients to their pre-noma level of function.

5.2 Introduction

Noma (cancrum oris) is a poorly understood, rapidly progressing infection of the oral cavity with a reported 90% mortality rate within weeks after the onset of first symptoms if untreated [154]. Noma begins as a mouth ulcer and, within days, progresses to oedema of the cheek followed by necrosis and the rapid destruction of the hard and soft tissues of the face [94]. Treatment with antibiotics, wound debridement and nutritional support in the early reversible stages of the disease greatly reduce mortality and morbidity [2]. Noma is thought to be multifactorial in nature [2]. The aetiology of noma is currently debated, organisms such as *Fusobacterium necrophorum* and *Prevotella intermedia* [52, 192] have been identified in noma cases but are not consistently present [2].

If the patient survives the acute stages, the disease can become inactive (with or without antibiotic treatment), after which patients often need complex surgical reconstruction in order to restore orofacial function and improve aesthetics [94]. Reconstruction often entails rebuilding the lips and cheeks and in some cases the eyelids and nose [4, 25]. However, each noma case is unique and as such, the surgical procedures used to treat noma differ [4].

Long-term physical sequelae of noma include displacement of the teeth and severe scarring and bony fusion between the maxilla and mandible [2, 4, 92, 94–96]. Sequelae around daily functioning may include difficulty eating, seeing, talking and breathing [57, 94, 96]. The social isolation or mental health sequelae of noma patients have not been documented in the literature but should not be underestimated.

Trismus (restriction of the mouth opening) is one of the most disabling sequelae [6] of noma and can lead to complications such as aspiration, malnutrition, poor oral hygiene, speech deficits, airway compromise and pain [97]. Trismus associated with noma can be caused by scarring around the temporo-mandibular joint capsule (extra-articular ankylosis) or by destruction and scarring of the temporo-mandibular joint itself (intra-articular ankylosis) [6, 38, 55, 193, 194].

Reported surgical techniques to address the spectrum of noma defects include pedicled supraclavicular flaps for the treatment of large unilateral facial defects [100], Abbe, Estlander, and fan flaps for the reconstruction of the lips and corner of the mouth [4, 102], forehead, deltopectoral, radial forearm and free flaps for the reconstruction of the cheek [4, 55] and Abbe, radial forearm, free, medial forehead and local turnover flaps for the reconstruction of central defects (upper lip and nose) [4, 55, 92]. Mouth opening is improved by performing bone-bridge excision, sometimes associated with contralateral coronoidectomy [55].

Outcomes of noma treatment are difficult to ascertain due to inconsistent patient follow-up. This is mostly due to the remote locations of the home villages of patients. One of the only studies on long-term outcomes of trismus release in noma patients was based in northwest

Nigeria (n=36) and showed that after a mean follow-up time of 43 months, results were poor with only 39% of patients showing improvement in mouth opening [6].

The NCH in northwest Nigeria, run by the Nigerian Ministry of Health and supported by MSF since 2014, offers care to noma patients including reconstructive surgical interventions. We present a description of the follow-up of a case series of patients treated surgically at the NCH to inform ongoing clinical treatment and areas for future study. Our study adds to the existing noma case series and is unique as we have followed-up patients over a longer period (median of 18 months) in comparison to other studies which had follow-up periods of between two and six weeks [5, 92, 99].

5.3 Methods

5.3.1 Study setting

We conducted a case series study with patients who had been surgically treated for noma at the NCH more than six months before data collection and who lived in Sokoto or Kebbi States. Data collection took place from April to June 2018.

5.3.2 Data collection

Data collection was done in two stages. The first stage was based on data collected at admission and for the duration of their stay at the NCH (routine data). The second stage of data collection occurred during follow-up visits conducted in the home villages of the patients.

5.3.2.1 Routine data

The routinely collected data were stored in a bespoke database at the NCH. Information gathered on each of the patients included demographics, diagnosis upon admission (chronic is defined as the absence of ongoing acute infection) and nutritional status.

Surgical data collected included the number and type of surgical procedures and surgical complications (infection, dehiscence, flap necrosis, flap failure). American Society of Anaesthesiologists (ASA) scores were assigned to patients prior to surgery (indicating the fitness of patients before surgery) (Table 5.1). Anaesthesia complications during and after surgery were recorded (difficult airway, hypothermia, equipment failure). The nose, outer lining, inner lining, trismus, upper lip, lower lip, particularities (NOITULP) classification system was used by a surgeon with experience in the treatment of noma to grade patients upon admission. This classification system delineates the extent of orofacial damage and related functional compromise, according to fractional loss of anatomical units (nose, outer and inner cheek lining, upper and lower lip) and trismus categories ranging from normal mouth opening (>40 mm) to no mouth opening [38] (Table 5.2).

5.3.2.2 Follow-up data

Data collected included weight (kilograms; kg), height (centimetres; cm), age (years), MUAC, for children aged six months to five years and maximum mouth opening. Height was measured using a height board for those under and including five years of age and a tape measure for those older than five years. One manual floor scale was used for weighing all participants, this was calibrated daily. Training for anthropometry measurements was conducted before data collection commenced. Age estimated to the closest year was self-reported by either the

Table 5.1 ASA classification system.

ASA Score	Score definition
ASA I	A normal healthy patient
ASA II	A patient with mild systemic disease
ASA III	A patient with severe systemic disease
ASA IV	A patient with severe systemic disease that is a constant threat to life
ASA V	A moribund patient who is not expected to survive without the operation
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes
ASA- American Society of Anaesthesiologists	

Table 5.2 NOITULP scale – classification for noma (nose, outer lining, inner lining, trismus, upper lip, lower lip, particularities) [4].

	Fractional *loss* of anatomical unit				
	0	**1**	**2**	**3**	**4**
Nose	No loss	1-25% lost	26-50% lost	51-75% lost	76-100% lost
Outer lining	No loss	1-25% lost	26-50% lost	51-75% lost	76-100% lost
Inner lining	No loss	1-25% lost	26-50% lost	51-75% lost	76-100% lost
Upper lip	No loss	1-25% lost	26-50% lost	51-75% lost	76-100% lost
Lower lip	No loss	1-25% lost	26-50% lost	51-75% lost	76-100% lost
Trismus*	T0: normal mouth opening > 40 mm	T1: mouth opening 20-40 mm	T2: mouth opening 0-20mm	T3: no mouth opening	NA
Particularities**	No particularities	Brief description of particularity:			

NA- not applicable;

*Trismus is not an anatomical unit but a functional problem – the inability to open the mouth properly. It has been included in the system because of its clinical relevance (e.g. for intubation);

**Particularities represent pathologic findings pertinent to reconstruction, i.e.: Loss of lower eyelid tissue (Eyelid retraction by a scarred cheek is not to be noted); Affection of the orbit; loss of an eye is seen quite commonly; Palatal defects; Maxillary sinus defects; Loss of pre-maxilla; Loss of skin of the chin; Defects of both cheeks.

patient (if ≥18 years) or their caretaker. Mouth opening was measured by trained research assistants using a ruler. The maximum mouth opening measurements were measured as the millimetres of mouth wide open minus the millimetres of mouth closed (incisor-to-incisor where possible or alveolar ridge to alveolar ridge).

As there was no validated quality of life scale in Hausa, we asked questions related to the patients' ability to eat and drink, their self-reported changes in appearance and how they currently experienced social inclusion in their community. These questions were based on tools used in prior reconstructive surgery studies [195–199]. Questions were extracted from these tools. The questions were translated in Hausa and back translated into English to ensure accuracy of translations. These questions have not to our knowledge been used in other noma studies. Quality of life questions were asked to adult respondents directly and to child respondents if the child felt comfortable discussing the issues with the interviewer. If children were aged under seven years or felt uncomfortable talking with the interviewers, the children's caretakers were asked the questions.

5.3.3 Data analysis

5.3.3.1 Data analysis routine data

A descriptive analysis was conducted. Median and IQR were reported for non-normally distributed continuous values; means and SDs were reported for values with normal distributions. For children aged six months to five years, MUAC measurements were used to classify the nutritional status of children upon admission as having severe acute malnutrition (SAM; MUAC <115 mm), moderate acute malnutrition (MAM; MUAC ≥116 mm ≤125 mm) or global acute malnutrition (GAM; MUAC <126 mm) [200]. For children aged six to 15 years, body mass index (BMI) was calculated and gender specific WHO BMI charts were used

to categorise children according to BMI for age. Children were classified as underweight (BMI <5th percentile), normal (6th–84th percentile), overweight (85th and 95th percentile) and obese (above the 95th percentile) [201]. For individuals aged 16 years and older, weight and height were used to classify individuals' BMI ranges as underweight: under 18.5 kg/m^2, normal: 18.5 to 25kg/m^2, overweight: 25 to 30kg/m^2, obese: over 30kg/m^2 [202].

5.3.3.2 Data analysis follow-up

Nutritional status at follow-up was assessed by the same means as at admission: SAM, MAM, GAM and BMI were calculated. Mouth opening measurements were used to grade patients according to the NOITULP scale trismus categories at follow-up by the research team in conjunction with a consultant level surgeon. Quality of life answers were stratified by age group (below and above 15 years).

All analyses were conducted in Stata 15 (StataCorp LP, College Station, TX, USA).

5.3.4 Ethics

The MSF, UDUTH and Sokoto and Kebbi State Ministry of Health ERBs approved the study protocol. Informed consent was sought at follow-up. Consent to review medical records was explicitly sought. All participants were treated in accordance with the ethical principles of the Helsinki Declaration.

5.4 Results

5.4.1 Demographic information of enrolled patients

We included 37 (82.2%) of the 45 eligible patients. The remaining eight could not be located due to inaccessible roads or the person having moved from the listed village of residence. All

patients were alive at follow-up. Of these 37 patients, 21 (56.8%) were male, 34 (91.9%) were from Sokoto and 12 (34.3%) were aged above 15 years at admission as were 17 at follow-up (patients were aged between four and 50 years at follow-up). Most patients (n=35; 94.5%) were diagnosed as having chronic noma upon admission. The main reported reasons for seeking care were cosmetic (n=25; 67.6%) and the related stigmatisation (n=24; 64.9%) with only 14 (37.8%) reporting functional disability as a reason for seeking care (Table 5.3). The median number of months between last surgery and follow-up was 18 (IQR 13, 25 months).

5.4.2 NOITULP classification at admission

At admission, the most severely affected anatomical area was the outer cheek (n=9; 36.0% of patient's had lost between 26% and 50%) (Figure 5.1 and Figure 5.2).

5.4.3 Surgical procedures

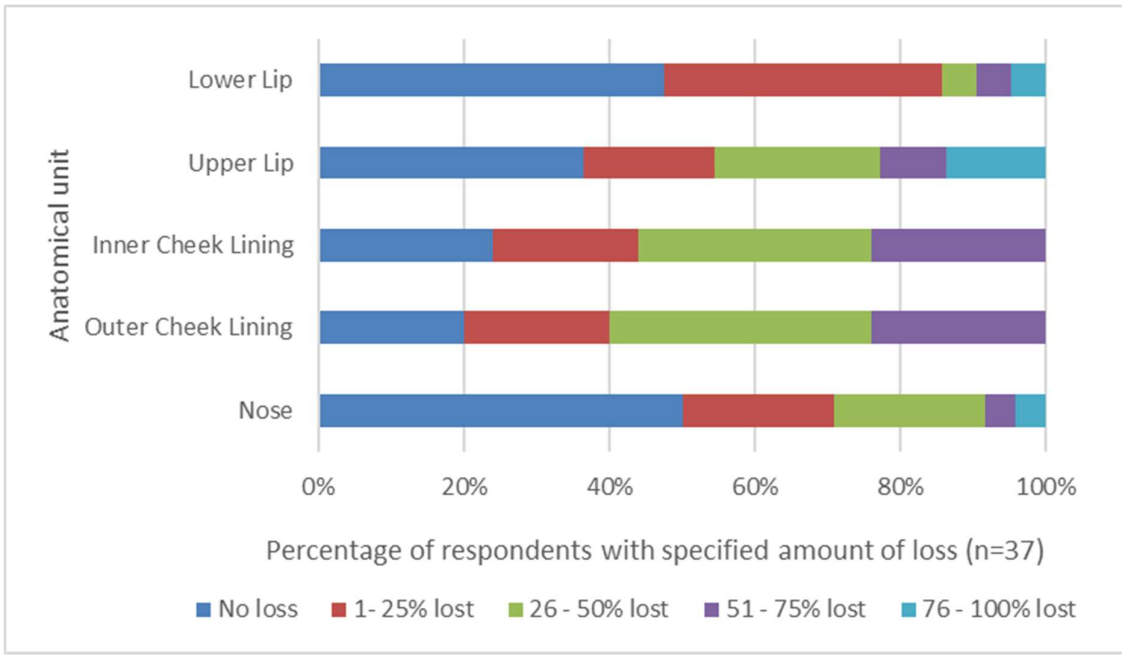
Of the 37 patients included in our study, 12 (32.4%) had one surgery, 15 (40.5%) had two to three surgeries, and the remaining 10 (27.0%) had four or more surgeries. In total, 92 surgeries were conducted during which 125 procedures were performed. The mean duration of each surgery was 90 minutes (SD 49 minutes). The most frequently used surgical procedure was a deltopectoral flap (n=16 patients; 43.2%) followed by trismus release (n=12 patients; 32.4%) (Table 5.4). No blood transfusions were required for any patients during their surgeries.

Eight surgical complications were noted in seven patients (18.9%), one patient had a superficial infection and an abscess. Complete dehiscence was reported in two patients (5.4%). One (2.7%) of each of the following complications were reported: flap failure, flap necrosis, flap detachment, neck pain needing physiotherapy and infection on corner of mouth. There were no donor site complications and no deaths.

Table 5.3 Respondent characteristics at admission.

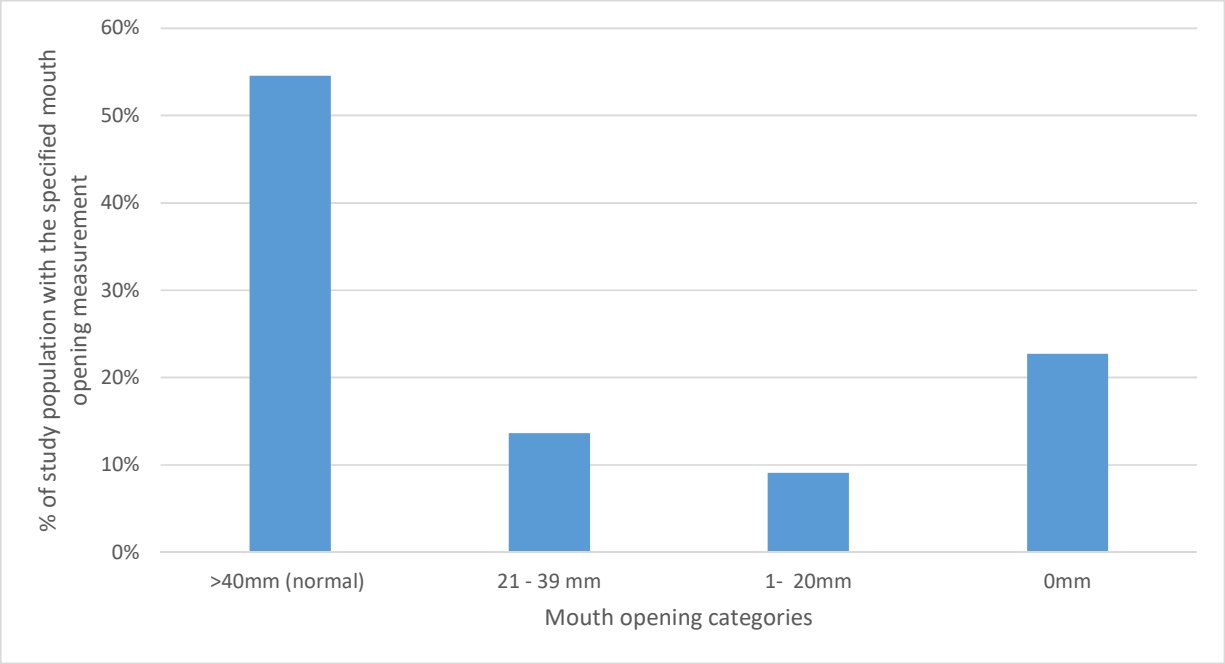
Demographic characteristic		n= 37 (%)
Sex	Female	16 (43.2%)
	Male	21 (56.8%)
State	Kebbi	3 (8.1%)
	Sokoto	34 (91.9%)
Patient age upon admission (years)	0-5	13 (37.1%)
	6-15	10 (28.6%)
	>15	12 (34.3%)
Patient education	None	1 (2.8%)
	Arabic Studies	34 (94.4%)
	Primary school	1 (2.8%)
Noma diagnosis on admission	Acute noma	2 (5.4%)
	Chronic noma	35 (94.6%)
Had treatment for noma prior to coming to NCH	No	22 (59.5%)
	Yes	15 (40.5)
Kinds of previous noma treatment	Antibiotics	11 (73.3%)
	Traditional	4 (26.7%)
Self-reported comorbidities reported upon admission at the NCH	Malaria	10 (27.0%)
	HIV	0 (0.0%)
	TB	0 (0.0%)
	Measles	14 (37.8%)
Any vaccination before hospital admission	No	17 (46.0%)
	Yes	20 (54.1%)
Health care seeking reason	Cosmetic	25 (67.6%)
	Stigmatization	24 (64.9%)
	Functional disability	14 (37.8%)
NCH- Noma Children's Hospital, Sokoto, Nigeria		

Figure 5.1 Fractional loss of anatomical unit at admission for study cohort (n=37).



* Missing information: nose (n=13); outer and inner cheek lining (n=12); upper lip (n=15); lower lip (n=16).

Figure 5.2 Trismus classification at admission for study cohort (mm = mouth opening measurement in millimetres) (n=37).



* Missing information on trismus at admission (n=15).

Table 5.4 Surgical procedures performed on study cohort, 37 patients*.

Surgical procedure	n=37 (%)
Deltopectoral flap	16 (43.2%)
Release of trismus	12 (32.4%)
Commissuroplasty and lip reconstruction	11 (29.7%)
Estlander flap	10 (27.0%)
Forehead flap	6 (16.2%)
Nasal reconstruction	5 (13.5%)
Fan flap	5 (13.5%)
Cheek rotation flap	2 (5.4%)
Other procedures	14 (37.8%)
*More than one procedure was performed per patient	

5.4.4 Anaesthesia information

All patients who had data available on the type of anaesthesia received (n=35) had undergone general anaesthesia. ASA scores were assigned for the 87 surgeries for these 35 patients: 69 (79.3%) surgeries had an ASA score of I, 17 surgeries (19.5%) had a score II and one surgery (1.15%) had a score of III. Four (10.8%) patients had anaesthesia complications noted during five surgeries. Three surgeries had unanticipated difficult airways (difficulty with facemask ventilation, difficulty with endotracheal intubation); there was one case of hypothermia and one case of anaesthesia equipment failure.

5.4.5 Nutritional status

Of the 37 patients included in the study, five (13.5%) had an improved nutritional status at follow-up and in four (10.8%) patients the nutritional status had deteriorated. The other patients had an unchanged nutritional status. Of the three patients under five years of age at admission, two (66.7%) patients aged between six months and five years were classified as having SAM and one (33.3%) patient was classified as having GAM using MUAC measurements. At follow-up, all three (100%) patients fell within the normal range indicating that these three children had an improved nutritional status at follow-up. In the six to 15 year age group (n=17), 12 (70.6%) children were categorised as normal weight at admission, four (23.5%) of these children were underweight at follow-up, and the others (47.1%) were normal. Two patients (11.8%) were underweight at admission, one (5.9%) of these was classified as normal at follow-up and the other was still underweight (5.9%). One (5.9%) patient was overweight at admission and normal at follow-up. For those aged 16 years and above (n=17), mean BMI was 19.0 (SD 3.3) upon admission and 18.7 (SD 3.5) at follow-up. The difference between these points is minimal and both measurements fall within the WHO classified normal range.

5.4.6 Trismus

There were 17 trismus release procedures conducted on 12 patients (8 = 1 procedure, 3 = 2 procedures, 1= 3 procedures). At follow-up, the median maximum mouth opening for those aged 15 years and under (n=7) was 15.3 mm (IQR 7mm, 18mm) and 10 mm (IQR 2mm, 20mm) for those aged 16 years and older (n=5). Although we had mouth opening measurements at follow-up that could be translated into the NOITULP mouth opening score for all patients, at admission we only had the allocated NOITULP score and not the actual mouth opening measurements for eight patients. As such, a comparison of the pre- and post-operative mouth opening NOITULP classification for these eight patients is seen in Table 5.5. No patient had a normal mouth opening status at the follow-up visit (all classified as T2, 0-20 mm).

5.4.7 Quality of life at follow-up

All respondents reported that the surgery had improved their quality of life in one facet or another. Respondents in the under 15 year age group reported that the surgery had led to decreased social isolation (n=17; 85.0%) and improvements in functional aspects such as eating (n=16; 80.0%) and talking (n=16; 80.0%). Respondents in the 15 year and older age group reported improvements in social acceptance (n=17; 100.0%) and enhanced self-esteem following aesthetic improvement (n=17; 100.0%) (Table 5.6).

Table 5.5 Mouth opening categories on admission and follow-up.

Patient	Age at follow-up	Admission	Follow-up
Patient 1	7	T2: mouth opening 0-20 mm	T2: mouth opening 0-20 mm
Patient 2	7	T3: no mouth opening	T2: mouth opening 0-20 mm
Patient 3	8	T1: mouth opening 20-40 mm	T2: mouth opening 0-20 mm
Patient 4	8	T0: normal mouth opening: >40 mm	T2: mouth opening 0-20 mm
Patient 5	10	T3: no mouth opening	T2: mouth opening 0-20 mm
Patient 6	18	T3: no mouth opening	T2: mouth opening 0-20 mm
Patient 7	20	T3: no mouth opening	T2: mouth opening 0-20 mm
Patient 8	22	T2: mouth opening 0-20 mm	T2: mouth opening 0 20 mm

Table 5.6 Self-reported quality of life assessment at long-term follow-up.

Quality of life indicator	≤15 year olds* n=20 (%)	>15 year olds* n=17 (%)
The surgery has improved your quality of life	18 (90.0%)	16 (94.2%)
At this point in time, I can go to school	10 (50.0%)	13 (76.5%)
At this point in time, I have friends	17 (85.0%)	17 (100.0%)
I am now included in the community	15 (75.0%)	17 (100.0%)
I can now get married	5 (25.0%)	2 (11.8%)
I can eat more easily than before the surgery	16 (80.0%)	16 (94.1%)
I can drink more easily than before the surgery	15 (75.0%)	16 (94.2%)
People can now understand what I am saying more easily than before the surgery	16 (80.0%)	16 (94.2%)
I feel more happy with the way I look than before the surgery	15 (75.0%)	17 (100.0%)
		*Age at follow-up

At the follow-up visits, patients and caretakers were asked if and how the surgery had changed their lives. Some feedback from patient caretakers was negative, and they did not want any further care:

> *"The surgery was not successful and I do not want to come back to the hospital."* (Patient age 8 year old).

Other caretakers reported difficulties with restricted mouth opening and related functional issues:

> *"The opening of the mouth is very small making it difficult to eat or drink*." (Patient age 29 year old).

There was some mixed feedback showing improvements in quality of life but continued difficulty with mouth opening:

> *"The mouth opening is a bit difficult because the side stitches are tight. However she can eat and talk well."* (Patient age 28 year old).

And some other patients reported positive functional changes and social acceptance:

> *"He was shy and angry before the surgery and he is now able to eat and go to school. He used to not be audible but now he talks loud and clear."* (Patient age 10 year old).

> *"He is very happy to have the treatment and he can meet different people since the wound is closed and healed*." (Patient age 10 year old).

5.5 Discussion

Our findings suggest after surgical care, all patients reported improvements in at least one aspect of their quality of life, with many reporting functional improvement in eating, drinking and speech, despite minimal evidence that trismus had improved. This corroborates findings from an Ethiopian study, which showed that post-operative follow-up revealed significant improvement in the lives of noma patients [111]. Most of the patients had more than one surgery, and the most commonly used procedure in our cohort was the deltopectoral flap which is utilized in the reconstruction of the cheek, the most commonly affected anatomical area. Children aged over 15 years reported more social and aesthetic improvements in their lives than the younger children (going to school, being accepted into the community, having more friends). This could be indicative of the stage of life these respondents are at, in comparison to the likely more home bound younger children who might experience less social isolation due to their appearance.

Our case series confirms the complexity and unique manifestation of noma, and the need for numerous surgical procedures to obtain an acceptable functional and cosmetic result. As most patients had more than one surgery, this needs to be taken into account for program planning and patients should be informed of the need to potentially return to the hospital multiple times for these surgeries in order to manage treatment expectations. The most commonly performed procedures were the deltopectoral flap, release of trismus, commissuroplasty and lip reconstruction, Estlander flap, forehead flap and nasal reconstruction. The procedures performed rely on regional flaps and local tissue and are in line with other reported surgical techniques used to treat noma [4, 24, 55, 92, 100, 102, 203]. Other providers have described the use of free flaps [20, 114]; however, given the technical and resource demands of

microsurgery, these techniques are not currently utilised at the NCH. The surgical program instead enlists older but reliable reconstructive techniques that are less risky in this context.

Noma cases are at high risk of developing trismus resulting in difficulties in speech, chewing, and maintaining healthy oral hygiene practices [6]. This case series has highlighted that despite surgical intervention, none of the patients in this cohort regained a normal mouth opening. Respondents reported ongoing concerns with their restricted mouth opening and the impact this restriction had on their lives. Similar studies with noma patients noted that the results of trismus release in noma patients was extremely poor [6, 193]. A northwest Nigerian study reported that 43 months after surgery the mean mouth opening of 36 patients was 10 mm [6]. A similar study with 95 patients from Niger and Burkina Faso reported that after three years, mean mouth opening was 21 mm [55]. Our results were similar to these studies and showed that all patients had a mouth opening of between 0 and 20 mm at follow-up (median mouth opening of our cohort (aged ≤15 years 15 mm; aged >16 years 10 mm).

This outcome is not unique to noma. The overall success rates of curing trismus in inflammatory processes other than noma (oral submucous fibrosis, chronic non-bacterial osteomyelitis) in the paediatric population can be low [204, 205]. In the majority of noma patients (as well as patients with other inflammatory causes of trismus), the trismus is extra-articular [55]. Noma can disrupt the peri-articular bony tissues of the subcondylar area, which is the location of the growth plate of the mandible. Other research into mandibular trauma has also reported that this disruption of the growth plate has resulted in increased fibrosis and trismus [97, 205–207], and we can hypothesise this is also a contributory factor in noma. Similarly, this area of the mandible can be disrupted by surgery to correct trismus (such as gap or interpositional arthroplasty) [5, 204]. This disruption is mitigated by delaying trismus

release until the mid-teen years to avoid, or at least decrease, the need for revision trismus surgery. Delaying trismus release surgery until skeletal maturity is likely to be effective for noma patients to reduce the post-surgical reduction in mouth opening. This delay should only occur if a child with noma can drink and eat enough calories to continue to feed, grow and gain weight. In these cases longer-term follow-up will be necessary as they will almost certainly need to undergo a revision procedure in future. While there are no specific rules or recommendations for trismus release and ankylosis repair in the literature, in studies and meta-analyses demonstrating high success rates for inflammatory causes, the patients are typically in the teenage years [204]. The success rates for paediatric trismus surgery are far higher in congenital and traumatic causes, where the surrounding capsule and other structures are unaffected [204]. A very important further step which has been shown to maintain adequate mouth opening and resulting quality of life after trismus release surgery is longer-term post-operative physiotherapy which can enable patients to have an improved mouth opening [55, 204]. We do not have physiotherapy treatment or uptake information for patients included in the study, however; the NCH program currently includes rigorous physiotherapy following trismus release while at the hospital, patients are also provided with an exercise list to complete when at home after discharge and they are assessed by the physiotherapist at the follow-up appointments at the hospital.

Our study has illuminated three potential changes for program planning and potential interventions. Firstly, as the anaesthesia complications were notable, it is important that surgical teams should include anaesthesia professionals who are specialised in difficult airway management. Secondly, as some patients remained malnourished, it is important to conduct nutritional follow-up with all patients. Lastly, vaccine preventable diseases and a lack of vaccines are a risk factor for the development of noma [2]. The inadequate vaccination status

of the patients included in this study shows that these populations should be the target for public health interventions, which could reduce the number of noma cases along with a host of other diseases.

Eighteen patients who were eligible to be included in the study were lost to follow-up, this could have introduced selection bias into the study and altered our findings. Most patients in this study reported improvements in quality of life; however, these questions were only asked at follow-up and not prior to surgery. Social desirability bias could have influenced the quality of life answers, particularly given that trismus was not markedly improved in most cases. As there is no validated tool for assessing quality of life following surgery for noma, comparisons with other study results will be difficult. In order to improve our assessment of quality of life changes, it would be beneficial to use a standardised, validated assessment tool at admission and follow-up [208]. Furthermore, the retrospective review of routinely collected data limited the type and quality of data available for analysis. We have now implemented a prospective study to assess the outcomes of patients that will address many of the weaknesses of this current case series as the same data will be systematically collected at standardized time points (admission, pre-surgery, post-operatively; six and 12 months after the date of last surgery).

Following their last surgical intervention, noma patients do experience some improvements in their quality of life, but debilitating long-term sequelae persist. Reconstructive surgery does appear to restore form and function in some patients. However, noma is a preventable condition that, if detected early can be effectively treated with antibiotics before the devastating consequences described in this cohort of patients occur. Therefore, public health interventions should prioritise strategies that address known risk factors through community-based health system approaches which target prevention, early detection and rapid treatment of acute noma.

Chapter 6 Noma and traditional healing

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Additional resources

The question guides and informed consent forms used in this chapter can be found in Appendix 6.4 and Appendix 7.4.

Relevance of this paper to the thesis

The research for this paper was conducted in Sokoto State, northwest Nigeria, and explores traditional healers' perceptions of noma, the relationship dynamics between traditional healers and caretakers of noma patients, traditional health care practices for noma and the potential to include traditional healers in noma prevention initiatives and partnerships. This manuscript offers insight into the pluralistic nature of the Nigerian health system, with a specific focus on the role traditional healers' play in the pathway to care for noma patients. It is clear from our findings that traditional healers do treat noma patients (mostly in the early, crucial, reversible stages of the disease) and that they would be willing to refer noma patients directly to the NCH which could greatly decrease the time it takes patients to receive care, which could thus decrease morbidity and mortality of noma.

Contribution of the student and co-authors

EF, AL, EV, JGC and BS conceptualised the project. EF developed the protocol with input from all authors. HMB and EF conducted the data collection. EF conducted the data analysis with guidance from EV and JGC. EF, EV and JGC interpreted the findings. EF wrote the first draft of the manuscript. All authors critically reviewed the manuscript and provided final approval.

6.1 Abstract

6.1.1 Background

Noma, a neglected disease mostly affecting children, with a 90% mortality rate within weeks after the onset of noma if untreated, is an orofacial gangrene that disintegrates the tissues of the face in <1 week. Noma can become inactive with early-stage antibiotic treatment. Traditional healers, known as mai maganin gargajiya in Hausa (the most commonly spoken language in northwest Nigeria), play an important role in the health system and provide care to noma patients in Nigeria. We interviewed caretakers of noma patients and traditional healers and explored perceptions of noma, relationship dynamics, health care practices and intervention opportunities.

6.1.2 Methods

We conducted IDIs with 12 caretakers who were looking after noma patients admitted to the NCH and 15 traditional healers in their home villages in Sokoto State, northwest Nigeria. Interviews were audio-recorded, transcribed and translated. Manual coding and thematic analysis were utilised.

6.1.3 Results

Traditional healers offered specialised forms of care for specific conditions and referral guidance. They viewed the stages of noma as distinct conditions with individualised remedies. Caretakers trusted traditional healers.

6.1.4 Conclusion

Traditional healers could play a crucial role in the early detection of noma and the health-seeking decision-making process of patients. Intervention programmes should include

traditional healers through training and referral partnerships. This collaboration could save lives and reduce the severity of noma complications.

6.2 Introduction

Noma (cancrum oris) is a rapidly progressing gangrenous infection of the oral cavity, which mostly affects children aged two to five years. If left untreated, noma is associated with a reported 90% mortality rate within weeks after the onset of first symptoms [1, 154]. Those who survive have severe facial disfigurements and multiple physical impairments including difficulties in eating, seeing and breathing [2]. Noma manifests in stages which are categorised by the WHO: simple gingivitis; acute necrotizing gingivitis (accompanied by fetid breath), oedema, gangrene (hard and soft tissue destruction), scarring and sequelae [1]. The total destruction of the cheek can take place in less than one week [1]. During the early stages of noma, infections can become inactive if patients are treated with antibiotics, wound cleaning and nutritional support; thus decreasing morbidity and mortality [2]. In many cases, however, patients live in remote locations and access to health care takes considerable time.

Primary research on noma is limited, hence knowledge sharing about the disease is impeded. The most commonly reported risk factors are malnutrition, poverty, immunosuppression, co-infections, poor vaccination coverage, lack of access to quality health care, not receiving colostrum at birth and caretakers (also known as caregivers) being someone other than the mother [2, 56, 209]. The majority of cases are currently reported in Africa [3, 7, 16, 18, 20–23] and Asia [21, 24–32]. However, over the past 15 years, there have been sporadic reports of cases originating and being treated in Turkey [33], Afghanistan [34], Italy [35], the United Kingdom [36] and the United States [11] .

The Nigerian Ministry of Health supported by MSF implements prevention and treatment programmes for noma at the NCH in Sokoto, northwest Nigeria. The program includes a strong outreach component focussing on finding cases and awareness raising about noma with community members and health workers.

The health system in Nigeria is comprised of three levels: primary (local government), secondary (state government) and tertiary (federal government) [210]. These levels of the health system operate in tandem alongside traditional medicine. Mai maganin gargajiya (the Hausa name for traditional healers) play an important role in health care globally [211] and in Nigeria, with an estimated 80% of the population exclusively using this form of care [212]. A Nigerian study reported that close to 10% of rural dwellers and 4% of urban dwellers in Nigeria were traditional healers, proportions much higher than those trained in biomedicine [213]. Patronage of traditional healing waned due to restrictions and the introduction of biomedicine, but recently, there has been an increase in seeking this form of care due to the ability of traditional healers to provide physical, psychological and spiritual care [214]. Traditional healers are said to either reside in the villages within which they serve, or to move around from village to village providing care as they go [215]. Traditional healers practices include utilizing remedies such as plants and trees [213, 216–219], piercing and cuts [220] and prayer [221].

As prevention and early detection are the most important strategies in reducing the impact of noma, it is crucial to consider the role of traditional healers in the pathway to care for noma patients. We interviewed caretakers of noma patients and traditional healers to explore their perceptions of noma, the relationship dynamics between the two; traditional healers' health care practices for the different stages of noma; and the feasibility of creating referral

partnerships with traditional healers. The information generated through this research will be used to guide noma outreach strategies.

6.3 Methods

6.3.1 Setting

Interviews with caretakers of noma patients were conducted at the NCH and interviews with traditional healers were conducted in their home villages in Sokoto State, northwest Nigeria. Among 110 noma patients who were admitted at NCH from January to December 2018, 53 (48.2%) had early-stage noma, 50 (45.5%) were female and 58 (52.7%) came from Sokoto State. The median age of self-reported onset was three years (IQR 1, 7 years) and 40 (36.4%) patients had sought care from traditional healers before coming to the hospital.

6.3.2 Study design

A qualitative study was conducted between April and June 2018. Semi-structured interview guides with open-ended questions were used, and the course of the interviews were left open so that any new themes that emerged could be fully explored.

6.3.3 Recruitment and sampling

IDIs were conducted with 12 caretakers (looking after child patients admitted to the NCH at the time of data collection) who were recruited using convenience sampling. The interviews were carried out by HMB, a first language Hausa speaker who was thoroughly trained before data collection commenced and who has experience working with noma patients, accompanied by the Principal Investigator, EF. The researchers interviewed caretakers who were present at the hospital during the data collection period. The head matron of the hospital invited caretakers to participate in the study. As the caretakers were at the hospital for extended

periods of times (up to six months), they were known to the head matron. We met with the matron and requested that she invite caretakers from both rural and urban locations to increase the variety of potential participants. Fifteen traditional healers (people in the community who have taken on the role of providing non-biomedical health care and have not received biomedical training) were recruited through purposive sampling. The outreach team at the NCH compiled a list of traditional healers working in Sokoto State where the MSF program was based (between a 30 minute and three hour drive from the hospital). Traditional healers were then contacted from this list by telephone. If they could not be reached by phone, the research team visited their villages and invited them to participate.

All participants were informed of the aims of the study prior to the interviews taking place. The researchers conducted interviews until data saturation occurred, saturation being the point at which no new information emerged from the interviews [160].

6.3.4 Data collection

Interview guides were developed for both interview groups (caretakers and traditional healers) in English, translated into Hausa by HMB and then back-translated by an independent Hausa speaker to ensure accurate translation. Any inconsistencies were rectified and the final version was used for pilot interviews, after which additional adjustments were made and the guides were then finalised. Interviews were conducted in Hausa and audio-recorded in quiet, private, locations. During the interviews, photographs of the five different stages of noma were shown to traditional healers to help interviewees discuss their knowledge and health care practices for the various stages of the disease. Interviews lasted approximately 30-45 minutes. No one else besides the researchers and participants were present during the interviews.

6.3.5 Data analysis

Audio-recorded interviews were transcribed into Hausa and then translated verbatim into English by HMB and checked by EF. Data saturation was discussed between investigators and once this occurred, data collection ended. Transcripts were manually coded by EF. EV and EF read the translated transcripts several times, and then codes that emerged were highlighted. The codes were then discussed within the research team, firstly between HMB and EF and then with three other members of the research team (EV, JGC and BS) [222]. Thematic analysis was undertaken to identify patterns in the data with attributed codes [222].

6.3.6 Ethics

The MSF, UDUTH, and the Sokoto State Ministry of Health ERBs approved the study protocol. Procedures followed were in accordance with the ethical standards of the Helsinki Declaration. Written informed consent for interviews and audio-recordings were obtained in Hausa. For participants who were illiterate, the consent form was read aloud to them and a thumbprint was then requested in place of a signature.

6.4 Results

We interviewed 12 caretakers of noma patients and 15 traditional healers. Caretakers were predominantly the mothers of patients (10/12); one was the grandmother of a patient, and the other the father. The median age of caretakers was 38 years and ranged from 22 to 55 years. Traditional healers were mostly male (13/15). The median age of male traditional healers was 55, ranging from 35 to 80 years, and they reported practicing traditional medicine for a median number of 30 years, ranging from two to 50 years. Female traditional healers were younger (35 and 40 years) and had worked as a traditional healer for short periods (two and three years respectively).

Three main themes emerged during data analysis: 1) the role and experiences of traditional healers, particularly in the management of noma cases; 2) relationship dynamics between caretakers and traditional healers; and 3) knowledge and perceptions of noma and treatment health care practices for the different stages of the disease.

6.4.1 The role and experiences of traditional healers in Sokoto, northwest Nigeria

Traditional healers reported that they played specific roles in the community, were well known and believed that their healing skills were understood and appreciated in the areas where they lived and worked:

> *"Everybody in this village small or big… knows that it is my work" (Traditional Healer (TH) 8).*

Even though the traditional healers resided in the communities within which they worked, some were well known in a wider geographical region, and reported that patients visited them from hundreds of kilometres away, some even travelling across borders:

> *"Based on my ability, people are coming [from] everywhere [even] all the way [from] Tawa [in Niger]. They are all coming to search for help from me" (TH 15).*

Traditional healers reported learning their craft in different ways, including inheriting the knowledge from family members and others through dreams and spirits:

> *"I inherited [traditional healing knowledge] from my grandfather" (TH 3).*
>
> *"This craft, I got it from a spirit. In my dreams I am told what [treatments] to get and so I go and get them and then I will mix it" (TH 9).*

Many traditional healers stated that they had specializations and only treated specific diseases. One traditional healer reported treating an array of diseases, whereas others noted one or two. None of the traditional healers specifically mentioned noma, although some of them mentioned treating elements of it (such as ciwon daji [cancer] and iska [spirit]).

> *"We have remedies for gudawa (dysentery), shawara (typhoid) and for basur (haemorrhoids)" (TH 1).*
>
> *"I sell remedies for ciwon baya (back pain) and zufanjiki (general swelling of the body)" (TH 4).*

These diseases were reportedly treated by the traditional healers with a variety of methods. Most of the remedies offered were obtained from sources surrounding their villages, such as trees and plants. Remedies included giving patients dried herbs, grinded plants "to soak" and then to drink, ointments to rub onto the skin and piercing of the skin to create "bleeding marks". In conjunction with other aspects of their healing traditional healers used spiritual beliefs including reciting the Qur'an to their patients.

6.4.2 Relationship dynamics between caretakers and traditional healers

Caretakers of noma patients reported seeking care from a range of health services in the community including hospitals, pharmacists (informal care providers who sell medication) and traditional healers.

> *"I prefer going to the hospital because they care most about a person's health" (Caretaker (C)7).*
>
> *"I like going to the pharmacist because you can go very quickly and buy the medication" (C4).*

Caretakers had differing perceptions of traditional healing: some said they made use of traditional healers' health care services because they were effective or accessible and some because they were affordable:

"If we go, we get better" (C9).

"Some people prefer visiting traditional healers if they are ill as they will quickly get treatment [in comparison] to [the time it would take at the] hospital" (C 10).

"I went there [to a traditional healer]. I find it much better, very much better, as there is less cost" (C6).

Other interviewees said that they had heard positive things about the services offered but had not personally visited a traditional healer before. One caretaker said:

"My neighbours used to go and they are happy about it and told me to try it but I did not try it" (C1).

Caretakers who had visited traditional healers for general health issues, noted a positive relationship with them, and described the type of care offered as efficient:

"When we went he immediately said what it was, he then gathered the remedies and gave them to me. He said "do as I say, do it like that". By His grace when we did it like that, [the treatment] worked" (C9).

The same positive relationship was noted by traditional healers:

"A lot of people are buying and drinking [our remedies] and feel good about it" (TH1).

Trust in the relationship between caretaker and traditional healer was mentioned by both parties:

> *"I am trusted by people. Honestly, a lot of babies that are weaned that could not stop crying or choked while taking the breast are brought to me and are [treated] successfully" (TH 1).*
>
> *"Ah, honestly we trust them because the healer is like our father" (C5).*

This trust was paired with accountability as partial payments were made upon care provision and the remaining payments made after the care provided was seen to be successful:

> *"[We] make a payment agreement that [the caretaker] will not [pay all] now. If I treat and he gets healed after [you can pay me]. If you did not heal, I do not want your money" (TH 8).*

6.4.3 Knowledge and perceptions of noma and health care practices for the disease

Many caretakers and traditional healers referred to noma as "*ciwon daji*" or "*daude*", which when translated from Hausa to English, refers to a general cancer which can occur anywhere in the body.

> *"We conclude that it was ciwon daji (cancer)" (C2).*

Some caretakers believed that noma was the "*disease of iska (spirit)*" and that it was "*brought by God*". Views differed about the causes of noma, with some caretakers believing that measles "*started"* noma in their child. There were also traditional healers, who believed that noma was caused by mumps:

"This work is that of mumps. Mumps make the teeth have inflammation. This the same as remedy for mumps. If it affects a person it will destroy their mouth and the mouth will smell" (TH12).

Some traditional healers reported never having seen or treated the disease, even when shown photos of it during interviews:

"I never saw it honestly… I have not done a matter like this" (TH2).

"I do not know anything about this disease" (TH3).

Caretakers reported seeking care at a variety of biomedical institutions including pharmacies, community health centres, clinics and hospitals, as well as from traditional healers, before coming to the NCH. The pathway to care was at times complex and time-consuming:

"So it was the starting point of the disease, we saw that her face was getting chubby and then we went to collect traditional treatment. We were mixing it and giving it to her to drink. We saw the cheek getting bigger so we took her to the hospital where they dressed the wound and closed the affected area. After two days he opened it and the area was spoiled and so we took her to [the big town]" (C 4).

"Before we came here we went to one hospital where he was given three injections. They referred us to the general hospital, and they referred us to a medical centre where we spent eleven days. Someone who works at the other hospital came and saw the disease and asked the medical centre to refer us to Sokoto" (C 5).

Some caretakers mentioned delays in accessing care; the main reasons were not having money to pay for transport and problems with finding childcare for their other children.

A variety of symptoms for the different stages of noma were described by caretakers and traditional healers. Many of the caretakers who were interviewed reported the first signs and symptoms of noma as a "*fever*"; "*skin rash like a single grain of millet*" and swelling:

> *"At first her eyes swelled. The following morning everywhere had swollen up; you cannot even see the eye" (C 8).*

When traditional healers were asked about their knowledge of the different stages of noma, the majority saw them as separate diseases and treated them as such. Traditional healers most often reported treating the earlier stages of noma (gingivitis and oedema), and referring children with the later stages of the disease to other forms of care. One traditional healer noted that "*[he] does not know noma disease*", but for the swelling stage of the disease he said "*there is remedy for it*", and for the necrosis stage he stated he "*does not know*" the remedy showing noma was not seen as a single disease, but as multiple conditions.

Gingivitis was usually treated with an ointment that was rubbed directly onto the gums:

> *"If the teeth are bleeding, I give a remedy. If a person puts it inside the mouth and [swills] it around the mouth, the [bleeding] will stop" (TH 8).*

Some traditional healers diagnosed the stage of noma associated with swelling of the cheek as "ciwon daji" (cancer) or "ciwon iska" (spirit), and offered care to the patients accordingly. Caretakers also reported being given this diagnosis and relevant remedies.

> *"[We are] taught it is ciwon daji (cancer). They find a branch of a tree and soak it to drink and to rub. That is what we were taught to do if the cheeks become big" (C2).*
>
> *"I will mix [the bark from three trees locally known as] tsada, tamarind and kaiwa and grind them and sieve them to drink in the morning and in the evening. [I use] the*

madarar tunwahiya [ground herbs], mix them all together and pour them onto the swollen area" (TH9).

Some traditional healers noted uncertainty about the stages of the disease and whether the stages were related. They had treated the swollen cheek stage which had a known remedy:

"I treat it but I do not know what the disease is unless I understand it is swelling. If it is swelling I can understand it and give treatment remedy" (TH3).

Traditional treatment options for a swollen cheek included piercing the cheek with a hot blade (initially placed in a fire) to decrease the swelling:

"If the remedy is drunk, it will go down or it will swell up to do piercing or it will burst" (TH8).

Caretakers also reported visiting traditional healers for assistance with piercing the swollen cheek:

"I visited…this piercer, the piercing was done, the following morning the [swelling] did not stop we came here [NCH]" (C10).

Traditional healers did not commonly report seeing patients in the necrosis stage of the disease, and as such, this stage was not widely known, although some were able to recognise it. One traditional healer described this stage as "*burnt meat*".

Caretakers reported being offered various remedies from traditional healers when visiting them with the child later diagnosed at the NCH as having noma. The remedies offered included "*ground herbs or tree branches…for drinking, rubbing and bathing"; and "to be mixed with pap [*a type of porridge staple made from maize, sorghum, or millet*] to drink".*

Caretakers reported mixed efficacy of these remedies:

> *"Last year when he was sick I took him [to the traditional healer] so this year when it came back I thought it is the same with the last one and I took him there, then I collected that remedy and it did not work so I took him to hospital" (C6).*
>
> *"I collected [the remedy] but I did not see any improvement" (C7).*

Traditional healers reported utilising referral to hospitals and doctors for unknown ailments, or conditions they felt would be best treated elsewhere.

> *"For the [diseases I] cannot [treat], I will send them to a doctor who can treat them" (TH5).*
>
> *"[I]f I see that [the disease] is much and beyond me and I cannot do the work I will refer him to the hospital. If it is too much [for me] I can only send a person to hospital" (TH9).*

Referring to all stages of noma treatment, one traditional healer stated that, *"For that disease, it is a doctor that gives help".* Other traditional healers reported not knowing where to refer noma patients.

One caretaker reported being referred to the NCH by a traditional healer who stated, "*This disease is beyond my power but some kids are taken to Sokoto [NCH]*".

And some traditional healers reported that now that they knew about the NCH, they would begin to refer any noma cases:

> *"As from today that we started the relationship, your issue [noma] is not a playing one as from today if I hear a person having it if I know your place I will take him" (TH13).*

When asked whether they would be interested in attending a training on noma, which would involve learning about the different stages of the disease, some traditional healers noted they were too old to travel, but most said they would be willing to attend and were enthusiastic about learning more about noma.

6.5 Discussion

Traditional healers play a role in the health system of northwest Nigeria; our findings showed that they are trustworthy, accessible, affordable care providers who offer specialised forms of care for specific conditions, and offer guidance on referral options. Traditional healers viewed the stages of noma as different conditions with individualised remedies rather than as one disease, which is similar to the biomedical approach in that each stage of noma has a specific treatment protocol [1]. There are however, crucial differences in the understanding of the aetiology and pathogenesis of the disease. Without the knowledge that the stages of noma are linked and are one condition, the impetus of referring noma cases in the early reversible stages of the disease may be lost. Traditional healers reported referring people to other providers when they were unable to treat a specific condition, and the majority stated that they would be willing to refer noma patients to the NCH and attend training on the disease. These are important indicators of the potential positive impact referral networks involving traditional healers could have.

There is no other literature looking at how traditional healers diagnose and treat noma, making comparisons with other findings challenging, with only one study suggesting that qualitative research methodologies are useful in understanding craniofacial conditions such as noma [223]. The naming of noma as ciwon daji which loosely translates to ‘cancer’ in English is also of

interest, as this is similar to a biomedical name for the disease which is frequently used, cancrum oris, meaning mouth cancer [64].

A third of caretakers at the NCH visited traditional healers before coming to the hospital. Our study corroborates other research findings that show that traditional healers are the first point of care for many people, especially those living in rural areas with little access to biomedical health facilities [224], and that the first line of treatment for 60% of children living in Nigeria who have a high fever from malaria would be traditional medicine [225]. The pluralistic nature of the Nigerian health system, where biomedical and traditional care are offered together in a dynamic system is not unique to this setting and has been seen in other contexts including Ghana [226], Nepal [218] and South Africa [227].

Our study showed that caretakers trusted traditional healing methods, and that care was sought from traditional healers due to the belief in its quality, as seen in a study from Cameroon [220]. Treatments offered by the traditional healers in our study such as ointments and piercings/bleeding marks were similar to those offered by healers in other studies [215, 228], as were the diversity of diseases treated [213, 217, 227–233].

Due to the rapid evolution of noma [2], it is imperative that patients are detected early and receive the appropriate treatment (antibiotics, wound cleaning and nutritional support) during the reversible stages of the disease. Some traditional healers reported recognising and treating the earlier stages of noma, and this, along with the fact that caretakers reported seeking care at traditional healers first, reinforces the importance of ensuring that traditional healers are able to detect cases of noma early and refer them to appropriate health care facilities. Not many traditional healers reported treating the later stages of the disease. This finding could be due

to the severe isolation patients with noma sequelae face or a lack of knowledge by patients, caretakers and traditional healers about the potential surgical treatments available, which could lead to care not being sought. This could also suggest that caretakers seek care elsewhere for the later stages of disease, or that, due to the rapid progression of the disease, the patients die before seeking care.

Partnering with traditional healers in order to set up robust referral networks for diseases has been implemented in a variety of settings [221, 234, 235]. A South African study noted that referrals by traditional healers were affected by the attitudes, subjective norms and perceived behavioural controls as influences on behaviour, which would need to be studied at a more in-depth level in our setting [236].

The willingness of traditional healers to be a part of referral networks and take part in a training, caretakers' positive views of traditional healing and their geographical proximity to patients provides a unique opportunity to build such partnerships. This could increase the frequency with which noma patients are detected at a community level and the speed with which they are referred, thus leading to efficient access to treatment in the crucial early, reversible stages of disease. Traditional healers could also identify patients with noma sequelae who require surgical care and refer them to the appropriate facilities. Training efforts should include a strong emphasis on the linkages between the noma stages, and the important need for rapid referral in the early stages. Future studies on the effectiveness and efficiency of referrals are needed as well as research assessing biomedical health care worker knowledge on noma as this could greatly impact the effectiveness of referral partnerships.

Study limitations include selection bias as we included caretakers of patients already accessing biomedical care through a convenience sampling approach. They may not have been an accurate representation of all caretakers of noma patients, especially of those who might make more use of traditional healers than biomedical care. There was also the potential for introducing social desirability bias as there could have been a reluctance to offer a wide range of opinions about traditional healers [237]. We were not able to interview traditional healers who had provided care for patients in the later stages of noma. This limits our insights into the care provided for these stages. We only included traditional healers who consented to being a part of the study, and there is the potential for the introduction of social desirability bias which may have meant we did not capture the full range of beliefs and treatments offered for the disease.

Our research has identified several different actors involved along the pathway to care of noma patients, including traditional healers, who need to be included in intervention activities. These findings show that traditional healers would be willing to attend trainings on the disease, and be a part of referral partnerships for noma patients. This collaboration could expedite care provision from the community level, which would ultimately save lives and reduce the severity of the complications associated with noma.

Chapter 7 Prevalence of noma stages

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Additional resources

The questionnaire and informed consent and assent forms used in this chapter can be found in Appendix 6.5 and Appendix 7.5.

Relevance of this paper to the thesis

One of the main gaps in knowledge around noma is the enumeration of the disease. This chapter presents robust, primary results of noma prevalence in Sokoto and Kebbi States, northwest Nigeria. The findings from this manuscript will be utilized in advocacy efforts and prevention programming.

Contribution of the student and co-authors

EF, AL, KB, SvdK, DBM, UM and CA conceptualised the project. EF developed the protocol with input from all authors. EF, MJO and JS collected the data. EF conducted the data analysis

with guidance from AL and CA. EF wrote the first draft of the manuscript. All authors critically reviewed the manuscript and provided final approval.

7.1 Abstract

7.1.1 Background

Noma, a rapidly progressing infection of the oral cavity, mainly affects children. The true burden is unknown. We aimed to estimate noma prevalence in children in northwest Nigeria.

7.1.2 Methods

Oral screening was performed on all ≤15 year olds, with caretaker consent, in selected households during this cross-sectional survey. Noma stages were classified using WHO criteria and caretakers answered survey questions. The prevalence of noma was estimated stratified by age group (0-5 and 6-15 years). Factors associated with noma were estimated using logistic regression.

7.1.3 Results

A total of 177 clusters, 3,499 households, and 7,122 children were included. In this sample, 4,239 (59.8%) were 0-5 years and 3,692 (52.1%) were female. Simple gingivitis was identified in 3.1% (n=181; CI 2.6-3.8), acute necrotizing gingivitis in 0.1% (n=10; CI 0.1-0.3), and oedema in 0.05% (n=3; CI 0.02-0.2). No cases of late-stage noma were detected. Multivariable analysis in the 0-5 year age group showed having a well as the drinking water source (aOR 2.1; CI 12-3.6) and being aged three to five years (aOR 3.9; CI 2.1-7.8) was associated with being a noma case. In six to 15 year olds, being male (aOR 1.5; CI 1.0-2.2) was associated with being a noma case and preparing pap once or more per week (aOR 0.4; CI 0.2-0.8) was associated with not having noma. We estimated that 129,120 (CI 105,294-152,947) individuals <15 years of age would have any stage of noma at the time of the survey within the two states. Most of these cases (94%; n=120,082) would be children with simple gingivitis.

7.1.4 Conclusions

Our study identified a high prevalence of children with simple and acute necrotizing gingivitis. Noma is important but neglected and therefore merits inclusion in the WHO Neglected Tropical Diseases (NTD) list.

7.2 Introduction

Noma, also known as cancrum oris, is a poorly understood, rapidly progressing infection of the oral cavity, with a reported 90% mortality rate [1]. If untreated, death usually occurs within weeks after the onset of symptoms [1, 2]. Treatment with antibiotics, wound debridement, and nutritional support in the early reversible stages of the disease greatly reduces mortality and morbidity [2]. Noma mostly affects children aged two to five years, and those who survive have severe facial disfigurements and multiple functional impairments including difficulties eating, seeing, and breathing, contributing towards stigmatization [2]. Noma starts as an inflammation of the gums leading to the rapid destruction of the hard and soft tissues of the face usually within one week [94]. The WHO has classified noma into stages [1]: Stage 0: simple gingivitis; Stage 1: acute necrotizing ulcerative gingivitis; Stage 2: oedema; Stage 3: gangrene; Stage 4: scarring; Stage 5: sequelae. Simple gingivitis ("Stage 0") is a precursor to noma. Acute necrotizing gingivitis is distinguished by orofacial necrosis and ulceration accompanied by severe halitosis. It is unknown what proportion of simple or acute necrotizing gingivitis cases progress to the later stages of noma, but it is thought to be a small fraction [1]. In the majority of later stage cases, infection causes the destruction of the cheek, while destruction of the jaw, lip, nose, and eye have also been reported [3]. Noma can become inactive with, and sometimes without, treatment. Once this occurs, patients can survive into adulthood but often require extensive reconstructive surgery and physiotherapy to correct the

resulting defects and improve function [1]. The aetiology of noma is unknown but thought to be multifactorial [2]. Noma typifies the complex interactions between extreme poverty, malnutrition, poor oral hygiene, poor access to routine childhood vaccinations, limited access to quality health care and immunosuppression resulting from comorbidities such as HIV [2].

In the 1800s, noma was widely reported in Europe [238] but is currently thought to be most prevalent in low-resource settings in Africa and Asia [104]. The oldest estimate of the burden of this disease that we could locate was from Edinburgh, United Kingdom, which indicated that noma was diagnosed once out of every 5,000 cases of children with an illness between 1860 and 1871 [65]. In 1998, the WHO estimated that 140,000 new cases of noma occur each year globally and that 770,000 patients were living with noma sequelae at that time, however the origin of this estimate and the stages included are unclear [19, 111]. Two 2003 Nigerian studies estimated the burden of disease ranged from seven cases per 1,000 children aged between one and 16 years (Denloye *et al.,* 2003) [42] to 6.4 per 1,000 children (Fieger *et al.,* 2003) [7]. The most recent study from 2019 estimated the period prevalence of noma from 2010-2018 was 1.6 per 100,000 population at risk in Nigeria [239]. These estimates are based on expert opinion, number of hospital admissions and retrospectively collected hospital-based data and it is unclear which stages of noma were included [49]. Our understanding of the current disease burden and epidemiology thus remains limited. There are few studies not only on the burden of disease but also on the pathogenesis and mortality rate. Although these aspects highlight the neglected nature of the disease, noma is not currently on the WHO NTD list.

Noma cases are frequently reported in Nigeria [6–8, 23, 37–39, 41–43, 50, 64, 71, 81, 89, 99, 100, 102, 148]. The Nigerian Centre for Disease Control recorded 37,646 noma cases from 2011 to 2017 [240]. However, these records may underestimate the true burden of cases, given

limited surveillance data and the potential for under-reporting (low rates of diagnosis, patients not accessing health care, reported high and rapid mortality) [240]. The majority of noma cases are reported from the northwest and northeast of the country [241]. At the 2018 National Noma Day Workshop, the Nigerian Ministry of Health confirmed that noma was a national public health priority, and highlighted the urgent need to generate robust evidence on the country's disease burden for programmatic planning [242]. This study contributes towards this need by estimating the prevalence of noma in northwest Nigeria using a robust cross-sectional population-based approach.

7.3 Methods

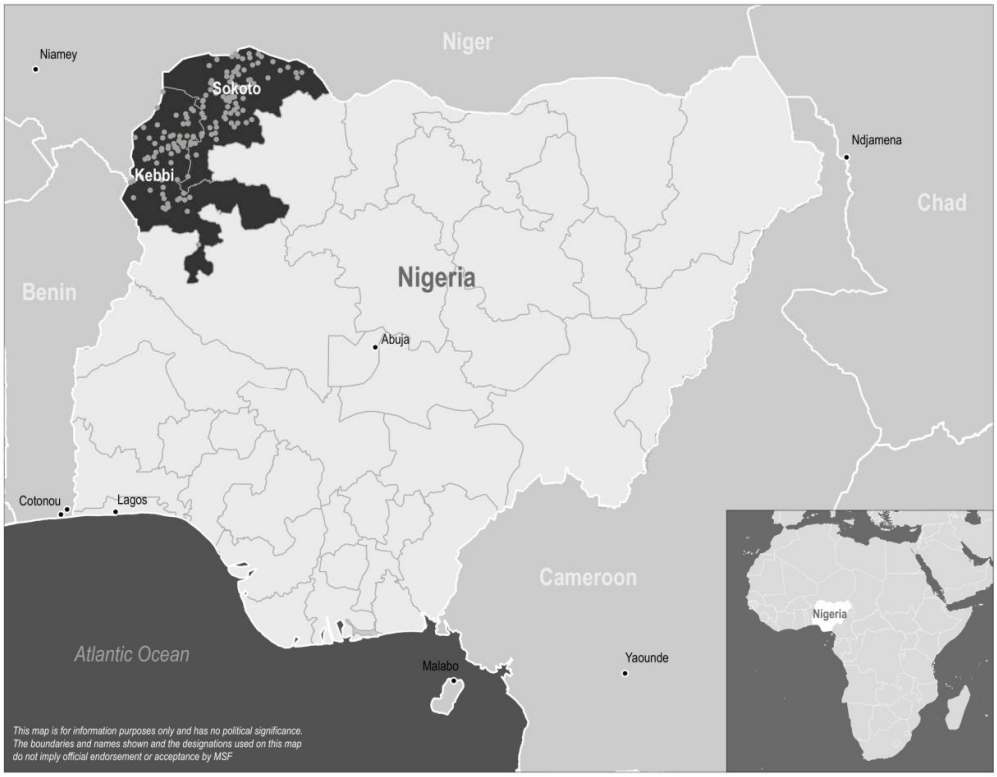
7.3.1 Study design and setting

A two-stage cluster-based cross-sectional survey was conducted in Sokoto and Kebbi States in northwest Nigeria (Figure 7.1).

7.3.2 Sampling

Based on the 2006 Nigerian census data (with a 2.4% annual population increase), Sokoto and Kebbi States have an estimated population of 4,798,979 and 4,203,978, respectively (2,063,560 and 1,807,710 aged under 15 years in Sokoto and Kebbi respectively) [243]. Sample size calculations indicated the need for inclusion of 3,615 households across 181 clusters with 20 households per cluster in order to estimate noma prevalence with precision of 0.4%. This calculation was based on the following assumptions: prior prevalence estimate, 1% [7]; design effect, 2; 1.98 children per household in the 0-4 year age group [244]; average household size, six [245]; and a 10% non-response rate.

Figure 7.1 Clusters where data was collected (pale grey dots) within Sokoto and Kebbi States, northwest Nigeria.



The number of villages (clusters) per ward were selected proportional to the population size of each administrative ward. A sampling frame of villages was created by ward in Sokoto and Kebbi using geo-sampling remote sensing methods. The OpenStreetMap database was compared against freely available satellite imagery to identify and verify village geo-locations and add new village geo-locations to the list. Villages were each assigned a number and a random selection was conducted. Once the teams reached the villages, they first visited the village head to ask permission to conduct the study and if this was given, the team then asked the village head to identify what the residents of the village would define as the central point of the village. Once at this central point, the adapted WHO EPI method of sampling was conducted to select the first compound [246]. At the central village point, the pen was spun and the team leader walked in the direction of the writing point of the pen to the edge of the village where the pen was spun again. The team leader then walked in a straight line (following the direction of the pen) and counted all the compounds along the path. The number 1 and N (total number of compounds) were inputted into a random number generator, and the compound allocated to the number generated was the first compound selected. When inside the selected compound, the number of households in each compound were counted (a household was defined as the children of one mother in the compound that lived in one hut). A random number was generated and the household allocated to that number was selected. If the house was empty, the interviewers proceeded to the next household to the left. If all households of a selected village were included in the study before completing the required number of households, the sampling was continued by selecting the geographically closest village.

7.3.3 Study participants

All children aged ≤15 years who lived in a selected household in sampled clusters were included in the study.

7.3.4 Data collection

Five research teams, each with five team members, of whom one was a nurse or doctor, and one the team leader, carried out data collection. To ensure standardisation of data collection methods, the teams were trained for one week prior to the commencement of data collection on the use of consistent measuring tools following the Standardised Monitoring and Assessment of Relief and Transitions (SMART) methodology which is an integrated method for assessing nutritional status in emergency situations [247]. Teams followed directions to selected clusters using a mobile mapping application (OsmAnd©) on data collection tablets (electronic mobile devices).

Consenting caretakers answered a structured questionnaire, collected on tablets using KoBoCollect, which covered: sociodemographic characteristics, living conditions, child's vaccination status, oral hygiene practices, food preparation, feeding practices and access to health care in the twelve months preceding the interview. For the questions around feeding practices, pap was defined in this context as a type of porridge staple made from maize, sorghum, or millet. Interviews were conducted in Hausa, and answers were coded automatically on the KoBoCollect tool into English.

In the sampled households, all eligible children underwent oral screening, which involved visual examination by a medical team member for any noma stage, based on the WHO classification [1]. The caretakers of children with simple gingivitis were advised to follow a strict oral health regimen (gargle with salt water or use water to clean mouth twice or more a day) as were acute necrotizing gingivitis cases who were also referred to the closest health centre. If children were identified as having any later stage of noma, they were referred directly to the NCH for care.

To assess the malnutrition status in children aged six months to five years, MUAC measurements were conducted using a flexible MUAC device with a precision of 1 mm.

Medical data (oral screening and MUAC) was collected on paper and later entered into a password-protected database by the study team.

Collected data were screened daily by the research team supervisors to identify inconsistencies and missing items and immediate feedback was given to the data collection teams.

7.3.5 Statistical analysis

We performed descriptive analyses of household characteristics in the study sample. Categorical variables are reported as frequencies and percentages. Continuous variables are summarised using medians and IQR. Missing data numbers are recorded in each table.

Wealth scores were calculated by assigning a value of one to each of the following items owned by the family: a mobile phone, motorbike, tractor and camel (these items were chosen based on consultation with local researchers who were knowledgeable about the context). The minimum wealth score was zero and the maximum was four.

Weighted prevalence and CI for all WHO noma stages were estimated, and stratified by age group (0-5 years and 6-15 years). The number of individuals with noma in Sokoto and Kebbi States was calculated by extrapolating the percentage prevalence from our study results to the total population in the 0-15 year age group for these states. This calculation took into consideration the cluster survey design and population age distribution of the two states. Using MUAC measurements, we estimated the weighted prevalence of SAM (MUAC <115 mm),

MAM (between MUAC ≥115mm and <125 mm) and GAM (MUAC <125 mm) in children aged six months to five years. The standard errors of the estimates were adjusted using the linearization method (syvset suite of Stata commands) to reflect the two-stage clustered design of the survey [248]. The estimates and standard errors were weighted to account for the actual population distribution of the two states, as our survey sample was observed to have under-represented participants aged six to 15 years when we compared our sample's age distribution to the population age distribution. The design effect (DEFF) was calculated to assess the ratio of variance under the sampling method used, in comparison to the variance of a simple random sample. This reflects the impact of the cluster sampling strategy. DEFF is reported for each prevalence and malnutrition estimate.

Univariable analysis with logistic regression was conducted to identify factors associated with noma Stages 1 and 2 in the total study sample, where the number of noma cases were too small to allow for multivariable analysis.

Univariable and multivariable analysis were conducted using logistic regression, to estimate factors associated with any noma stage (Stage 0-2); stratified by age group (0-5 years and 6-15 years). Variables chosen for inclusion in the multivariable analysis were those with ten or more cases [249] and a univariable strength of association equivalent to a p-value <0.2, after assessing collinearity among variables. To further understand the association with age, an age covariate with finer age categories (0-2 years, and three to five years, in the younger age group model; and six to ten years, and eleven to 15 years, in the older age group model, respectively) were included in the univariable analyses for both age group models, and in the 0-5 year old multivariable model.

All data analysis was conducted with Stata 15 (StataCorp LP, College Station, TX, USA).

7.3.6 Ethics

Ethical approval was obtained from the MSF, UDUTH and the Sokoto and Kebbi States Ministry of Health ERBs. Written informed consent was obtained from all literate caretakers; caretakers with insufficient literacy provided a thumbprint and a signature from a literate witness. For individuals aged eight to 17 years, the child provided assent and a caretaker provided written consent.

7.4 Results

The survey was conducted from 17 September to 5 November 2018, and included 3,499 households in 177 clusters, 92 clusters from Sokoto and 85 from Kebbi (four clusters were not accessible because of security issues), with 7,164 children aged <15 years. As 42 children did not have oral examinations, they were excluded from the analysis and the remaining 7,122 were included. The median caretaker age was 30 years (IQR 25-35); 3,423 caretakers (97.8%) were female; 2,194 (30.8%) were employed or self-employed, and the median household size was five people (IQR 4-7). Most children (n=4,239; 59.5%) were aged 0-5 years, 3,692 (52.1%) were female, 5,875 (83.0%) had no education, and 6,686 (94.4%) had a primary caretaker that was the mother (Table 7.1 and 7.2).

Table 7.1 Demographic characteristics of households in the noma prevalence survey population.

Households n=3,499	n (%)
Caretaker age, years median (IQR)	30 (25-35)
Caretaker Sex	
Female	3,423 (97.8%)
Male	76 (2.2%)
Caretaker income source	
Employed or self-employed	2,194 (30.8%)
Unemployed or other*	4,927 (69.2%)
Total household members median (IQR)	5 (4-7)
Drinking water source	
Bore hole in the village	644 (18.4%)
River	91 (2.6%)
Tap (running water)	578 (16.2%)
Well in the compound	1,512 (43.2%)
Other	674 (19.3%)
Treat water before drinking (Yes)	1,026 (29.3%)
Type of sanitation facility	
Flushing toilet	224 (6.4%)
Pit latrine (with slab)	650 (18.6%)
Pit latrine (no slab)	1,168 (33.4%)
Other**	1,457 (41.6%)

IQR- inter-quartile range

*Other caretaker income source includes being a housewife or student

**Other sanitation facility includes neighbours house, the bush, river

Table 7.2 Demographic characteristics of children in the noma prevalence survey population.

Children	Total n n=7,122 (%)*	0-5 year olds n n= 4,239 (%)	6-15 year olds n n= 2,841 (%)
Age groups (years)			
0-5	4,239 (59.8%)		
6-15	2,841 (40.1%)		
Missing	42*		
State			
Kebbi	3,291 (46.5%)	2,045 (48.2%)	1,246 (43.9%)
Sokoto	3,789 (53.5%)	2,194 (51.8%)	1,595 (56.1%)
Missing	42*	0	0
Child sex			
Female	3,692 (52.1%)	2,119 (49.9%)	1,573 (55.4%)
Male	3,388 (47.9%)	2,120 (50.0%)	1,268 (44.6%)
Missing	42*	0	0
Education of child			
None	5,875 (83.0%)	3,850 (90.8%)	2,025 (71.3%)
Any education	1,204 (17.0%)	388 (9.2%)	816 (28.7%)
Missing	42*	1	0
Primary caretaker of the child interviewed			
Mother	6,686 (94.4%)	4,061 (95.8%)	2,625 (92.4%)
Other (father, grandmother, grandfather)	394 (5.6%)	178 (4.2%)	216 (7.6%)
Missing	42*	0	0
*n= 42 missing age category			

7.4.1 Prevalence

Table 7.3 reports the prevalence of all stages of noma in the study population overall and by age group. Any stage of noma was identified in 3.3% of sampled children (n=194; CI 2.7-4.0). Stage 0 noma was identified in 3.1% (n=181; CI 2.6-3.8), Stage 1 in 0.1% (n=10; CI 0.1-0.3), and Stage 2 in 0.05% (n=3; CI 0.02-0.2). No children with Stages 3 to 5 noma were detected in our study population (Table 7.3). Based on these results 3,300 out of every 100,000 children in the 0-15 year age group would have any stage of noma (including simple gingivitis) and 150 out of every 100,000 children would have Stage 1 or 2 noma in the study area.

The prevalence of SAM in children aged six months to five years (n=3,993) was 3.7% (n=149; CI 3.2-4.4) and MAM 7.7% (n= 309; CI 6.7-8.7) (Table 7.3).

7.4.2 Factors associated with noma

Table 7.4 describes univariable analysis of risk factors for Stage 1 and 2 noma regardless of age category. This analysis showed that having eaten pap in the last 24 hours (OR 0.2; CI 0.1-0.9); the child eating pap once or more per week (OR 0.4; CI 0.1-0.9) and the caretaker preparing pap once or more per week compared to less frequent preparation of pap (OR 0.3; CI 0.1-0.8) were associated with not having Stage 1 and 2 noma. The child experiencing an illness in the 12 months prior to the interview was associated with being a Stage 1 and 2 noma case (OR 8.8; CI 1.1-69.5) (Table 7.4).

Table 7.3 Noma stage and malnutrition prevalence (overall and by age group).

	Total (n=7,122)*			0-5 year olds n=4,239*			6-15 year olds n=2,841 *			
	n (%)	CI	Deff	n (%)	CI	Deff	n (%)	CI	Deff	P (age comparison)
Any noma	194 (3.3%)	2.7, 4.0	1.9	63 (1.5%)	1.1, 2.0	1.3	129 (4.4%)	3.6, 5.4	1.6	<0.001
Noma stages										
None	6,928 (96.6%)	95.9, 97.2	1.9	4,176 (98.5%)	98.0, 98.9	1.3	2,712 (95.6%)	94.6, 96.4	1.6	<0.001
Stage 0: Simple gingivitis	181 (3.1%)	2.6, 3.8	1.8	56 (1.3%)	1.0, 1.8	1.3	123 (4.2%)	3.4, 5.2	1.5	
Stage 1: Acute necrotizing gingivitis	10 (0.1%)	0.1, 0.3	1.2	6 (0.1%)	0.07, 0.3	1.0	4 (0.1%)	0.04, 0.4	1.5	
Stage 2: Oedema	3 (0.05%)	0.02, 0.2	1.0	1 (0.02%)	0.0, 0.2	1.0	2 (0.1%)	0.02, 0.3	1.0	
Stage 3: Gangrene	0 (0%)	NA	NA	0 (0%)	NA	NA	0 (0%)	NA	NA	
Stage 4: Scarring	0 (0%)	NA	NA	0 (0%)	NA	NA	0 (0%)	NA	NA	
Stage 5: Sequelae	0 (0%)	NA	NA	0 (0%)	NA	NA	0 (0%)	NA	NA	
Malnutrition				**6 month – 5 year olds (n = 3,993)**						
Moderate acute malnutrition	NA	NA	NA	309 (7.7%)	6.7, 8.7%	1.5	NA	NA	NA	NA
Severe acute malnutrition	NA	NA	NA	149 (3.7%)	3.2, 4.4%	1.0	NA	NA	NA	NA

*42 missing age category

CI: 95% confidence interval; Deff: design effect, P: P-value comparing age groups

Table 7.4 Univariable analysis for Stage 1 and 2 noma.

		Study population		Univariable analysis		
		Proportion of all respondents; N=7,122; %(n/N*)	Proportion respondents with Stage 1 and 2 noma;N=13; % (n/N*)	OR	CI	P
Primary caretaker	Other	5.6% (394/7,080)	7.7% (1/13)		Reference	0.561
	Mother	94.4% (6,686/7,080)	92.3% (12/13)	0.5	0.07, 4.18	
Pap eaten in the 24 hours before interview	No	32.1% (2,271/ 7,080)	53.8% (7/13)		Reference	0.030
	Yes	67.9% (4,809/ 7,080)	46.2% (6/13)	0.2	0.07, 0.87	
Frequency of the child eating pap per week	<1 or never	30.4% (2,151/7,080)	46.2% (6/13)		Reference	0.049
	1 or more	69.6% (4,929/7,080)	53.8% (7/13)	0.4	0.13, 0.99	
Frequency of the caretaker preparing pap per week	<1 or never	29.9% (2,116/7,080)	53.8% (7/13)		Reference	0.018
	1 or more	70.1% (4,964/7,080)	46.2% (6/13)	0.3	0.11, 0.81	
Duration of breastfeeding at time of interview (months)	12+	89.4% (6,310/7,061)	84.6% (11/13)		Reference	0.782
	0-12	10.6% (751/7,061)	15.4% (2/13)	1.2	0.27, 5.63	
Colostrum given to the child at birth	No	12.0% (843/7,047)	15.4% (2/13)		Reference	0.366
	Yes	88.0% (6,204/7,047)	84.6% (11/13)	0.5	0.10, 2.32	
Child sick during last 12 months	No	30.0% (2,131/7,080)	7.7% (1/13)		Reference	0.041
	Yes	70.0% (4,949/7,080)	92.3% (12/13)	8.8	1.11, 69.49	
Did you seek health care for this child in the last year?	No	48.4% (3,428/,7,080)	23.1% (3/13)		Reference	0.221
	Yes	51.6% (3,652/7,080)	76.9% (10/13)	2.5	0.58, 10.51	
Vegetables eaten in the 24 hours before interview	No	68.2% (4,829/7,080)	76.9% (10/13)		Reference	0.461
	Yes	31.8% (2,251/7,080)	23.1% (3/13)	0.6	0.13, 2.50	

Wealth score (mobile phone, motorbike, tractor, camel)	0-1	63.5% (4,522/7,122)	84.6% (11/13)		Reference	0.106
	2-4	36.5% (2,600/7,122)	15.4% (2/13)	0.3	0.08, 1.27	
*N = total number of respondents who answered the question (excluding missing) OR = odds ratio; CI = 95% confidence interval; P = p-value from logistic regression model. Analysis adjusted for the survey design.						

The risk factors associated with any stage of noma (including Stage 0) for the 0-5 year age group are shown in Table 7.5. The multivariable analysis shows that two factors remained associated with being a noma case in the 0-5 year age group, namely, having a well as the source of drinking water (aOR 2.09; CI 1.22-3.60), and being aged three to five years (aOR 3.90; CI 2.04-7.47) (Table 7.5).

In the six to 15 year age group, the risk factors associated with any stage of noma (including Stage 0) are shown in Table 7.6. Multivariable analysis showed that males were more likely to be noma cases (aOR 1.52; CI 1.04-2.22), and that the caretaker preparing pap once or more per week was associated with not having noma (aOR 0.36; CI 0.16-0.82) in the six to 15 year old age group (Table 7.6).

Vaccination coverage rates in both age groups were low (21% of 0-5 year olds and 12% of six to 15 year olds had any immunisations noted on the vaccination card seen by the interviewer). No association between vaccination status and noma was seen in our study.

7.5 Discussion

We have shown that the prevalence of any stage of noma in Kebbi and Sokoto States is 3.3%. Based on the study results, we therefore estimate that 129,120 (CI 105,294-152,947) individuals <15 years of age would have any stage of noma at the time of the survey within the two states. Most of these cases (n=120,082, 94% of all cases) would be children with simple gingivitis (i.e. Stage 0) and approximately 7,101 (4% of all cases) and 1,937 (2% of all cases) of children would have Stage 1 and 2 noma, respectively. Our estimates exceeded those from Bello *et al.* 2010-2018 period prevalence estimates (1.6 per 100,000) [239] and

Table 7.5 Univariable and multivariable analysis of associations with any noma cases (Stage 0 to 5), 0-5 years.

		Study population		Univariable analysis			Multivariable analysis		
		Proportion of all respondents; N=4,239; %(n/N*)	Proportion respondents with any noma stage; N=63; % (n/N*)	OR	CI	P	aOR	CI	P
Child demographics									
Child age (years)	0-2	46.2% (1,957/4,239)	17.5% (11/63)		Reference	<0.001		Reference	<0.001
	3-5	53.8% (2,282/4,239)	82.5% (52/63)	4.1	2.20, 7.62		3.90	2.04, 7.47	
Birth order	1-2	39.9% (1,691/4,239)	30.2% (19/63)		Reference	0.174		Reference	0.398
	3 or more	60.1% (2,548/4,239)	69.8% (44/63)	1.5	0.83, 2.88		1.36	0.67, 2.79	
Feeding practices									
Duration of breastfeeding	12+ months	84.4% (3,565/4,226)	95.2% (60/63)		Reference	0.020			
	0-12 months	15.6% (661/4,226)	4.8% (3/63)	0.3	0.09, 0.81				
Colostrum given to baby	No	11.9% (502/4,221)	11.1% (7/63)		Reference	0.899			
	Yes	88.1% (3,719/4,221)	88.9% (56/63)	1.1	0.37, 3.09				
Frequency of the child eating pap per week	<1 or never	31.6% (1,340/4,239)	34.9% (22/63)		Reference	0.597			
	1 or more	68.4% (2,899/4,239)	65.1% (41/63)	0.9	0.47, 1.54				
Frequency of the caretaker preparing pap per week	<1 or never	30.8% (1,307/4,239)	34.9% (22/63)		Reference	0.505			
	1 or more	69.2% (2,932/4,239)	65.1% (41/63)	0.8	0.46, 1.46				
Animal products eaten in the 24 hours before interview	No	91.5% (3,879/4,239)	95.2% (60/63)		Reference	0.274			
	Yes	8.5% (360/4,239)	4.8% (3/63)	0.5	0.16, 1.67				

Grains eaten in the 24 hours before interview	No	19.3% (819/4,239)	22.2% (14.63)		Reference	0.607			
	Yes	80.7% (3,420/4,239)	77.8% (49/63)	0.8	0.45, 1.59				
Vegetables eaten in the 24 hours before interview	No	69.6% (2,952/4,239)	69.8% (44/63)		Reference	0.963			
	Yes	30.4% (1,287/4,239)	30.2% (19/63)	1.0	0.56, 1.73				
Health									
Are the teeth ever cleaned (self-reported)	No	13.8% (508/3,679)	9.7% (6.62)		Reference	0.300			
	Yes	86.2% (3,171/3,679)	90.3% (56/62)	1.5	0.69, 3.39				
Teeth cleaning frequency per day (self-reported)	Once or twice	85.1% (3,132/3,679)	88.7 (55/62)		Reference	0.370			
	Less than once	14.9% (547/3,679)	11.3% (7/62)	0.7	0.34, 1.50				
SAM, MAM	Normal	88.5% (3,535/3,993)	91.1% (51/56)		Reference	0.199			
	SAM	3.7% (149/3,993)	7.1% (4/56)	1.0	0.55, 6.85				
	MAM	7.7% (309/3,993)	1.8% (1/56)	0.2	0.03, 1.71				
GAM	Normal	88.5% (3,535/3,993)	91.1% (51/56)		Reference	0.666			
	GAM	11.5% (458/3,993)	8.9% (5/56)	0.8	0.26, 2.36				
Was the child vaccinated (self-report)	No	27.5% (1,165/4,239)	23.8% (15/63)		Reference	0.516			
	Yes	72.5% (3,074/4,239)	76.2% (48/63)	1.2	0.67, 2.20				
Vaccinations listed on vaccination card:									
Diphtheria	No	71.1% (635/893*)	75.0% (12/16)		Reference	0.688			
	Yes	28.9% (258/893)	25.0% (4/16)	0.8	0.21, 2.81				
Pertussis	No	73.7% (658/893)	75.0% (12/16)		Reference	0.840			
	Yes	26.3% (235/893)	25.0% (4/16)	0.9	0.24, 3.21				
Tetanus	No	82.1% (733/893)	75.0% (12/16)		Reference	0.584			
	Yes	17.9% (160/893)	25.0% (4/16)	1.4	0.40, 5.11				

Hepatitis A	No	93.4% (834/893)	93.8% (15/16)		Reference	0.900			
	Yes	6.6% (59/893)	6.3% (1/16)	0.9	0.11, 6.86				
Hepatitis B	No	77.4% (691/893)	68.8% (11/16)		Reference	0.415			
	Yes	22.6% (202/893)	31.3% (5/16)	1.6	0.52, 4.84				
Measles	No	38.0% (339/893)	31.3% (5/16)		Reference	0.628			
	Yes	62.0% (554/893)	68.8% (11/16)	1.3	0.43, 4.11				
Pneumococcal disease	No	69.4% (620/893)	75.0% (12/16)		Reference	0.686			
	Yes	30.6% (273/893)	25.0% (4/16)	0.8	0.19, 2.96				
Yellow fever	No	64.7% (578/893)	68.8% (11/16)		Reference	0.745			
	Yes	35.3% (315/893)	31.3% (5/16)	0.8	0.24, 2.75				
Meningitis	No	87.6% (782/893)	75.0% (12/16)		Reference	0.150			
	Yes	12.4% (111/893)	25.0% (4/16)	2.3	0.74, 7.26				
Polio	No	21.8% (195/893)	12.5% (2/16)		Reference	0.351			
	Yes	78.2% (698/893)	87.5% (14/16)	2.0	0.48, 8.12				
Any vaccination listed on vaccination card	No	79.2% (3,356/4,239)	74.6% (47/63)		Reference	0.415			
	Yes	20.8% (883/4,239)	25.4% (16/63)	1.3	0.70, 2.40				
Child sick during last 12 months	No	29.7% (1,260/4,239)	23.8% (15/63)		Reference	0.235			
	Yes	70.3% (2,979/4,239)	76.2% (48/63)	1.4	0.82, 2.28				
How often child was sick, last 12 months	0-1	50.9% (2,156/4,239)	50.8% (32/63)		Reference	0.994			
	2 or more	49.1% (2,083/4,239)	49.2% (31/63)	1.0	0.60, 1.68				
Did you seek health care for this child in the last year?	No	47.3% (2,006/4,239)	50.8% (32/63)		Reference	0.634			
	Yes	52.7% (2,233/4,239)	49.2% (31/63)	0.9	0.50, 1.53				

Difficulties accessing health care (cost, time, distance)	Didn't seek care	47.3% (2,006/4,239)	50.8% (32/63)		Reference	0.765			
	No difficulties	46.0% (1,949/4,239)	44.4% (28/63)	0.9					
	Yes difficulties	6.7% (284/4,239)	4.8% (3/63)	0.7					
Caretaker and household information									
Caretaker age (years)	Under 30	49.8% (2,109/4,239)	34.9% (22/63)		Reference	0.010		Reference	0.251
	30 or older	50.2% (2,130/4,239)	65.1% (41/63)	1.8	1.16, 2.94		1.38	0.80, 2.39	
Primary caretaker of the child interviewed	Other	4.2% (178/4,239)	7.9% (5/63)		Reference	0.166			
	Mother	95.8% (4,061/4,239)	92.1% (58/63)	0.5	0.18, 1.34				
Total number of household members	0-6	71.7% (3,039/4,239)	74.6% (47/63)		Reference	0.591			
	Above 6	28.3% (1,200/4,239)	25.4% (16/63)	0.9	0.48, 1.51				
Drinking water source	Other (borehole, river, tap	54.9% (2,326/4,239)	36.5% (23/63)		Reference	0.007		Reference	0.008
	Well	45.1% (1,913/4,239)	63.5% (40/63)	2.1	1.24, 3.66		2.09	1.22, 3.60	
Water treatment	No	71.2% (3,020/4,239)	73.0% (46/63)		Reference	0.759			
	Yes (strain through cloth, let stand and settle, boil)	28.8% (1,219/4,239)	27.0% (17/63)	0.9	0.54, 1.57				
Wealth score (mobile phone, motorbike, tractor, camel)	0-1	63.5% (2,693/4,239)	65.1% (41/63)		Reference	0.810			
	2-4	36.5% (1,546/4,239)	34.9% (22/63)	0.9	0.55, 1.60				

OR = odds ratio; aOR = adjusted odds ratio; CI = 95% confidence interval; P = p-value from logistic regression model. Analysis adjusted for the survey design. Variables with ten or more cases and a p<0.2 in the univariable analysis included in the multivariable model (child age, birth order, caretaker age, drinking water source).

*893= number of vaccination books seen by research team

Table 7.6 Univariable and multivariable analysis of associations with any noma cases (Stage 0 to 5), 6-15 years.

		Study population		Univariable analysis			Multivariable analysis		
		Proportion of all respondents; N=2,841; %(n/N*)	Proportion respondents with any noma stage; N=129; % (n/N*)	OR	CI	P	aOR	CI	P
Demographics									
Child age (years)	6-10	74.9% (2,127/2,841)	76.0% (98/129)		Reference	0.722			
	11-15	25.1% (714/2,841)	24.0% (31/129)	0.93	0.64, 1.36				
Child gender	Female	55.4% (1,573/2,841)	45.7% (59/129)		Reference	0.036		Reference	0.031
	Male	44.6% (1,268/2,841)	54.3% (70/129)	1.50	1.03, 2.20		1.52	1.04, 2.22	
Birth order	1-2	50.2% (1,426/2,841)	55.8% (72/129)		Reference	0.186		Reference	0.613
	3 or more	49.8% (1,415/2,841)	44.2% (57/129)	0.79	0.56, 1.12		0.90	0.61, 1.34	
Feeding practices									
Colostrum given to baby	No	12.1% (341/2,826)	11.7% (15/128)		Reference	0.856			
	Yes	87.9% (2,485/2,826)	88.3% (113/128)	1.06	0.57, 1.98				
Frequency of the child eating pap per week	<1 or never	28.5% (811/2,841)	36.4% (47/129)		Reference	0.042		Reference	0.136
	1 or more	71.5% (2,030/2,841)	63.6% (82/129)	0.68	0.47, 0.98		1.87	0.83, 4.21	
Frequency of the caretaker preparing pap per week	<1 or never	28.5% (809/2,841)	38.8% (50/129)		Reference	0.011		Reference	0.015
	1 or more	71.5% (2,032/2,841)	61.2% (79/129)	0.61	0.42, 0.89		0.36	0.16, 0.82	
Animal products eaten in the 24 hours before the interview	No	91.0% (2,585/2,841)	94.6% (122/129)		Reference	0.265			

	Yes	9.0% (256/2,841)	5.4% (7/129)	0.57	0.22, 1.52				
Grains eaten in the 24 hours before the interview	No	18.2% (516/2,841)	15.5% (20/129)		Reference	0.455			
	Yes	81.8% (2,325/2,841)	84.5% (109/129)	1.22	0.73, 2.04				
Vegetables eaten in the 24 hours before the interview	No	66.1% (1,877/2,841)	71.3% (92/129)		Reference	0.293			
	Yes	33.9% (964/2,841)	28.7% (37/129)	0.78	0.50, 1.23				
Health									
Are the teeth ever cleaned (self-reported)	No	3.1% (88/2,823)	4.7% (6/128)		Reference	0.372			
	Yes	96.9% (2,735/2,823)	95.3% (122/128)	0.63	0.23, 1.73				
Teeth cleaning method (self-reported)	Toothbrush	23.8% (677/2,841)	18.6% (24/129)		Reference	0.654			
	Ash or cloth	1.9% (55/2,841)	2.3% (3/129)	1.54	0.45, 5.32				
	Salt and water or stick	16.4% (466/2,841)	15.5% (20/129)	1.26	0.68, 2.32				
	None or other	57.8% (1,643/2,841)	63.6% (82/129)	1.44	0.82, 2.52				
Teeth cleaning frequency per day (self-reported)	Once or twice	95.2% (2,687/2,823)	93.0% (119/128)		Reference	0.275			
	Less than once	4.8% (136/2,823)	7.0% (9/128)	1.53	0.72, 3.26				
Any vaccinations listed on vaccination card	No	88.5% (2,513/2,841)	86.0% (111/129)		Reference	0.451			
	Yes	11.5% (328/2,841)	14.0% (18/129)	1.24	0.71, 2.17				
Polio vaccination (self-report)	No	29.8% (846/2,841)	24.0% (31/129)		Reference	0.131		Reference	0.113
	Yes	70.2% (1,995/2,841)	76.0% (98/129)	1.36	0.91, 2.01		1.40	0.92, 2.13	
Child sick last 12 months	No	30.7% (871/2,841)	24.0% (31/129)		Reference	0.148		Reference	0.138
	Yes	69.3% (1,970/2,841)	76.0% (98/129)	1.39	0.89, 2.18		1.51	0.88, 2.60	

How many times was child sick during last 12 months	0-1	51.1% (1,451/2,841)	46.5% (60/129)		Reference	0.379			
	2 or more	48.9% (1,390/2,841)	53.5% (69/129)	1.19	0.81, 1.74				
Did you seek health care for this child in the last year?	No	50.1% (1,422/2,841)	47.3% (61/129)		Reference	0.620			
	Yes	49.9% (1,419/2,841)	52.7% (68/129)	1.10	0.75, 1.63				
Difficulties accessing health care (cost, time, distance)	Didn't seek care	50.1% (1,422/2,841)	47.3% (61/129)		Reference	0.068		Reference	0.259
	No difficulties	43.9% (1,247/2,841)	41.9% (54/129)	0.99	0.63, 1.55		0.78	0.45, 1.36	
	Yes, there were difficulties	6.1% (172/2,841)	10.9% (14/129)	1.98	1.12, 3.51		1.44	0.73, 2.85	
Caretaker and household information									
Caretaker age (years)	Under 30	21.5% (611/2,841)	20.2% (26/129)		Reference	0.731			
	30 or older	78.5% (2,230/2,841)	79.8% (103/129)	1.08	0.69, 1.69				
Caretaker gender	Female	97.5% (2,770/2,841)	99.2% (128/129)		Reference	0.271			
	Male	2.5% (71/2,841)	0.8% (1/129)	0.32	0.04, 2.40				
Primary caretaker of the child interviewed	Other	7.6% (216/2,841)	8.5% (11/129)		Reference	0.712			
	Mother	92.4% (2,625/2,841)	91.5% (118/129)	0.87	0.43, 1.78				
Total number of household members	0-6	58.1% (1,650/2,841)	67.4% (87/129)		Reference	0.025		Reference	0.145
	Above 6	41.9% (1,191/2,841)	32.6% (42/129)		0.46, 0.95		0.74	0.49, 1.11	
Drinking water source	Other (borehole, river, tap)	57.8% (1,641/2,841)	54.3% (70/129)		Reference	0.498			
	Well	42.2% (1,200/2,841)	45.7% (59/129	1.16	0.79, 1.87				

Water treatment	No	69.1% (1,964/2841)	65.1% (84/129)		Reference	0.376			
	Yes (strain through cloth, let stand and settle, boil)	30.9% (877/2,841)	34.9% (45/129)	1.21	0.79, 1.87				
Wealth score (mobile phone, motorbike, tractor, camel)	0-1	62.9% (1,787/2,841)	70.5% (91/129)		Reference	0.063		Reference	0.190
	2-4	37.1% (1,054/2,841)	29.5% (38/129)	0.70	0.48, 1.02		0.77	0.52, 1.14	

OR = odds ratio; aOR = adjusted odds ratio; CI = 95% confidence interval; P = p value from logistic regression model; Analysis adjusted for the survey design. Variables with ten or more cases and a $p<0.2$ in the univariable analysis included in the multivariable model (child gender, birth order, frequency of the child eating pap per week, frequency of the caretaker preparing pap per week, polio vaccination, child sick last 12 months, difficulties accessing health care, total number of household members, wealth score

Fieger *et al.* in 2003 (640 per 100,000 children) [7]. Differences between the two could be due to the inclusion of earlier noma stages including stage 0 in the estimates, geographical differences (Bello *et al.* is north central Nigeria vs our northwest Nigeria), or due to methodological differences (Bello *et al.* used patient record review of patients presenting at hospital and Fieger *et al*. based their estimates on the number of clefts and mathematical modelling vs our community-based cross-sectional survey).

Despite only covering two states of one country, our prevalence estimates would account for 17% of the current global WHO prevalence estimates [19]. Even though direct comparisons between the WHO and current study estimates are difficult as the stages included in the WHO estimates were not reported, our findings do suggest that the true burden of noma worldwide may be higher than previously thought.

Results from this study highlight the under-reported and overlooked nature of noma. Even though oral diseases, such as noma, are largely preventable, they impact over 3.5 billion people worldwide (untreated dental caries are the most prevalent of these oral health issues), disproportionally affecting marginalised groups [250]. Oral diseases are frequently more neglected than other diseases in low- and middle-income countries, which may be linked to the fact that modern dentistry focuses on high-technology solutions, which are unaffordable and not currently feasible in low-resource settings [251]. This overarching neglect of oral diseases is magnified in the case of noma, as patients live in underserved, often rural locations [32]. Many cases will never seek care, and, even if they do, noma is unknown to many health care workers in endemic areas [21]. The condition may thus go undiagnosed, and rapid detection with opportunities for early treatment through improved oral hygiene, nutritional support and antibiotics, may be missed.

The presence of acute necrotizing gingivitis, which is rarely seen in healthy children, points to the need to assess and address risk factors at a community level with public health interventions. Treatment with antibiotics, nutritional support and a search for underlying diseases including HIV, measles and chronic malnutrition is essential in preventing progression to the later stages of noma [252].

Strong surveillance systems have been the cornerstone of many successful NTD control programmes [253, 254]. The WHO has stated that robust surveillance helps to better understand the burden and distribution of disease, and to identify high risk populations so that evidence-based decision-making can be used to target interventions in resource-constrained contexts [255]. A further benefit of robust surveillance is an increase in the number of cases identified, diagnosed and treated [256]. Due to the neglected nature of noma, surveillance activities for active noma cases are hampered and it is unlikely that current surveillance mechanisms adequately identify deaths from noma at community level. The mortality rate associated with noma is unknown, but estimated to be as high as 90% if the disease is left untreated [1]. Deaths may be primarily due to starvation, aspiration pneumonia, respiratory insufficiency or sepsis [25, 74], and not be attributed to noma, further reducing the potential for accurate reporting of disease burden. Our findings suggest that improved efforts to enumerate the burden of disease are necessary.

This study highlights the need for a single classification system for the differential diagnosis of each stage of noma, which would be beneficial in standardizing reporting of noma globally by the clinical and research noma community. In published work, noma is often classified into two stages (acute and chronic noma [6, 8]) or with the Montandon system (classifies noma according to the location of the defect) [55]. The lack of standardization complicates

comparison between different studies. The WHO noma staging system [1] is the most comprehensive to date and includes an early-stage noma definition which is useful as it identifies those at risk of progressing to later-stage noma. However, it lacks specificity as it overlaps with commonly seen ailments such as simple gingivitis and acute necrotizing gingivitis and therefore may overestimate the burden of disease. It is currently unknown what the risk factors are for progression, nor what proportion of patients do progress to the later stages of disease. Explicit reference to which WHO stages of noma are included in prevalence and incidence estimates as well as improved detail of the method employed in these estimations would greatly improve our ability to compare findings across studies. The lack of consistency of approach to assessing the incidence and prevalence of noma in the literature and the lack of real investment in assessing the true incidence and prevalence of this condition particularly in regions that bear the highest global burden, contributes to the ongoing neglect of this disease and the populations it affects.

Study findings indicate that children aged between three and five years had a higher prevalence of noma in comparison to those aged two years or less, a finding corroborated by other studies [53, 67, 68, 71]. We hypothesise that this finding is likely due to the relationship between child feeding practices in Nigeria and malnutrition as a risk factor for noma. Our study did not identify an association between malnutrition and noma. However, other studies have shown that rural Nigerian children typically transition to a limited diet after being breastfeed until 24 months of age [181, 257]. This has shown to result in higher levels of malnutrition and stunting [257] and therefore, a potentially higher risk of developing noma. This discrepancy in our findings in comparison to other studies, could be due to the fact that our population had early-stage noma, whereas other studies could have identified the association between malnutrition

and late-stage noma. It is also possible that late-stage noma could cause malnutrition if the child was having difficulties eating due to the noma infection.

Our findings showed that older (aged six to 15 years) male children were more likely to have any stage of noma in comparison to older female children. We do not know what would explain this finding as we would not expect an inherent difference in gender in noma development. However, this association could point to risky behavioural traits that may be more common in males in this setting. This finding warrants further research.

We showed that various factors relating to pap preparation and consumption were linked to not having Stage 1 and 2 noma amongst the whole study sample and of any stage noma in the six to 15 year old age group. It is difficult to explain this finding as it could be due to a lack of access to food or that pap made more frequently has less chance of becoming contaminated (thus causing less disease) as it is stored for shorter periods of time. A Nigerian study showed that when mothers prepared food far in advance, contamination was more likely to occur [258]. A further Nigerian study in Kebbi State showed that pap was contaminated with high levels of Salmonella in comparison to other commonly eaten foods [183]. This association with food preparation affected children in the older age group who are more reliant on this food source compared to the younger children.

This study further indicated that having a well as the main water source in comparison to other water sources such as a borehole, river or tap, was associated with having noma in the 0-5 year age group. Well water has a high risk of contamination from nearby pit latrines or livestock [56], and the consumption of contaminated well water is a risk factor for diarrhoea [118], which in turn is a commonly identified comorbidity for children with noma [59].

Vaccination coverage in all eligible children included in the study was low. Even though this result prevented us from exploring whether vaccination is associated with noma prevention, it does confirm findings from other studies in rural Sokoto State, where up to 70% of children were not vaccinated against measles and other common childhood diseases [8]. Low immunisation coverage is an important indicator of struggling societal systems in need of multi-sectoral improvements, including access to quality timely health care, access to safe drinking water, improved nutrition, and security. Prevention efforts should also include early detection training with health care workers, and setting up effective referral pathways. These initiatives are resource-intensive and require large-scale investment of time, money and human resources.

This study had a large sample size and robust approach to sampling and analysis, and we are confident that prevalence estimates are broadly representative of the study area. However, a few limitations should be considered. This cross-sectional study was conducted on a disease with an extremely rapid clinical progression with onset to death taking as little as two weeks [1]. Thus, it is possible that Neyman bias was present and we only identified a fraction of noma cases that occur. The research team did come across Stage 5 noma patients in study villages, but not in households included in the study. These patients were referred to the NCH for care. The sample size was calculated using the only available, but nonetheless, relatively out-of-date data with the household size used only representing Sokoto and not Kebbi, this could have influenced the findings of the study. It is possible that if we had reached the calculated number of clusters (181) or had a study with a larger sample size, we could have identified children with the later stages of disease. Some of the answers were self-reported by caretakers, which could have introduced social desirability bias that either inflated or deflated the risk factor associations found in the study. This aspect was mitigated by anonymising the survey and

trying to phrase questions in contextually acceptable ways. Data on some risk factors, such as comorbidities, water quality, and malnutrition in older children was not collected, limiting our ability to identify associations with these factors. It is difficult to interpret the results of questions asking about consumption of any food and specific foodstuffs in the 24 hours prior to the interview and associations with noma as respondents with noma could have difficulty eating in general and would thus have been less likely to report eating at all. The measurement of malnutrition using only the MUAC was a limitation as this tool is useful to diagnose severe acute malnutrition but noma is reported to be associated with chronic malnutrition often accompanied by stunting. Finally, the challenging security situation limited the areas the research teams could access. This may have introduced selection bias, and an under-estimation of noma and malnutrition prevalence, as we did not visit the hardest to reach communities who were likely most vulnerable to noma infection. Future research on the burden of noma should be combined with existing surveillance systems for other disease and research activities such as malnutrition and vaccination surveys.

Noma meets the criteria of a NTD as defined by the WHO: it is a preventable disease that affects children in low-resource contexts; children that survive will have life-long physical and mental health sequelae; and there is a poor understanding of the disease, its pathogenesis and global burden [259].

This study has shown that the prevalence of any stage of noma is higher than previous estimates. While we did not find any later stages of the disease, the high rates of simple gingivitis and the presence of known risk factors for noma (low vaccination rates, malnutrition and poor access to health care) suggest the need for improved coverage of preventative interventions and access to care in northwest Nigeria. Our prevalence estimates are greater

than those for snakebite in Nigeria (497 per 100,000 people), which the WHO recently recognised as a NTD [260]. Noma prevention and control will require a concerted health systems approach. Adding noma to the WHO's list of NTDs will facilitate global attention for noma and the allocation of much needed resources to those countries where noma continues to be a persistent public health problem.

Chapter 8 Discussion and recommendations

This chapter presents a synopsis of the key findings of the thesis in relation to the initial aims and objectives, the overarching themes and the recommendations for policy, practice and future research.

8.1 Synopsis

The main aim of this thesis was to refine our understanding of the biopsychosocial features of noma, its epidemiology and treatment in northwest Nigeria. Through the various studies included in the thesis, we were able to address the three key objectives:

1. Assess the distribution of noma among children in Sokoto and Kebbi States, northwest Nigeria.
2. Identify factors associated with noma in this setting, including factors influencing health-seeking behaviour and risk factors for the development of noma.
3. Gain an understanding of the biomedical and non-biomedical care provided to noma patients in this setting.

Firstly, we examined the literature on noma (Chapter 2) which clearly demonstrates the paucity of knowledge on the distribution of noma globally and in Nigeria. The literature review further illustrated the changing distribution of noma from the 1800's to 2019. Crude estimates of global prevalence and incidence found in this review have not been updated since 1998 [19]. Secondly, recognising the need to update and expand on current prevalence data for noma in Nigeria, we conducted a community-based cross-sectional prevalence study in the two northwest Nigerian states of Sokoto and Kebbi (Chapter 7). The study included 177 clusters, 3,499 households, and 7,122 children. The prevalence of noma for 0-15 year olds in this area was 3.3%. Although no late stage noma patients were identified, the relatively high prevalence

of simple gingivitis (3.1%) demonstrates that this remains a population at risk for developing late stage noma. Most prevalence and incidence data reported from Nigeria prior to this study arose from hospital-based surveillance systems, which are likely to only detect more serious cases that have successfully sought care [7, 42, 239]. Our study represents the first population-based noma prevalence study in Nigeria and provides a more comprehensive view of disease distribution in these states.

Thirdly, we identified factors associated with noma in this setting, including factors influencing health-seeking behaviour. Chapter 3, a qualitative study showed the varied beliefs about noma causes including birds and insects, interference from the spirit world and preceding cases of disease (measles was specifically mentioned). These beliefs impacted the health-seeking decisions of caretakers, with several seeking care at traditional healers who treat not only the physical but also the spiritual manifestations and causes of disease. Reasons for traditional healer use were also noted by caretakers in Chapter 6 and include issues surrounding trust, affordability and distance to care when compared to biomedical services. Even though biomedical care was free for patients at the NCH, other costs such as childcare and a loss of income posed additional barriers to this type of care.

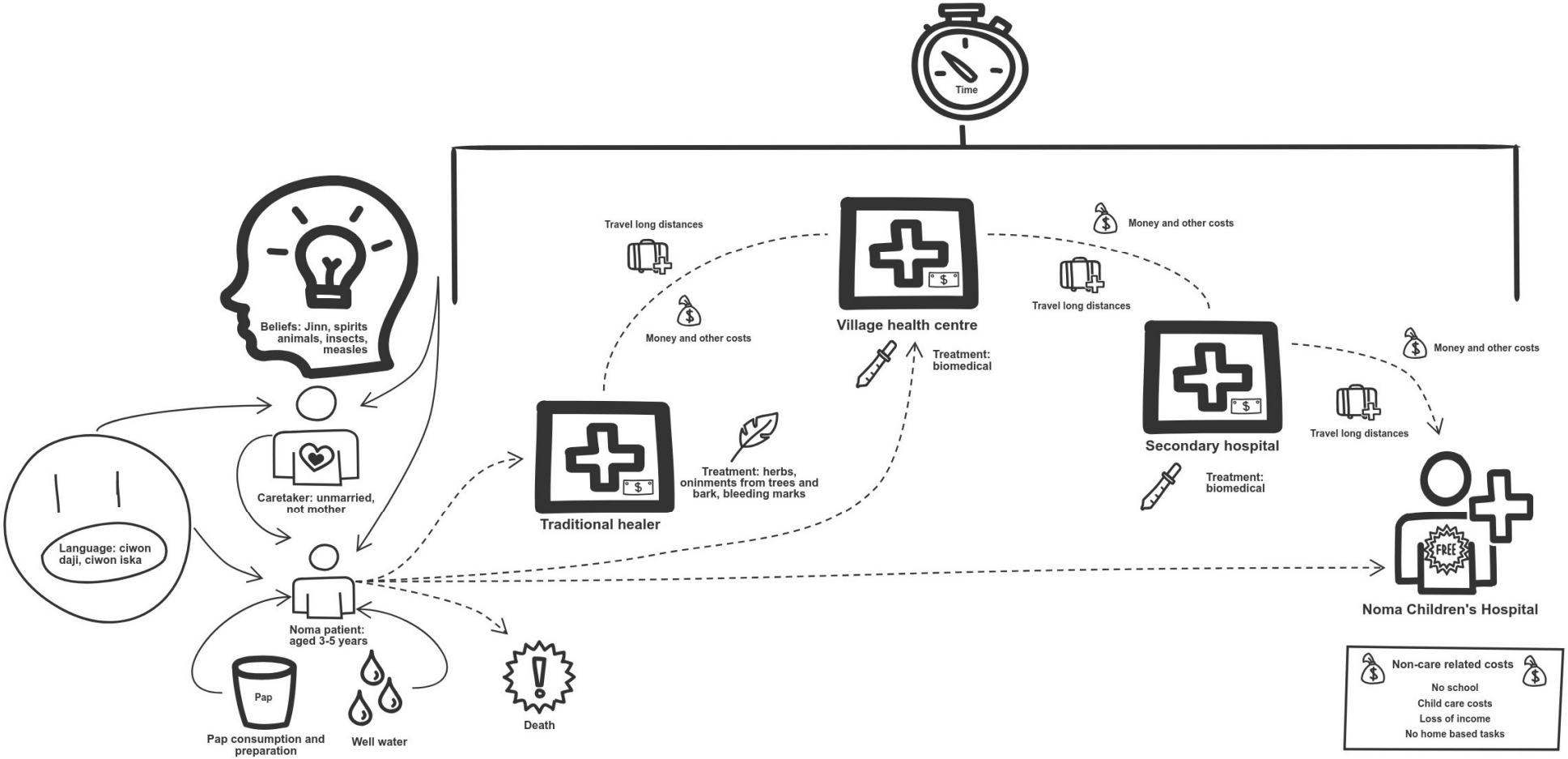
Fourth, risk factors for the development of noma were explored in both the case control study (Chapter 4) and the prevalence study (Chapter 7). Notable risk factors centred on food, water and caretakers and child demographics. These included: pap being consumed more than once per week, pap being prepared less than once a week, a well point as the main water source, the mother not being the primary caretaker, the caretaker being unmarried and the child being aged between three and five years. The differences in risk factors identified in these chapters is likely due to the different sample populations included in these studies. Cases in the case

control study were hospital-based, compared to the community-based identification of cases in the prevalence study.

Fifth, we explored the biomedical surgical care available at the NCH as well as the care provided by traditional healers living in the villages of the patients in Sokoto State. The literature review (Chapter 2) showed the importance of seeking care in the early reversible stages of disease and the positive impact receiving antibiotic treatment, nutritional support and wound debridement had on noma mortality and morbidity. The review also highlighted the limitations of biomedical care for noma patients. These included the lack of outreach to communities at risk, health care workers' low levels of knowledge about the disease, and the inadequate amount of follow-up conducted after surgical treatment to provide care such as physiotherapy and assess longer-term outcomes. These limitations were echoed in the outcomes study (Chapter 5) which showed that surgical care reportedly improved patients' quality of life, but had limited improvements in patients' functional outcomes.

In Chapter 6, traditional healers reported that they believed the different stages of noma were different diseases. Treatment of noma in the oedema phase included herbs, ointments and the creation of bleedings marks. However, several healers noted they had not treated the later stages of the disease. Traditional healers also reported referring these patients to biomedical health care centres, reflecting their recognition and acceptance of biomedical care alongside traditional interventions. Qualitative studies in Chapters 3 and 6 highlight the importance of traditional healers as a first point of call for noma patients. However, this can result in delayed access to biomedical care at a crucial point in the patient pathway when progression of the disease is most preventable. Figure 8.1 below illustrates an example of the various

Figure 8.1 Example pathways to care for noma patients in northwest Nigeria.



pathways to care for noma patients in northwest Nigeria, the factors associated with the disease in this setting and the care options available to patients.

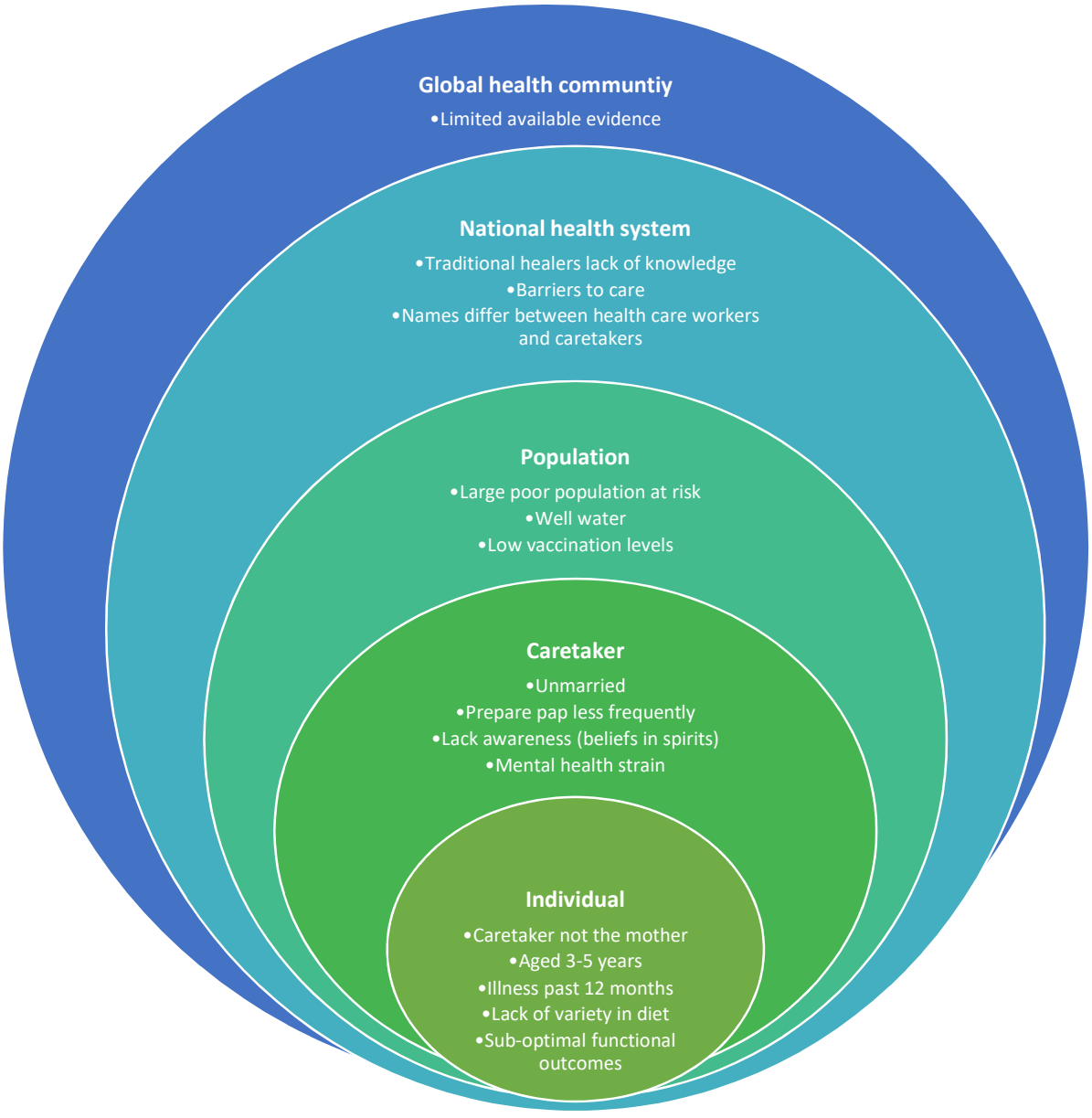
8.2 Noma: an invisible and neglected disease

Noma is a disfiguring disease that affects vulnerable populations who live in underserved communities. A pervasive theme across this thesis is that noma patients and the disease itself remain invisible within the communities they reside, the health systems that are supposed to serve them and the global health community. These layers of invisibility are all interwoven and exercise influence upon one another (Figure 8.2). If a disease is invisible, it will likely be neglected.

At the United Nations Human Rights Council in 2011, Jean Ziegler stated that *"Noma is a neglected disease: neglected by the medical community, by governmental authorities, by major private donors and by public opinion. The persistence of noma in today's world raises doubts not only about our morality, but it comes to prove that the human rights of children, the most vulnerable members of the international community are being severely ignored and violated"* [261]. Noma has been labelled a neglected disease by several other authors for many decades as indicated by the titles below:

- Noma : a neglected scourge of children in sub-Saharan Africa (1995) [238]
- Noma: a neglected enigma (2013) [209]
- Noma: neglected, forgotten and a human rights issue (2015) [58]
- Noma: overview of a neglected disease and human rights violation (2017) [57]

Figure 8.2 Invisible noma: depiction of the levels of invisibility of noma as shown in the thesis.



Despite these pleas over many decades and the evidence generated that indicates the neglected nature of noma, the disease remains neglected on several fronts discussed in more detail below.

At the first layer are the individuals experiencing the direct consequences of noma. Our research has shown that noma affects children aged between three and five years who are predominantly cared for by someone other than their mothers. These children were shown to have a poor variety in their diet and a recent history of illness. Such factors highlight the vulnerable and marginalised nature of noma patients who predominantly live in areas of socioeconomic need and have limited voices of their own. Our studies further showed that caretakers of noma patients were frequently unmarried and often female. Movements of females in this setting are limited to their residential compounds due to cultural and religious norms [136]. This heightens the invisibility and neglect of noma patients who rely on female caregivers to access care.

Our findings showed an additional layer of invisibility is added to noma patients and caretakers due to the significant stigma associated with the disease. Caretakers and patients are ostracised by family and friends, resulting in mental health strain, a finding corroborated by others [162–164]. The outcomes study in Chapter 5 demonstrated that when noma patients are provided with surgical care, stigma and social isolation are reduced. Patients reported less invisibility and greater societal inclusion by attending school, having friends and perceiving marriage as a possibility after their surgery showing that access to timely care can reduce stigma and the resulting invisibility.

A third layer of invisibility occurs at the population level. Noma cases are frequently reported in low socioeconomic populations such as those found in northwest Nigeria [11, 32, 38, 41, 70, 262, 263]. Our community-based prevalence study showed that there is a large population at risk of developing later stage noma. Populations living in poverty are at times ignored, and as such, the diseases affecting these marginalized populations are also ignored by the governments and health systems that serve them [58, 70].

In northwest Nigeria, our studies showed that participants had limited access to biomedical health services and low vaccination coverage rates. These factors add weight to previous studies which found that a lack of access to quality care and vaccine preventable comorbidities were associated with increased risk of noma [2, 8, 147]. In the absence of a functional and accessible health system infrastructure, noma precursor conditions and cases cannot be detected or timeously managed, further compounding the political and social invisibility of this disease.

This invisibility in the biomedical health system was mirrored in Chapter 6 where traditional healers noted that many of them had not seen cases of the later stages of disease. As traditional healers are frequently the first port of call for any health issues, this could indicate noma patients are either kept at home or, due to the rapid progression of the disease, die before seeking care. Thus ensuring patients remain unseen and unnoticed by traditional and biomedical healthcare providers.

The thesis literature review has shown that despite the major developments in healthcare and health research since noma was first identified, noma remains a poorly understood disease in the global health community. There are only a handful of robust epidemiological studies [3, 8,

10, 17, 20, 22, 23, 34, 40–43, 56, 107, 117] making comparison between our study results and others difficult. The invisibility of noma within the global health community could be explained by the reported relative rarity of the condition and the fact that geographic clustering of cases has tended to occur in hard-to-reach communities such as northwest Nigeria. This means that even for those who do want to study the disease, conditions are challenging. A further reason could be the limited presence of noma in international health dialogues. This limits the amount of resources allocated to researching noma, adding to the circular nature of the invisibility of noma within the global health community.

Based on the invisibility and neglect of noma, we offer several recommendations for policy, practice and further research.

8.3 Recommendations for policy

The strongest policy recommendation from this thesis is to further support the advocacy of the addition of noma to the WHO NTD list [57, 58, 113, 209, 238, 261]. NTDs are characterised as diseases that do not have a strong political voice, affecting people with a low status in public health priorities, living in remote, rural areas, in conditions of poverty [259]. Noma meets all of these criteria.

However, the WHO have stated that there are two main reasons for the deliberations over including noma on the WHO NTD list. Firstly, there have been discussions over whether to classify noma as an infectious disease or as a dermatological condition [264]. This difficulty in classification should not however cause a delay as there are NTDs that are infectious diseases (leishmaniasis), and others that are not infectious (snake bite), and there are others that are dermatological in nature (scabies). The second reason for deliberation is that noma is not

strictly a tropical disease [264]. Tropical diseases are labelled as those found in the areas around the equator between the lines of the Tropic of Capricorn and the Tropic of Cancer [265]. This point is valid, the maps in Chapter 2 have shown the global distribution of noma. However, several diseases on the WHO NTD list including snakebite [266], scabies [267], dengue [268], rabies [269], leprosy [270] and Chagas [271] are present in non-tropical regions but are still included on the list. Therefore, geographical distribution should not stop noma from being added to the WHO NTD list. It is also possible that the non-inclusion on the WHO NTD list is linked with the fact that acute noma can be treated with relatively inexpensive and widely available antibiotics meaning it is not a target for pharmaceutical companies which contrasts with other diseases on the list which have significant interest for these companies, including snake bite.

The addition of noma to the WHO NTD list could raise awareness about the disease and boost much needed funding for prevention, treatment and research. For example, since the inclusion of snakebite onto the WHO NTD list, this cause has received several large scale donations such as USD$102 million from the Wellcome Trust [272]. Many funders rely on the WHO NTD list to make donation decisions, including the Bill and Melinda Gates Foundation, USAID and UK Aid. In 2014, diseases on the WHO's NTD list received an estimated USD$300 million in donations [259]. Furthermore, the addition of noma to the WHO NTD list could boost national awareness and funding. In Nigeria, there have been successful eradication campaigns for other diseases such as Guinea-worm in 2009 [273]. This cost the Nigerian Ministry of Health USD$2 million [273]. This figure far outweighs the 2018 available budget for noma from all sources which stood at USD$138,780 [241].

8.4 Recommendations for practice

The thesis provides recommendations for practice including health system strengthening, training initiatives and the adoption of a singular noma classification system.

8.4.1 Health system strengthening

To decrease the number of noma cases, three main areas of improvement to the health system have been identified: increasing access to care, preventative activities and the creation of a robust surveillance network. As these are broad health systems initiatives, they would be beneficial in curbing the incidence of noma and other childhood diseases simultaneously.

8.4.1.1 Access to care

Our findings identified several barriers to care in the northwest Nigerian setting including time, money and distance. These challenges lead to the need for several improvements in health care access. The number of health centres and health care workers needs to be increased, as does their distribution into rural areas [129, 274]. Whilst noma does occur in urban settings, the risk factors for noma are more frequently found in rural areas. Increased rural health services would need to be paired with health financing programmes which would aim to remove the catastrophic health expenditure faced by many families of noma patients. A further area of focus should be the creation of effective and efficient referral mechanisms. This would mean that noma patients could access the type of care they need in the crucial early stages of the disease. Improving access to healthcare would not only reduce the incidence of noma but also other common childhood illnesses.

8.4.1.2 Preventative activities

This thesis has shown that noma has devastating consequences, and even for those who survive and are able to access surgical treatment, outcomes in terms of functionality are limited. As such, focus should be placed on preventing noma. By removing the main risk factors associated with noma development (low vaccination rates, malnutrition and poor oral hygiene) there would be a reduction in the incidence of noma and other childhood diseases.

The creation of a functioning vaccination system that reaches even the most rural communities is an important first step in the prevention of noma. This system would need to be adequately resourced and provide continual high coverage. Due to mistrust in vaccines in this setting, this system would need to be paired with an awareness campaign about the safety and efficacy of vaccines which should involve community and religious leaders [275–277].

Programmes focussing on improving the nutritional status of children could be a further effective mechanism in the prevention of noma. This would yield numerous other health benefits to this population. As stated in this thesis, most acute noma cases occur in children aged between two and five years and so interventions should focus on caretakers of young children. These should include providing prenatal care and nutritional assistance for mothers as the first one thousand days of a child's life (including time spent *in utero*) have been shown to be instrumental in the health outcomes of children [278]. Infants born with a low birth weight are also at higher risk of contracting noma [239].

Oral health care is a major public health issue in Nigeria where there is a high prevalence of dental caries and periodontal diseases [145]. Poor oral health is a recognised risk factor for noma [34]. Limited access to oral health services is an issue in this context. There are an

estimated 1.2 dentists per 100,000 population members [145]. A school- and community-based oral health programme would provide access to dental care. This has proven to be an effective option in Ibadan, Nigeria [279] and could be an effective means of diagnosing and treating the early reversible stages of noma in other Nigerian states. However, interventions within dental health programs alone may limit the health care system's ability to help these children most effectively and so system wide interventions are needed.

These three preventative activities could be achieved through the deployment of mobile health care workers. Such workers could provide immunization services, monitor nutritional and oral health status, identify cases that need referral and deliver health education talks. These efforts could build trust in the health system and offer protection from a host of childhood diseases [184, 280]. Moreover, these mobile healthcare workers could improve the functioning and geographical reach of other routine healthcare services.

8.4.1.3 Surveillance

A strong recommendation from this thesis would be the strengthening of the surveillance system for noma in Nigeria in particular, but also in other endemic countries. An improved surveillance system would assist in gaining a better understanding of the incidence, spatio-temporal distribution and burden of diseases, which, in turn, is essential for prevention, control and elimination [281, 282]. The smallpox and polio eradication programmes provide convincing examples of the critical role played by a globally organised approach in linking surveillance data to targeted, swift and effective public health responses [281].

Noma is a notifiable disease in Nigeria, however, the Nigerian Centre for Disease Control believe the case numbers being reported are a gross under-estimation of the true burden of

disease [240]. There is a need to strengthen the national noma surveillance system. At this point, the most effective form of surveillance would likely be a combination of active health facility-based (new cases detected in health facilities by health care professionals) and population-based surveillance (cases identified in a defined population or at a community level who are not presenting at a health centre). In 2017, the Nigerian Centre for Disease Control adopted the Surveillance and Outbreak Review Management System, a digital surveillance tool which is now functional in 15 health facilities across 11 states [283]. This could be a useful tool (once fully rolled out) for the rapid surveillance of noma at a health facility level. To ensure the effectiveness of this surveillance system, large scale training for health care workers and surveillance officers would be required (discussed below).

One unique method of surveillance which has been effective in the mapping of onchocerciasis (river blindness) is the use of rapid screening in high risk areas [282]. This could be useful in terms of noma in that active community-based surveillance initiatives could first target communities with high levels of known noma risk factors. These could include areas with low vaccination rates or areas with recent measles outbreaks, high levels of malnutrition or food insecurity, areas where most citizens use well water or in water scare settings and areas where government clinics or non-governmental organisation partners (such as Operation Smile, Mercy Ships, Smile Train or MSF) have identified noma cases.

8.4.2 Training initiatives

The MSF and Nigerian Ministry of Health outreach team train community members and health care workers on the stages of noma and appropriate treatment protocols for each stage. This team visits approximately 30 villages each month training approximately 500 community members. Whilst this is an impressive effort, the thesis suggests there is still a substantial

knowledge gap that further training could fill. The main focus areas should include community awareness raising and health care worker trainings.

8.4.2.1 Healthcare worker training

Wide scale healthcare worker trainings with biomedical and non-biomedical care providers (nurses, doctors, dentists, pharmacists, traditional healers and traditional birth attendants) could facilitate better surveillance initiatives, more efficient treatment and referrals to the correct points of care and assist with generating interest in noma. These trainings should focus on educating health care workers on the early signs and symptoms of the disease, identification of the different stages of disease and the timeframes for progression between stages, the risk factors for the disease (to encourage discussions around prevention), the language used to describe the disease (to enable improved patient interaction) and the appropriate treatment regimens for each stage. These trainings should be paired with the creation of efficient referral pathways between biomedical health centres and from non-biomedical health care providers to biomedical health centres. In other African settings, traditional healers have been recruited to serve as community health workers through training and support by nearby health facilities [284]. This could be a strategy for the effective inclusion of traditional healers in noma interventions.

8.4.2.2 Community-based awareness raising and training

Awareness about the biomedical causes and treatment protocols for noma in northwest Nigerian communities is limited, indicating a need to improve awareness about the disease. Awareness raising campaigns should focus on educating community members looking after children who are at risk of developing noma. These awareness campaigns should include the importance of a well-balanced diet, hygienic pap preparation practices, the importance of

boiling well water, healthy oral hygiene practices, the early signs and symptoms of noma and the urgency with which health care should be sought. The various names for noma identified in this thesis should be included in these awareness campaigns to ensure community members know which disease the campaigns are targeting. The beliefs about the causes of disease should also be discussed in face to face trainings and included in other messaging methods. Radio adverts, fliers handed out at village events and posters hung in prominent positions in the villages (mosque, shop, health centre) could be effective means of alternative communication. These would need to be well illustrated to accommodate for the low levels of literacy in noma endemic countries. Public messaging tools should be paired with a hotline number which allows for speedy referrals. Testing the success of each awareness raising approach will be important to determine the most affordable and effective methods for scaling programmes.

Including community leaders (religious leaders, village chiefs, village elders and school teachers) will assist in gaining community trust and acceptance for all initiatives (prevention, treatment and research). Community leaders are frequently the first port of call for patients if they are seeking advice or financial assistance to take their children to health care facilities. Tailor-made trainings for this group should include information on the importance of supporting unmarried mothers and caretakers of children who are not the biological mother in raising their children specifically at times when the child is sick. Information should also be given about the causes and treatment options available for noma, the early signs and symptoms, the speed with which care needs to be sought and the best referral options for patients from their communities.

8.4.3 Single noma classification system

There are numerous classification systems and descriptions of the staging of noma in the literature, making comparisons of study results difficult. These include classifying noma into two stages, acute and chronic noma [10, 31, 32], the Montandon system which focuses classification on the area of the face implicated [55], the WHO noma classification system which classifies noma according to distinct stages of clinical progression [1] and the NOITULP grading tool which classifies noma cases based on the percentage loss of each anatomical unit [38]. This thesis has utilised two of these tools, namely the WHO noma classification tool and the NOITULP grading tool. However, these tools have limitations. The WHO classification system is useful as a surveillance tool; it is sensitive but not adequately specific. It is intended to assist surveillance staff and affected communities in identifying the stages of noma. As the tool includes the more commonly seen ailments of simple gingivitis and acute necrotizing ulcerative gingivitis to ensure populations at risk are identified, and the fraction of patients with these conditions who go on to develop the later stages of noma is unknown, the tool may overestimate the true burden of disease. This tool also classifies the later stages of disease as inactive which is not necessarily true as the defect created by noma heals with contracture and as the child grows the scar contracts and this can cause further damage including the exposure of teeth or the opacification of the exposed eye leading to blindness of the affected eye. The NOITULP scale is not a classification of noma stage, but a classification of anatomical loss of the nose, the outer cheek and the inner lining of the cheek, the upper lip and lower lip, and the degree of trismus [38]. This is a useful tool to determine priorities for surgical reconstruction and understanding the outcomes of surgical care of later stage noma patients, but cannot be used as a diagnostic tool. Further research is needed to assess the most appropriate tools to use, but even with these limitations, the adoption of the WHO tool for surveillance along with the NOITULP scale for surgical classifications would allow for standardisation in noma

reporting for each stage of the disease as well as the clinical outcomes. This could lead to clearer estimates of each stage of noma being identified and allow for easier comparison of study results. The WHO tool should also be embedded in training materials such as information booklets and educational messaging.

8.5 Recommendations for further research

Future research should be paired with education and training for respondents and in areas where the research is conducted. Topics covered should be based on the needs identified for the target populations. These may include the naming of the disease, risk factors and appropriate referral practices. This would mean that research initiatives have a positive impact for the respondents and communities in which the research tasks place.

Further robust studies need to be undertaken to examine the associations found in this thesis. Along with these studies, based on the findings of the thesis, the main recommendations for future research are to better enumerate the burden and distribution of noma, gain an understanding of the proportion of cases that progress from one stage to the next, and the risk factors for this progression, create evidence around the main gaps in biomedical health care workers knowledge about the disease, conduct an economic evaluation of the impact of noma and to validate a Hausa quality of life tool.

8.5.1 Distribution and burden of noma

The thesis assessed the prevalence of noma in two states in Nigeria. One of the main gaps in knowledge remains the national distribution and burden of disease. Specifically, the incidence of noma is unknown. A prospective cohort study would enable an assessment of the incidence of noma, and offer an opportunity to more accurately assess risk factors for the disease. A set

number of randomly selected villages could be included, and all children in those villages could undergo oral examinations once a month over a year long period. This would enable the detection of all stages of noma. This study would however, be resource- and time- intensive, especially considering the rare nature of noma.

We recognize that there are many other issues these communities face. Cross-cutting initiatives that address more than one disease, strengthen reporting structures and upskill human resources may be more beneficial than vertical noma initiatives. Future initiatives to gain a better understanding of the distribution and burden of noma could be incorporated into vaccine coverage surveys, surveillance initiatives for other diseases listed as high priorities in the country (lassa fever, yellow fever, cholera and measles [283]) or malnutrition surveys. Nigeria conducts SMART nutrition surveys twice a year in the areas most prone to malnutrition (northern Nigeria) and nationally once every two years [285]. The 2018 national SMART survey included 19,471 children aged between 0 and 59 months across all 36 states in Nigeria [285]. If oral health screening was included in these surveys, this would provide national estimates for the prevalence of any stage of noma and would provide the largest data source on noma prevalence in Nigeria (and globally).

8.5.2 Progression to later stage noma and death

This thesis has shown there is a lack of evidence around the proportion of cases who move from each stage of noma to the next, as well as the risk factors for this progression. This knowledge would offer useful information to identify opportunities for interventions. A cohort of patients with simple gingivitis could be followed and offered the WHO prescribed standard of care [1]. This would allow for an assessment of the number of cases that develop to the later stages of disease, and an assessment of the risk factors for progression. Alternatively, a

randomised trial could be conducted with one arm receiving the standard of care, and another arm receiving interventions specifically designed for noma treatment (mouth wash etc.). This study would also offer information on the most effective treatment protocols to stop cases from developing the later stages of disease. If specific risk factors are found for progression during this crucial time, intervention options could be taught during health care worker and community awareness campaigns. There are several ethical issues, particularly around what treatments are offered to each arm of the trail (the use of placebos would not be ethical in this instance as there are known effective treatments). It is also possible that providing the standard of care would prevent cases from developing to later stage noma, which would lead to an under-estimation of the proportion of cases that progress. These studies are also logistically complex and the sample size would be very large which could prove difficult in this context.

An alternate idea would be to conduct a modelling study to assess the contribution of specific factors to the progression of the disease. Factors such as immunosuppression, malnutrition, child and caretaker demographics and feeding practices could be included in these models which may offer predictions on the roles each factor plays in the progression of the disease which could then provide evidence for prevention programmes.

As this thesis has shown, the true mortality rate of noma is unknown. Ascertaining noma mortality in the absence of intervention using a prospective study design is not ethical, but a retrospective mortality survey at a community level or paired with a malnutrition survey may provide this information. Using a structured verbal autopsy, with questions focussing on assessing if the cause of death was from noma, it would be possible to ascertain how many deaths could be attributed to the disease. Recall bias would be a limitation in this study.

8.5.3 Knowledge, attitudes and perceptions of health care workers

This thesis has elucidated gaps in knowledge of traditional healers, and the literature review revealed that biomedical knowledge on noma was sub-optimal. A cross-sectional study assessing biomedical health care workers' knowledge, attitudes and perceptions of noma in Nigeria could yield useful information which highlights the gaps in knowledge of health care workers. These points could be the main items covered in health care worker trainings. Tailoring these trainings around the identified gaps in knowledge could increase the effectiveness of this intervention.

A further approach to determining health care workers' knowledge of noma would be to assess which medical school and tropical medicine curricula include sections on noma. This would be useful to assess both in Nigeria and other noma-afflicted countries but also more broadly among international tropical medicine programs which attract students from regions across the globe. These include the Liverpool School of Tropical Medicine (UK); London School of Hygiene and Tropical Medicine (UK); Institute of Tropical Medicine (Peru); Royal Tropical Institute (Amsterdam) and the Kenya Institute of Tropical Medicine and Infectious Diseases (Kenya).

8.5.4 Economic evaluation

The thesis has shown the impact the disease has on both the patient and the caretaker in terms of the emotional toll as well as the impact on quality of life. In 2013, the Swiss Tropical Public Health Institute group calculated that 1-10 million disability adjusted life years were lost due to noma, the estimate is wide due to uncertainties about incidence, mortality, and surgical rehabilitation [57]. This estimate is similar to the 2010 Global Burden of Disease study for disability adjusted life years of other neglected tropical diseases (0.14-3.32 million years)

[286], highlighting the comparable nature of the economic burden of noma. Further studies assessing the economic impact of noma may highlight the significant costs of this disease for both the patient, the health system and society. This would provide useful information for advocacy, funding and policy efforts.

8.5.5 Quality of life scale in Hausa

As indicated in the outcomes study, there is currently no validated quality of life scale in Hausa (the predominantly spoken language in northwest Nigeria). This makes it difficult to robustly measure the improvement in noma patient's quality of life. This measure should be the focus of treatment programmes and needs to be incorporated in initiatives set up to monitor the efficacy of surgical treatments. Designing and validating such a tool would provide an opportunity to minimize the neglect of this aspect of noma care and would be useful for a range of other assessments in this setting. A previous study assessing quality of life changes for noma patients in Ethiopia utilised a semi-structured interview [111] which provided useful insights into the noma specific changes to this metric and could be used as a basis for the standardised noma assessment tool.

8.6 Conclusion

In conclusion, this thesis provides a unique view of the biopsychosocial features, epidemiology and treatment options for noma in northwest Nigeria. Noma is a disease which is indicative of a weak health system and socio-economic environments of extreme deprivation.

Intervention programmes should include wide-spread health system improvements which could address a host of risk factors for noma, and simultaneously other childhood diseases. These include increasing access to quality health care (including vaccinations) and referral

mechanisms, predominantly in rural areas, and the creation of a robust surveillance network. Health financing initiatives would need to be paired with these improvements. Nutritional programs aimed at caretakers of young children and community based oral health initiatives could also be effective mechanisms to curb the number of noma cases. Trainings with healthcare workers and community members are necessary to ensure awareness of noma is improved in endemic settings.

The combined findings of this thesis highlight the neglected nature of noma and make a strong case for placing noma on the WHO NTD list. This addition could garner awareness and open up much needed funding streams which would allow for further research, sufficient surveillance systems, general public health interventions and ultimately the eradication of noma.

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Appendices

Appendix 1 MSF documents

1.1 Letter of support from MSF

ARTSEN ZONDER GRENZEN

Naritaweg 10
Postbus 10014
1001 EA Amsterdam
T 020 520 87 00
info@artsenzondergrenzen.nl
www.artsenzondergrenzen.nl

19th April 2018

To Whom It May Concern,

RE: Elise Farley, PHD Candidate (student number FRLELI001)

On behalf of Médecins Sans Frontières (Holland), I am writing this letter of support for Elise Farley to complete her PhD through the University of Cape Town, utilizing data gathered during the course of her employment with MSF as an Epidemiologist. Elise has worked with MSF officially since June 2017 and has been involved in missions in Nigeria and South Sudan. Her time in Nigeria has and will be spent working on the Operational Research initiatives of the Noma project, in Sokoto, northwest Nigeria and it is through these projects she will gather the data that will be used for her PhD.

We support her PhD candidacy and the use of data gathered through MSF initiatives. A formal data sharing agreement has been signed with Elise which dictates the use of the data gathered.

Sincerely,

Signature Removed

Dr. Sidney Wong
Medical Director MSF OCA

Médecins Sans Frontières - Artsen Zonder Grenzen
Operational Centre Amsterdam
Naritaweg 10
1043 BX Amsterdam

Tel: +31 (0) 20 520 8945
E: sidney.wong@amsterdam.msf.org

1.2 Data sharing agreement with MSF

Data Sharing Agreement

between

Médecins Sans Frontières - Holland

and

Elise Farley

This agreement between MSF-Holland (disclosing party) and Elise Farley (recipient party) is entered into on 16th April 2018.

Disclosing party: **MSF-Holland (hereinafter referred to as "MSF")**

Name of contact person: Sidney Wong, Medical Director

Plantage Middenlaan 14
1018 DD Amsterdam
The Netherlands

Recipient party: Elise Farley
9 Southdown, 144 2nd Ave,
Harifield Village, 7700
Cape Town, South Africa

Description/ name of data set:

The data that is shared on the basis of this agreement has been collected by MSF for the purpose of the study entitled:

1) Risk factors for diagnosed Noma in northwest Nigeria, 2017- A Sequential Mixed Method Study Protocol (Case control and qualitative)
2) Long term follow up of Noma patients after surgical, nutritional and mental health interventions at the Noma Children's Hospital in northwest Nigeria, 2018
3) Determining the prevalence of all stages of Noma in northwest Nigeria
4) Noma and traditional healing in northwest Nigeria, 2018- A qualitative study with caretakers of Noma patients and traditional healers

MSF is the full owner of any data related to said study/ program.

Purpose of use: To add sound, useful information to the scant body of knowledge on Noma.

Method of transferring data:
All data will be transferred in an encrypted format with the encryption key stored separate from the dataset. Each party agrees to maintain this dataset either on the supplied CD or on a secure server.

The purpose of this Agreement is to set forth the terms, conditions, and obligations concerning the sharing of data between the parties.

Therefore, MSF and Elise Farley agree to share the aforementioned data under the following conditions:

1. MSF certifies that no personal health identifiers are included in this data set or that appropriate patient consent has been obtained for all identifiable data.

2. Both parties agree to maintain confidentiality and privacy safeguards that were originally created as part of the protocol or data collection. Both parties agree not to release information about specific identifiable subjects to anyone. Only people mentioned in the protocol will have access to the database.

3. During handling and storage of the data, all parties agree to abide by universally recognised ethical principles. In particular, due consideration will be given to issues of individual consent, confidentiality, and involvement of concerned communities.

4. Each party agrees to cooperate with the principle investigator (PI) in selective reporting of focused results so as to protect the integrity of subsequent research activities and uses of the shared data by the originating party.

5. The parties to this agreement agree not to use the transferred data for commercial purpose, and not to claim any intellectual property rights on the data.

6. Both parties view dissemination of research findings, both by publication and oral presentation, as an essential objective of the research. Therefore Parties are encouraged to publish the results of their work in a collaborative fashion for the benefit of the public.

7. A copy of each manuscript or abstract shall be submitted to MSF at least 30 days before submission for publication in a journal or presentation at an international meeting. MSF Publication shall be based on written consent of MSF and accompanied by an acknowledgement that MSF and the host country supplied the data. Guidelines for authorship of the International Committee of Medical Journal Editors Committee will be used to establish authorship.

8. The ownership of the data remains with MSF.

9. The information and data provided through this agreement shall only be used for the above mentioned purpose and according to the outlined terms and conditions. Neither party shall

use the personal information/ data provided under this agreement for any purpose other than that set out in this agreement.

10. This Agreement shall be in full force and effect from the first date written above for a period of three years. This Agreement may be terminated with thirty (30) days written notice by either party or mutual agreement of the parties.

    Upon completion of the agreement, the recipient party will return all copies of the collected data and the cleaned database. MSF commits to storing the data for at least 5 years.

11. In the event of the termination of this Agreement, the personal information shared under this Agreement shall be returned to the disclosing party.

The undersigned individuals represent that they are fully authorized to execute this Agreement on behalf of the respective parties, perform the obligations under this Agreement, and make all representations, warranties, and grants as set forth herein.

MSF is willing to provide the data for use as indicated above according to the outlined conditions, and the recipient party and MSF agree to comply with those conditions.

IN WITNESS WHEREOF this Agreement has been signed on behalf of the disclosing party by the Medical Director of MSF:

Signature Removed

Dr. Sidney Wong

[Name] [Date] [Signature]

IN WITNESS WHEREOF this Agreement has been signed on behalf of the recipient party by

Signature Removed

Elise Farley 16.04.2018

[Name] [Date] [Signature]

Appendices (*Protocol or concept paper to be attached)*

Appendix 2 Ethical approvals

2.1 UCT ERB ethical approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 552-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: sumeyah.eriefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

05 November 2018

HREC REF: 425/2018

Dr U Mehta
Division of Public Health & Family Medicine
5th Floor
Falmouth Building-FHS

Dear Dr Mehta

PROJECT TITLE: NOMA IN NORTHWEST NIGERIA - LANGUAGE AND BELIEFS, RISK FACTORS, TREATMENT OUTCOMES, LINKS WITH TRADITIONAL HEALING AND PREVALENCE (PHD Candidate - Ms E Farley)

Thank you for your response letter dated 12 September 2018, addressing the issues raised by the Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 November 2019.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: Ms Elise Farley will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator must obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

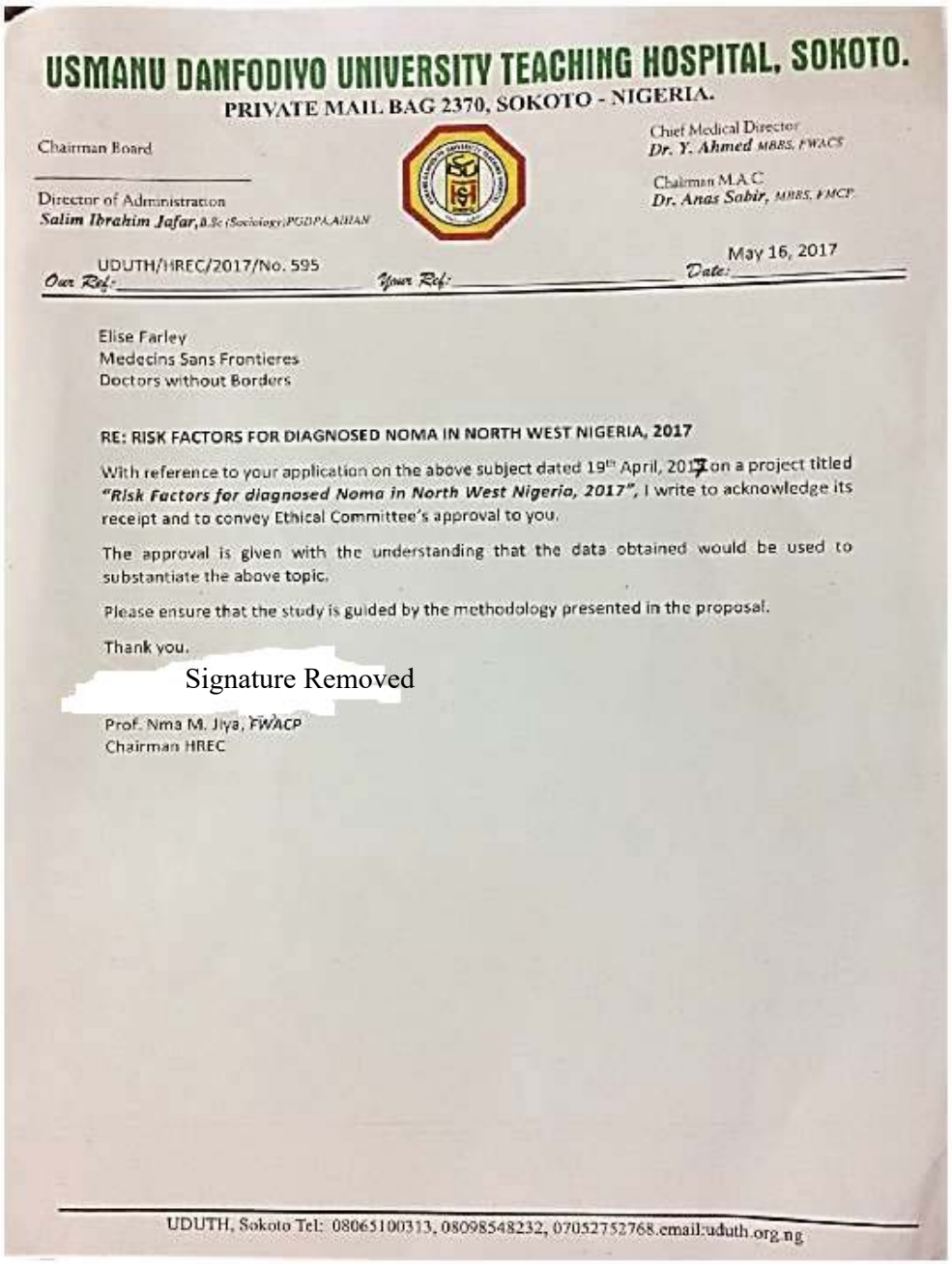
Signature Removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.

2.2 Risk factors and language and beliefs study ethical approvals

2.2.1 *UDUTH ethical approval - risk factors and language and beliefs study*



USMANU DANFODIYO UNIVERSITY TEACHING HOSPITAL, SOKOTO.

PRIVATE MAIL BAG 2370, SOKOTO - NIGERIA.

Chairman Board

Director of Administration
Salim Ibrahim Jafar, B.Sc (Sociology) PGDPA,ABIAN

Chief Medical Director
Dr. Y. Ahmed MBBS, FWACS

Chairman M.A.C
Dr. Anas Sabir, MBBS, FMCP

Our Ref: UDUTH/HREC/2017/No. 595 Your Ref: Date: May 16, 2017

Elise Farley
Medecins Sans Frontieres
Doctors without Borders

RE: RISK FACTORS FOR DIAGNOSED NOMA IN NORTH WEST NIGERIA, 2017

With reference to your application on the above subject dated 19th April, 2017 on a project titled ***"Risk Factors for diagnosed Noma in North West Nigeria, 2017"***, I write to acknowledge its receipt and to convey Ethical Committee's approval to you.

The approval is given with the understanding that the data obtained would be used to substantiate the above topic.

Please ensure that the study is guided by the methodology presented in the proposal.

Thank you.

Signature Removed

Prof. Nma M. Jiya, FWACP
Chairman HREC

UDUTH, Sokoto Tel: 08065100313, 08098548232, 07052752768.email:uduth.org.ng

2.2.2 *MSF ethical approval - risk factors and language and beliefs study*

Ethics Review Board
Instituted by *Médecins Sans Frontières*

Dr Sidney Wong
Medical Director
Médecins Sans Frontières - Artsen Zonder Grenzen
Operational Centre Amsterdam
Plantage Middenlaan 14
1018 DD Amsterdam

02 May 2017

Re: Ethics approval of "Risk factors for diagnosed Noma in Northwest Nigeria, 2017: Sequential Mixed Method Study Protocol", Version 3.0, dated 1 may 2017, (ID: 1710)

Dear Dr Wong,

Thank you for your reply to our review of the above-mentioned protocol. We are happy with the answers provided by the investigators. **We thus approve the protocol for a period of 12 months, until 01 May 2018**. Please ensure that all people associated with this particular research are duly informed about the changes introduced compared to the initially submitted version, and that they all receive a copy of the approved protocol.

If the study is not started within the next twelve months, you should submit a request for amendment of the study schedule one month before this approval expires. If the study is not completed within the next twelve months, you should request an extension of approval at least one month before this approval expires.

Any substantial changes you might wish to make to the protocol must be submitted to the Ethics Review Board through a request for amendment, for further review and approval. Anything that may occur during the research that may affect ethical acceptability of the project, including adverse effects on participants or unforeseen events, must be reported to the Ethics Review Board. We would also like to remind you that the Ethics Review Board will routinely check the reported and published outcome measure(s) against the outcome measure(s) listed in the approved protocol. If the outcome measures are changed during the course of the research, a request for amendment should be submitted to the Ethics Review Board.

Please notify us once the study is completed or if it is stopped. The ERB considers that a study is finished when there is no more contact with study participants and when data are collected, cleaned and analysed and, as applicable, samples have been analysed and coded/anonymised. We would appreciate receiving the final research report.

Please send us in due time the approval by Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee. Please notify us once this study is initiated.

We wish you much success with the research.

Yours sincerely,

Signature Removed

Raffaella Ravinetto
Chairperson, Ethics Review Board

2.2.3 *Kebbi ethical approval - risk factors and language and beliefs study*

KEBBI STATE MINISTRY OF HEALTH

(HEADQUARTERS)

GWADANGAJI SECRETARIAT COMPLEX, BIRNIN KEBBI, KEBBI STATE (NIGERIA)

e-mail: kebbistatemoh@yahoo.com

P.M.B 1040

Ref MOH/SUB/4027/VOL.I/14

Date 5th July, 2017

The Medical Coordinator,
Medicines Sans Frontiers (OCA)
26 Agaie Road,
Sokoto, Nigeria.

RE: REQUEST FOR APPROVAL/INTRODUCTORY LETTER

I am directed to write and refer to your request on the above subject and to inform you that after a review of the attached documents by the Health Research Ethics Committee and found the documents quite fulfilling and satisfactory.

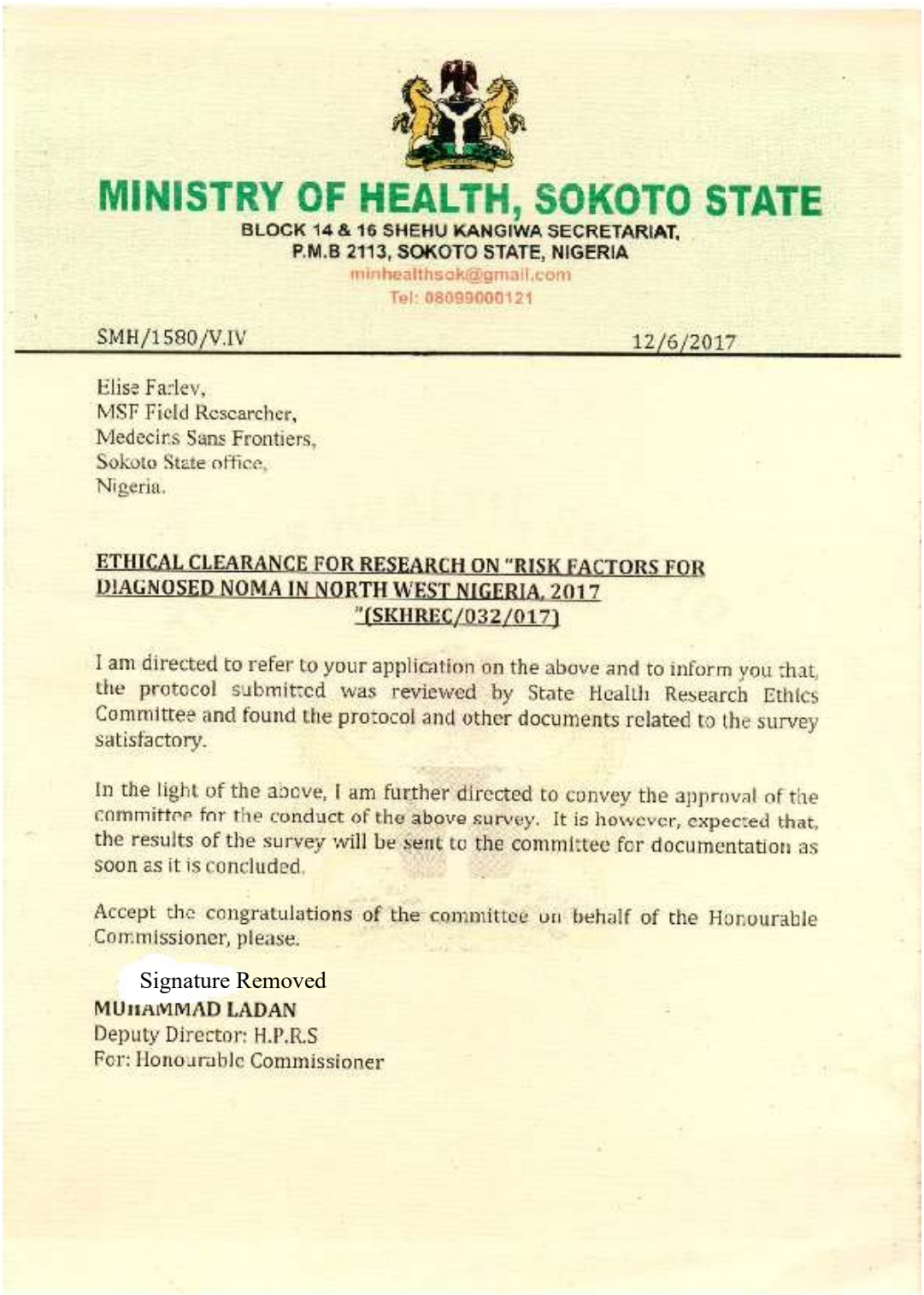
I wish to convey the approval of the committee on the plan study survey undertaking by your organisation to the eight Noma patients in Kebbi State, please note that you should endeavour to illicit feedback on your findings to the State Health Research Ethics Committee for proper documentation. .

Accept the assurance and esteem of the Honourable Commissioner's please.

Signature Removed

Bello Bagudu Diggi
Deputy Director Public Health
For:-Hon. Commissioner

2.2.4 *Sokoto ethical approval - risk factors and language and beliefs study*



MINISTRY OF HEALTH, SOKOTO STATE

BLOCK 14 & 16 SHEHU KANGIWA SECRETARIAT,
P.M.B 2113, SOKOTO STATE, NIGERIA
minhealthsok@gmail.com
Tel: 08099000121

SMH/1580/V.IV 12/6/2017

Elise Farley,
MSF Field Researcher,
Medecins Sans Frontiers,
Sokoto State office,
Nigeria.

ETHICAL CLEARANCE FOR RESEARCH ON "RISK FACTORS FOR DIAGNOSED NOMA IN NORTH WEST NIGERIA, 2017 "(SKHREC/032/017)

I am directed to refer to your application on the above and to inform you that, the protocol submitted was reviewed by State Health Research Ethics Committee and found the protocol and other documents related to the survey satisfactory.

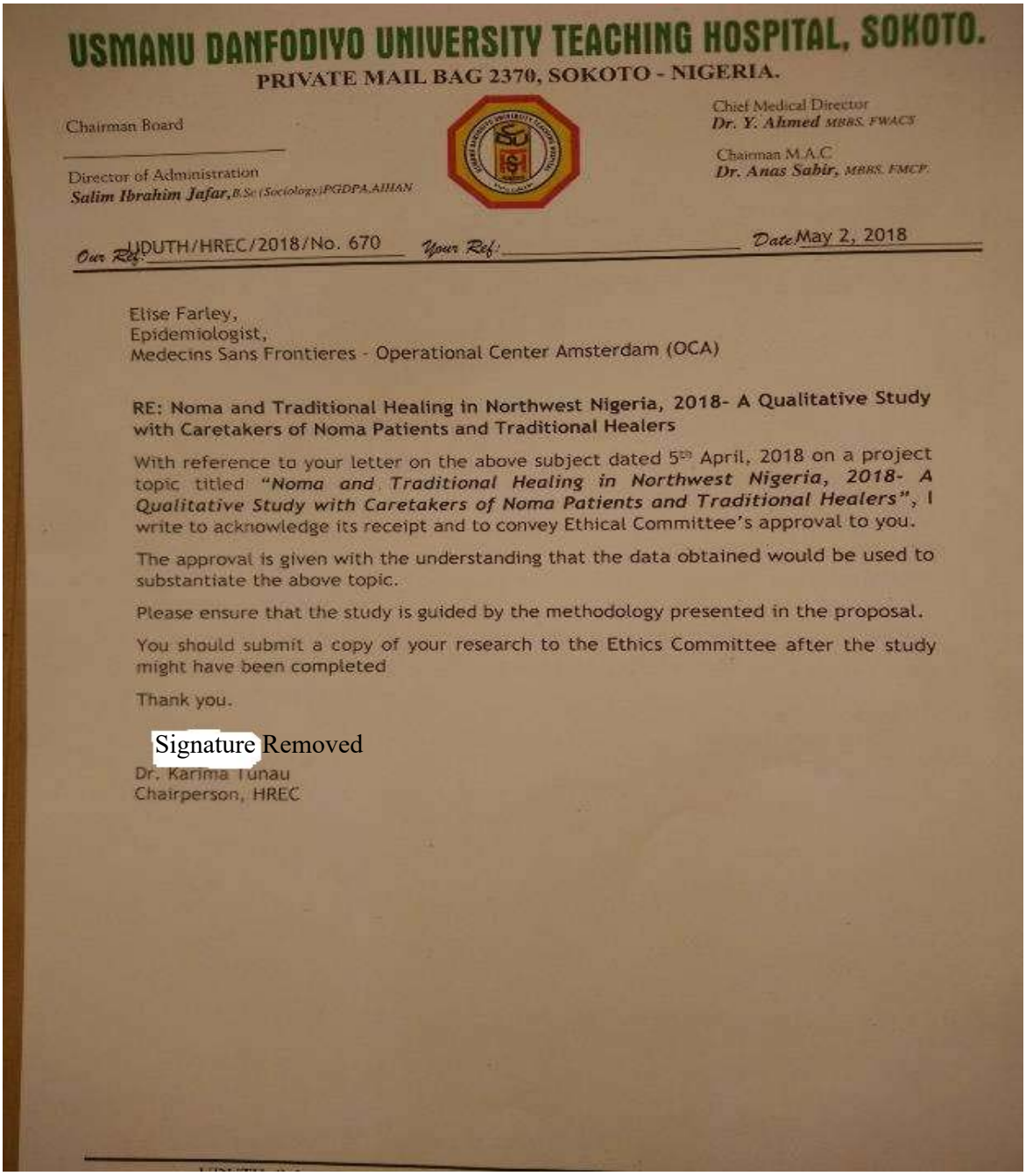
In the light of the above, I am further directed to convey the approval of the committee for the conduct of the above survey. It is however, expected that, the results of the survey will be sent to the committee for documentation as soon as it is concluded.

Accept the congratulations of the committee on behalf of the Honourable Commissioner, please.

Signature Removed
MUHAMMAD LADAN
Deputy Director: H.P.R.S
For: Honourable Commissioner

2.3 Traditional healer study ethical approvals

2.3.1 *UDUTH ethical approval - traditional healer study*



USMANU DANFODIYO UNIVERSITY TEACHING HOSPITAL, SOKOTO.

PRIVATE MAIL BAG 2370, SOKOTO - NIGERIA.

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Salim Ibrahim Jafar, *B.Sc (Sociology) PGDPA,AIHAN*

Chief Medical Director
Dr. Y. Ahmed *MBBS, FWACS*

Chairman M.A.C
Dr. Anas Sabir, *MBBS, FMCP*

Our Ref: UDUTH/HREC/2018/No. 670 Your Ref: Date May 2, 2018

Elise Farley,
Epidemiologist,
Medecins Sans Frontieres - Operational Center Amsterdam (OCA)

RE: Noma and Traditional Healing in Northwest Nigeria, 2018- A Qualitative Study with Caretakers of Noma Patients and Traditional Healers

With reference to your letter on the above subject dated 5th April, 2018 on a project topic titled ***"Noma and Traditional Healing in Northwest Nigeria, 2018- A Qualitative Study with Caretakers of Noma Patients and Traditional Healers"***, I write to acknowledge its receipt and to convey Ethical Committee's approval to you.

The approval is given with the understanding that the data obtained would be used to substantiate the above topic.

Please ensure that the study is guided by the methodology presented in the proposal.

You should submit a copy of your research to the Ethics Committee after the study might have been completed

Thank you.

Signature Removed
Dr. Karima Tunau
Chairperson, HREC

2.3.2 *MSF ethical approval - traditional healer study*

Ethics Review Board
Instituted by *Médecins Sans Frontières*

Dr Sidney Wong
Medical Director
Médecins Sans Frontières - Artsen Zonder Grenzen
Operational Centre Amsterdam
Plantage Middenlaan 14
1018 DD Amsterdam

01 June 2018

Re: Ethics approval of "Noma and traditional healing in northwest Nigeria, 2018: A qualitative study with caretakers of Noma patients and traditional healers", Version 2, dated 3 May 2018, (ID: 1824)

Dear Dr Wong,

Thank you for your reply to our review of the above-mentioned protocol. We are happy with the answers provided by the investigators and thus approve the protocol. Please ensure that all people associated with the research receive a copy of the final, approved protocol.

Please note that:

- *if the study is not started within the next twelve months*, this approval will not be valid anymore, and you should submit a *Request for Amendment* (with the new schedule and the rationale for the delay);
- *after the study has started*, any planned substantial revisions/changes to the protocol must be submitted to the Ethics Review Board through a *Request for Amendment*, for further review and approval;
- any occurrences *during the research* that may affect its ethical acceptability, such as serious adverse events or other unforeseen events, must be reported to the Ethics Review Board;
- *once the study is completed or if it is stopped prematurely*, the Ethics Review Board should be notified with an *End of Study Notification*. Please also send us copies of the final research report and any related publications.

Please send us in due time the approval by the *Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee*, and notify us once this study is initiated.

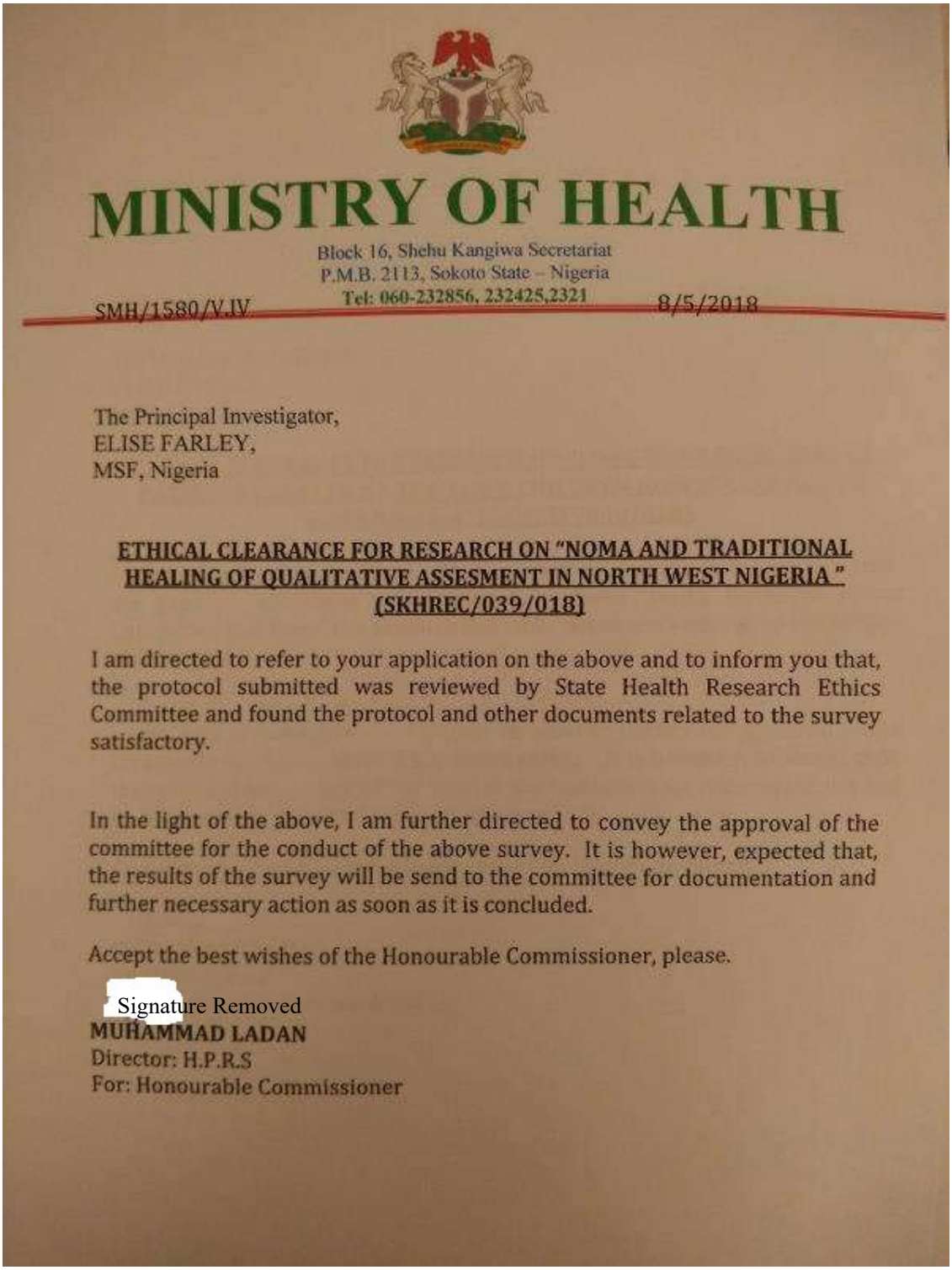
We wish you much success with the research.

Yours sincerely,

Signature Removed

Raffaella Ravinetto
Chairperson, Ethics Review Board

2.3.3 *Sokoto ethical approval - traditional healer study*



MINISTRY OF HEALTH

Block 16, Shehu Kangiwa Secretariat
P.M.B. 2113, Sokoto State – Nigeria
Tel: 060-232856, 232425,2321

SMH/1580/V.IV 8/5/2018

The Principal Investigator,
ELISE FARLEY,
MSF, Nigeria

ETHICAL CLEARANCE FOR RESEARCH ON "NOMA AND TRADITIONAL HEALING OF QUALITATIVE ASSESMENT IN NORTH WEST NIGERIA." (SKHREC/039/018)

I am directed to refer to your application on the above and to inform you that, the protocol submitted was reviewed by State Health Research Ethics Committee and found the protocol and other documents related to the survey satisfactory.

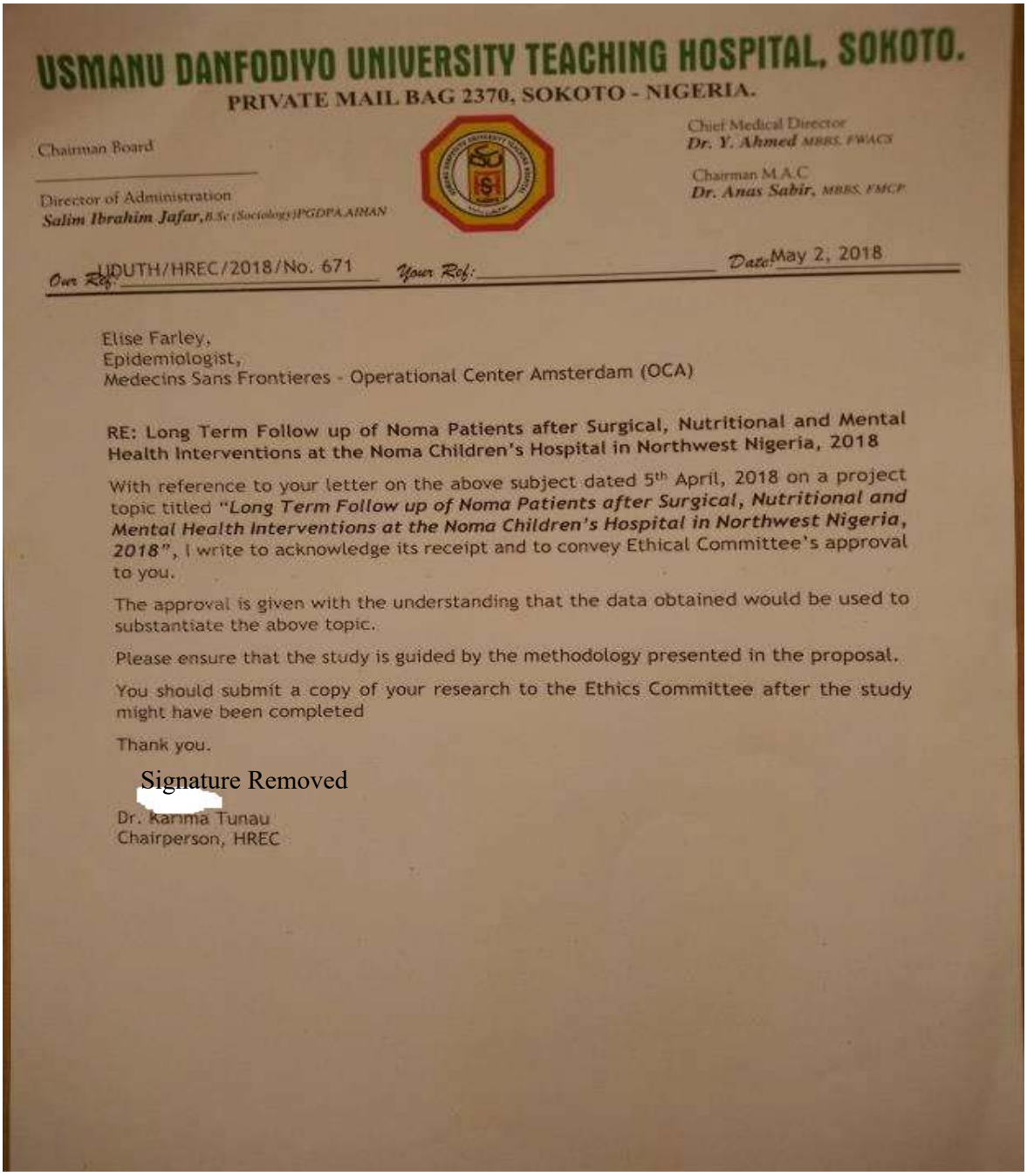
In the light of the above, I am further directed to convey the approval of the committee for the conduct of the above survey. It is however, expected that, the results of the survey will be send to the committee for documentation and further necessary action as soon as it is concluded.

Accept the best wishes of the Honourable Commissioner, please.

Signature Removed
MUHAMMAD LADAN
Director: H.P.R.S
For: Honourable Commissioner

2.4 Outcomes ethical approvals

2.4.1 *UDUTH ethical approval - outcomes study*



USMANU DANFODIYO UNIVERSITY TEACHING HOSPITAL, SOKOTO.
PRIVATE MAIL BAG 2370, SOKOTO - NIGERIA.

Chairman Board

Director of Administration
Salim Ibrahim Jafar, B.Sc (Sociology) PGDPA AIRAN

Chief Medical Director
Dr. Y. Ahmed MBBS, FWACS

Chairman M.A.C
Dr. Anas Sabir, MBBS, FMCP

Our Ref: UDUTH/HREC/2018/No. 671 Your Ref: Date: May 2, 2018

Elise Farley,
Epidemiologist,
Medecins Sans Frontieres - Operational Center Amsterdam (OCA)

RE: Long Term Follow up of Noma Patients after Surgical, Nutritional and Mental Health Interventions at the Noma Children's Hospital in Northwest Nigeria, 2018

With reference to your letter on the above subject dated 5th April, 2018 on a project topic titled *"Long Term Follow up of Noma Patients after Surgical, Nutritional and Mental Health Interventions at the Noma Children's Hospital in Northwest Nigeria, 2018"*, I write to acknowledge its receipt and to convey Ethical Committee's approval to you.

The approval is given with the understanding that the data obtained would be used to substantiate the above topic.

Please ensure that the study is guided by the methodology presented in the proposal.

You should submit a copy of your research to the Ethics Committee after the study might have been completed

Thank you.

Signature Removed

Dr. Karima Tunau
Chairperson, HREC

2.4.2 *MSF ethical approval - outcomes study*

Ethics Review Board
Instituted by *Médecins Sans Frontières*

Dr Sidney Wong
Medical Director
Médecins Sans Frontières - Artsen Zonder Grenzen
Operational Centre Amsterdam
Plantage Middenlaan 14
1018 DD Amsterdam

27 June 2018

Re: Ethics approval of "Long term follow up of Noma patients after surgical, nutritional and mental health interventions at the Noma Children's Hospital in northwest Nigeria, 2018", Version 3 dated 13 June 2018 (ID: 1829)

Dear Dr Wong,

Thank you for your reply to our review of the above-mentioned protocol. We are happy with the answers provided by the investigators and thus approve the protocol. Please ensure that all people associated with the research receive a copy of the final, approved protocol.

Please note that:

- *if the study is not started within the next twelve months*, this approval will not be valid anymore, and you should submit a *Request for Amendment* (with the new schedule and the rationale for the delay);
- *after the study has started*, any planned substantial revisions/changes to the protocol must be submitted to the Ethics Review Board through a *Request for Amendment*, for further review and approval;
- any occurrences *during the research* that may affect its ethical acceptability, such as serious adverse events or other unforeseen events, must be reported to the Ethics Review Board;
- *once the study is completed or if it is stopped prematurely*, the Ethics Review Board should be notified with an *End of Study Notification*. Please also send us copies of the final research report and any related publications.

If you have not already done so, please send us in due time the approvals from the *Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee* and the *Sokoto and Kebbi Ministry of Health Ethics Departments*, and notify us once this study is initiated.

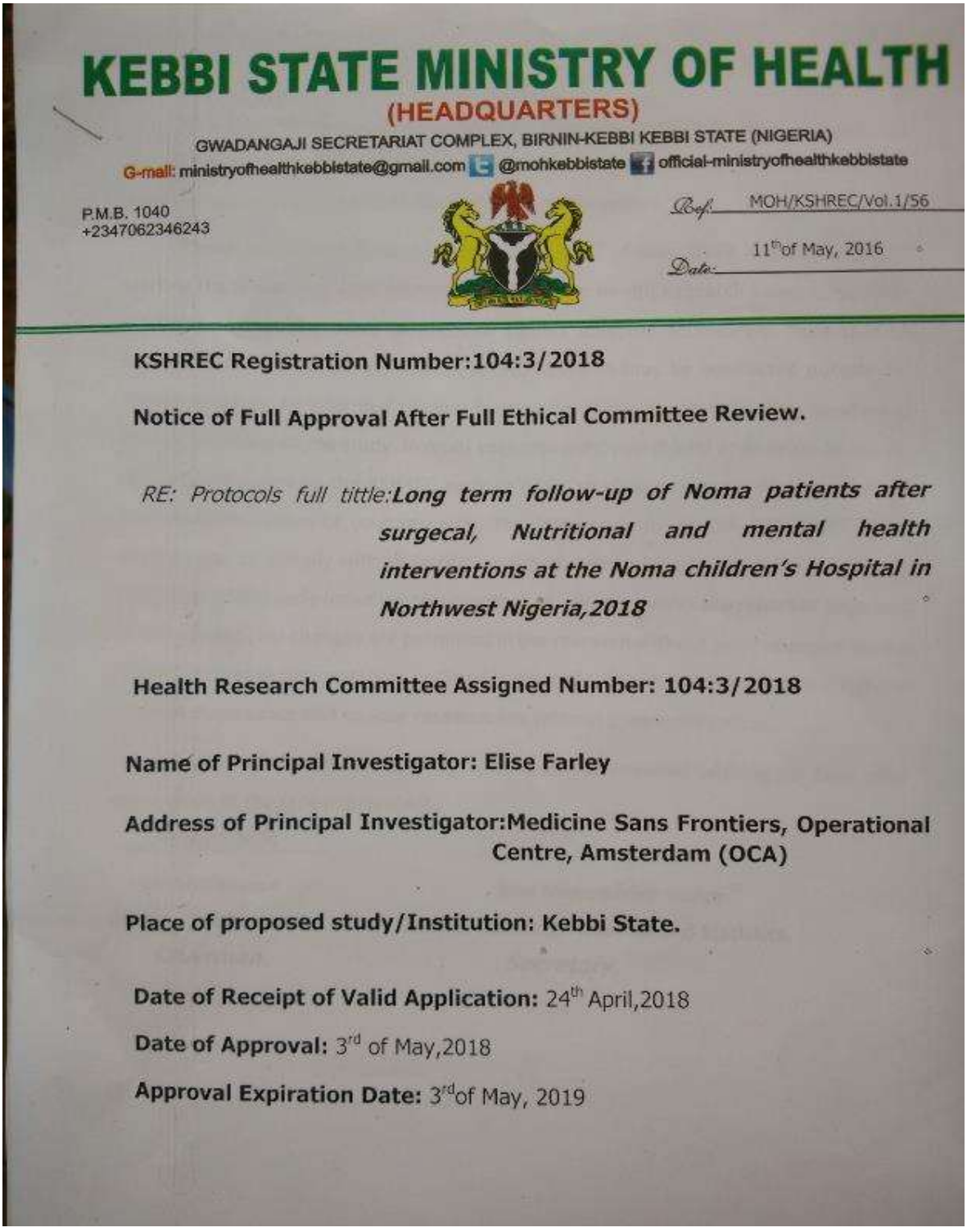
We wish you much success with the research.

Yours sincerely,

Signature Removed

Raffaella Ravinetto
Chairperson, Ethics Review Board

2.4.3 *Kebbi ethical approval - outcomes study*



KEBBI STATE MINISTRY OF HEALTH

(HEADQUARTERS)

GWADANGAJI SECRETARIAT COMPLEX, BIRNIN-KEBBI KEBBI STATE (NIGERIA)

G-mail: ministryofhealthkebbistate@gmail.com @mohkebbistate official-ministryofhealthkebbistate

P.M.B. 1040
+2347062346243

Ref: MOH/KSHREC/Vol.1/56

Date: 11th of May, 2016

KSHREC Registration Number:104:3/2018

Notice of Full Approval After Full Ethical Committee Review.

RE: Protocols full tittle: ***Long term follow-up of Noma patients after surgecal, Nutritional and mental health interventions at the Noma children's Hospital in Northwest Nigeria,2018***

Health Research Committee Assigned Number: 104:3/2018

Name of Principal Investigator: Elise Farley

Address of Principal Investigator:Medicine Sans Frontiers, Operational Centre, Amsterdam (OCA)

Place of proposed study/Institution: Kebbi State.

Date of Receipt of Valid Application: 24th April,2018

Date of Approval: 3rd of May,2018

Approval Expiration Date: 3rdof May, 2019

This is to inform you that the research described in the submitted protocol, the consent forms and other participant information materials have been reviewed and givin full approval by the Health Research Ethics Committee.

Thisapproval dates from 3rd of May,2018 to 3rd of May, 2019. If there is delay in starting the research, Please inform the Kebbi State Health Research Ethics Committee (KSHREC) so that the dates of approval can be adjusted accordingly. Note that no participant accrual or activity related to this research may be conducted outside the stipulated dates. All informed consent forms used in this study must carry duration of KSHREC approval of the study. In multi year research, you should endeavour to submit your annual report to the KSHREC early in order to obtain renewal of your approval and avoid disruption of your research. The State code for Health RESEARCH Ethics requires you to comply with all institutional guidelines,rules and regulations and with the tenets of the code including ensuring that all adverse events are reported promptly to the KSHREC. No changes are permitted in the research without prior approval by the KSHREC except in circumstances outlined in the code. The KSHREC reserves the right to conduct compliance visit to your research site without prior notification.

A copy of the final research/project report is required withing 60 days after completion of the research/project.

Signature Removed

Kabiru Alhassan

Director Public Health

Chairman.

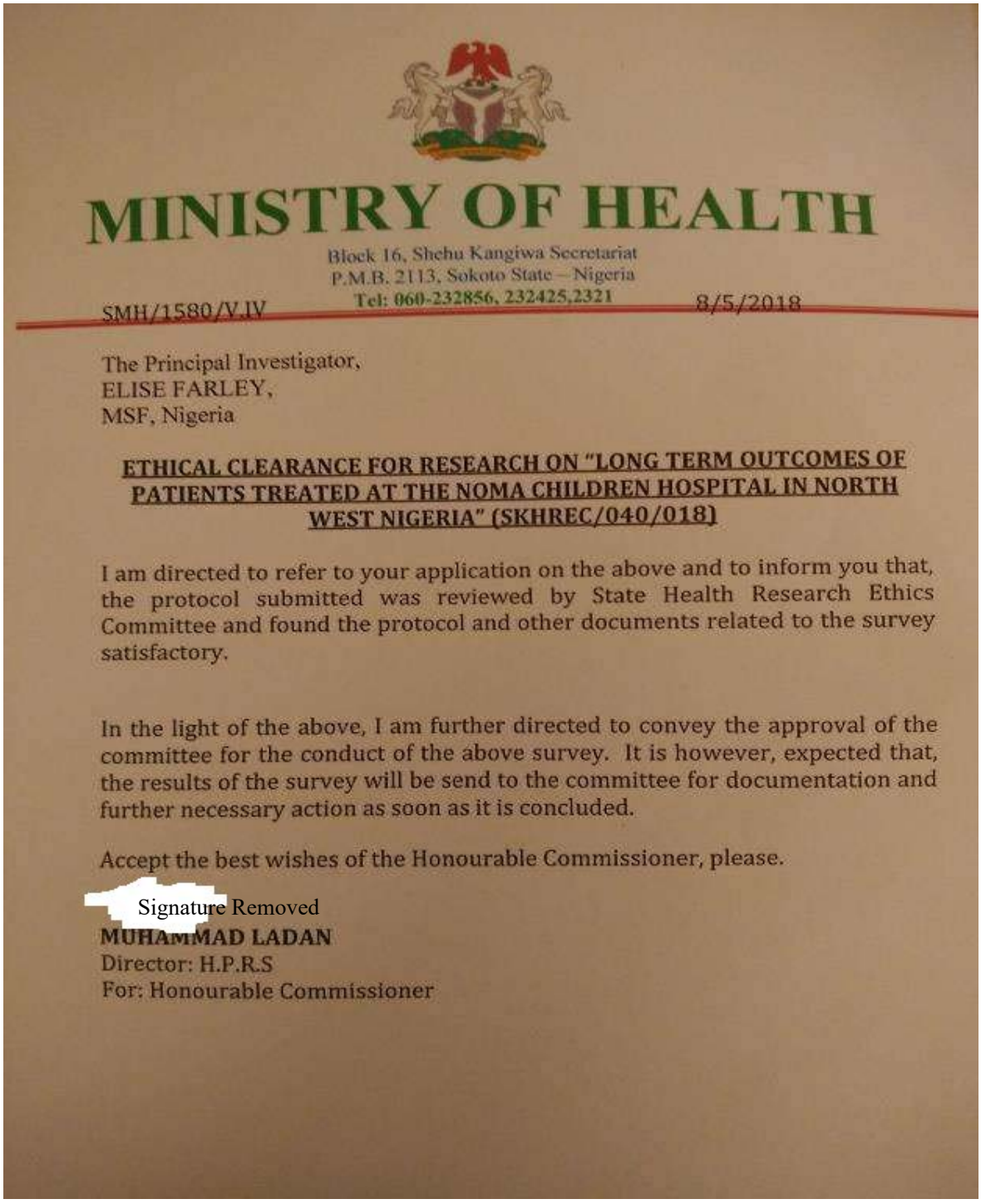
Signature Removed

Sani Muhammed Bunza

Director Planning, Research and Statistics.

Secretary.

2.4.4 *Sokoto ethical approval - outcomes study*



MINISTRY OF HEALTH

Block 16, Shehu Kangiwa Secretariat
P.M.B. 2113, Sokoto State – Nigeria
Tel: 060-232856, 232425,2321

SMH/1580/V.IV 8/5/2018

The Principal Investigator,
ELISE FARLEY,
MSF, Nigeria

ETHICAL CLEARANCE FOR RESEARCH ON "LONG TERM OUTCOMES OF PATIENTS TREATED AT THE NOMA CHILDREN HOSPITAL IN NORTH WEST NIGERIA" (SKHREC/040/018)

I am directed to refer to your application on the above and to inform you that, the protocol submitted was reviewed by State Health Research Ethics Committee and found the protocol and other documents related to the survey satisfactory.

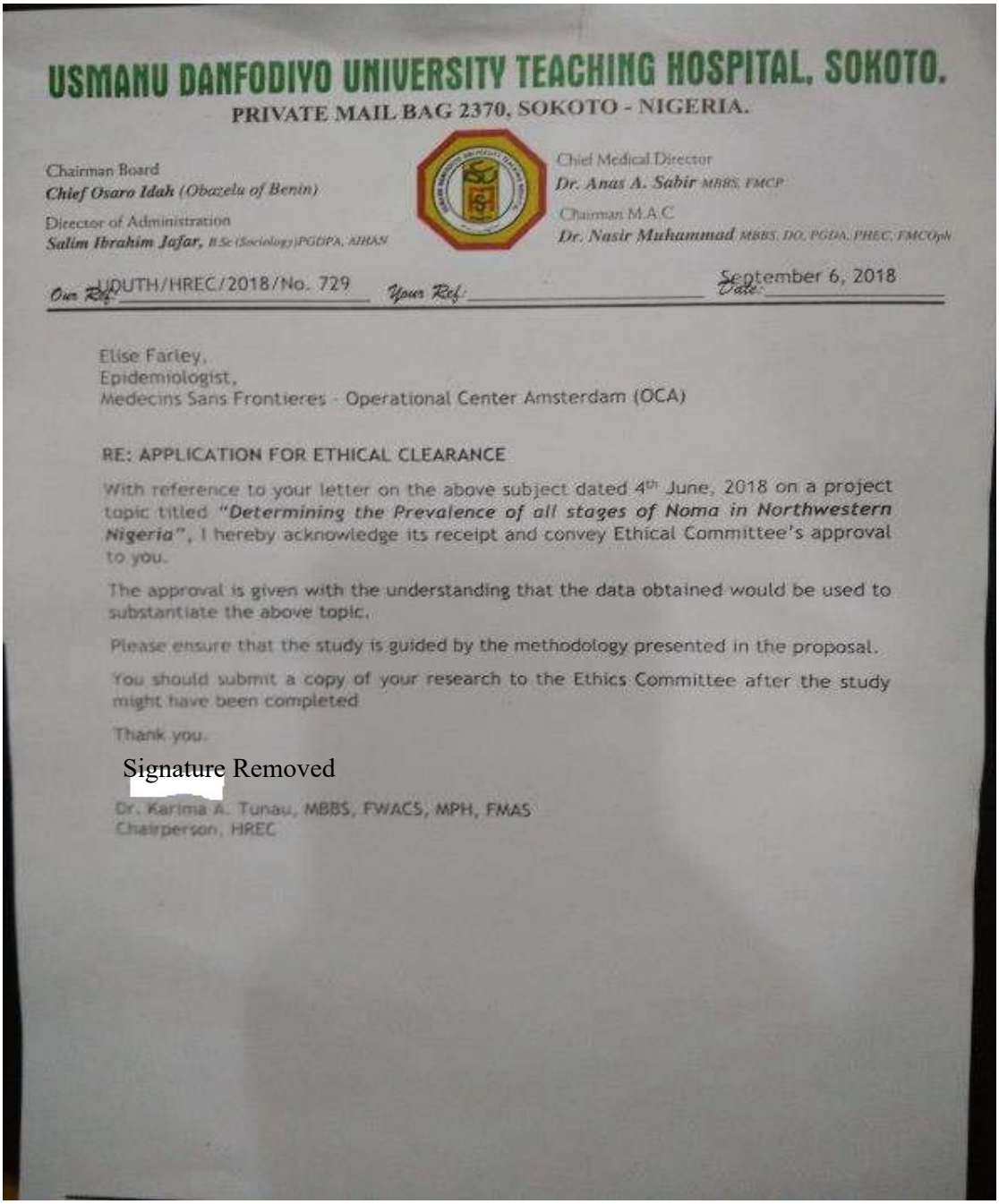
In the light of the above, I am further directed to convey the approval of the committee for the conduct of the above survey. It is however, expected that, the results of the survey will be send to the committee for documentation and further necessary action as soon as it is concluded.

Accept the best wishes of the Honourable Commissioner, please.

Signature Removed
MUHAMMAD LADAN
Director: H.P.R.S
For: Honourable Commissioner

2.5 Prevalence study ethical approvals

2.5.1 *UDUTH ethical approval - prevalence study*



USMANU DANFODIYO UNIVERSITY TEACHING HOSPITAL, SOKOTO.

PRIVATE MAIL BAG 2370, SOKOTO - NIGERIA.

Chairman Board
Chief Osaro Idah (Obazelu of Benin)
Director of Administration
Salim Ibrahim Jafar, B.Sc (Sociology) PGDPA, ARAN

Chief Medical Director
Dr. Anas A. Sabir MBBS, FMCP
Chairman M.A.C
Dr. Nasir Muhammad MBBS, DO, PGDA, PHEC, FMCOph

Our Ref: UDUTH/HREC/2018/No. 729 Your Ref: Date: September 6, 2018

Elise Farley,
Epidemiologist,
Medecins Sans Frontieres - Operational Center Amsterdam (OCA)

RE: APPLICATION FOR ETHICAL CLEARANCE

With reference to your letter on the above subject dated 4th June, 2018 on a project topic titled *"Determining the Prevalence of all stages of Noma in Northwestern Nigeria"*, I hereby acknowledge its receipt and convey Ethical Committee's approval to you.

The approval is given with the understanding that the data obtained would be used to substantiate the above topic.

Please ensure that the study is guided by the methodology presented in the proposal.

You should submit a copy of your research to the Ethics Committee after the study might have been completed

Thank you.

Signature Removed

Dr. Karima A. Tunau, MBBS, FWACS, MPH, FMAS
Chairperson, HREC

2.5.2 *MSF ethical approval - prevalence study*

Ethics Review Board
Instituted by *Médecins Sans Frontières*

Dr Sidney Wong
Medical Director
Médecins Sans Frontières - Artsen Zonder Grenzen
Operational Centre Amsterdam
Plantage Middenlaan 14, 1018 DD Amsterdam

cc: Renée Teernstra <Renee.Teernstra@amsterdam.msf.org>

01 August 2018

Re: Ethics approval of "Determining the prevalence of all stages of Noma in northwest Nigeria" Version 2 dated 4 July 2018 (ID 1848)

Dear Sid;

Thank you for your reply to our review of the above-mentioned protocol. We are happy with the answers provided by the investigators and thus approve the protocol. Please ensure that all people associated with the research receive a copy of the final, approved protocol.

Please note that:

- *if the study is not started within the next twelve months*, this approval will not be valid anymore, and you should submit a *Request for Amendment* (with the new schedule and the rationale for the delay);
- *after the study has started*, any planned substantial revisions/changes to the protocol must be submitted to the Ethics Review Board through a *Request for Amendment*, for further review and approval;
- any occurrences *during the research* that may affect its ethical acceptability, such as serious adverse events or other unforeseen events, must be reported to the Ethics Review Board;
- *once the study is completed or if it is stopped prematurely*, the Ethics Review Board should be notified with an *End of Study Notification*. Please also send us copies of the final research report and any related publications.

Thank you for providing us with a copy of the letter of approval from the *Sokoto State Health Research Ethics Committee*. Please notify us once this study is initiated.

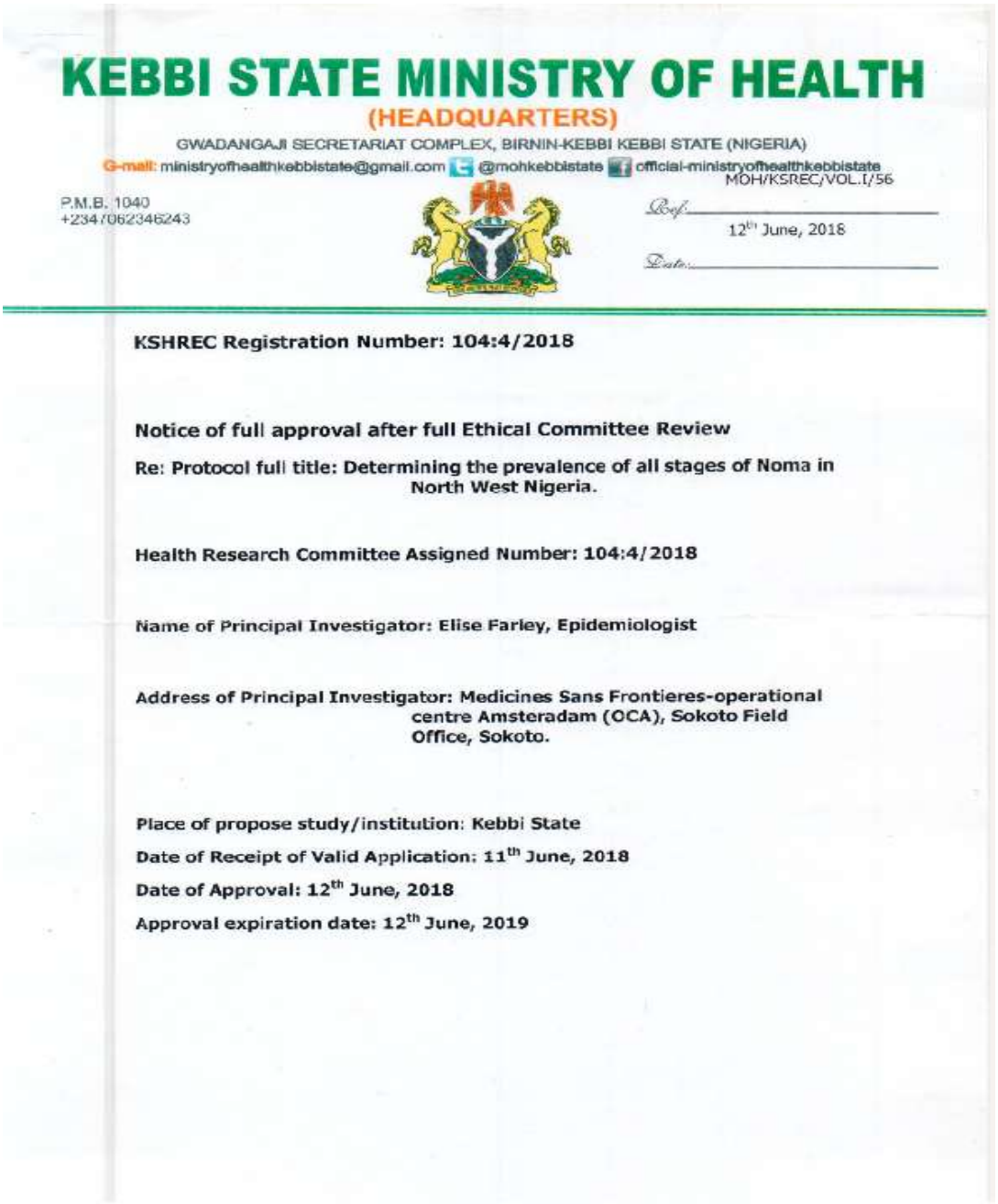
We wish you much success with the research.

Yours sincerely,

Signature Removed

Raffaella Ravinetto
Chairperson, Ethics Review Board

2.5.3 *Kebbi ethical approval - prevalence study*



KEBBI STATE MINISTRY OF HEALTH

(HEADQUARTERS)

GWADANGAJI SECRETARIAT COMPLEX, BIRNIN-KEBBI KEBBI STATE (NIGERIA)

G-mail: ministryofhealthkebbistate@gmail.com @mohkebbistate official-ministryofhealthkebbistate

P.M.B. 1040
+234 7062346243

MOH/KSREC/VOL.I/56

Ref:

12th June, 2018

Date:

KSHREC Registration Number: 104:4/2018

Notice of full approval after full Ethical Committee Review

Re: Protocol full title: Determining the prevalence of all stages of Noma in North West Nigeria.

Health Research Committee Assigned Number: 104:4/2018

Name of Principal Investigator: Elise Farley, Epidemiologist

Address of Principal Investigator: Medicines Sans Frontieres-operational centre Amsteradam (OCA), Sokoto Field Office, Sokoto.

Place of propose study/institution: Kebbi State

Date of Receipt of Valid Application: 11th June, 2018

Date of Approval: 12th June, 2018

Approval expiration date: 12th June, 2019

2.5.4 *Sokoto ethical approval - prevalence study*

MINISTRY OF HEALTH

Block 16, Shehu Kangiwa Secretariat
P.M.B. 2113, Sokoto State – Nigeria
Tel: 08026326999, mladansk2@yahoo.com

SMH/1580/V.IV 25/6/2018

ELISE FARLEY,
Epidemiologist,
Medicine Sans Frontiers- Operational Centre Amsterdam
Nigeria office.

ETHICAL CLEARANCE FOR RESEARCH ON "DETERMINING THE PREVALENCE OF ALL STATGES OF NOMA IN NORTHWEST NIGERIA: SKHREC/070/018)

I am directed to refer to your application on the above and to inform you that, the protocol submitted was reviewed by State Health Research Ethics Committee and found the protocol and other documents related to the survey to be satisfactory.

In the light of the above, I am further directed to convey the approval of the committee for the conduct of the above survey. It is however, expected that, the results of the survey will be sent to the committee for documentation and further necessary action as soon as it is concluded.

Accept the best wishes of the Honourable Commissioner, please.

Signature Removed

MUHAMMAD LADAN
Director: Health Planning, Research& Statistics,
For: Honourable Commissioner

Appendix 3 Scoping literature review documents

3.1 PRISMA checklist for scoping literature review

Section	Item	PRISMA-scar checklist item	Reported
TITLE			
Title	1	Identify the report as a scoping review.	Yes
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	NA
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	Yes
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	Yes
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	NA
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	Yes
Information sources	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	Yes
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Yes

Section	Item	PRISMA-scar checklist item	Reported
Selection of sources of evidence	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	Yes
Data charting process	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	Yes
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	Yes
Critical appraisal of individual sources of evidence	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	Yes
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	Yes
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	Yes
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	Yes
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Yes
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	Yes
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	Yes
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	Yes
Limitations	20	Discuss the limitations of the scoping review process.	Yes

Section	Item	PRISMA-scar checklist item	Reported
Conclusion	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	Yes
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	Yes

3.2 Scoping literature review data extraction tool

Noma scoping review extraction tool

Notes on using a data extraction form:

- Be concise
- If you cannot find information, note down 'Cannot Find'

Include or exclude	
Include ☐	Exclude ☐
If excluding, reason:	

Title:	
Author:	
Journal:	
Year of publication:	

Study type:	**RCT**	Yes / No
	Cross-sectional	Yes / No
	Cohort	Yes / No
	Case control	Yes / No
	Qualitative	Yes / No
	Case series	Yes / No
	Case report	Yes / No
Meets research goal:	Yes / No / Unclear	
Geographical location first author:		
Setting:		

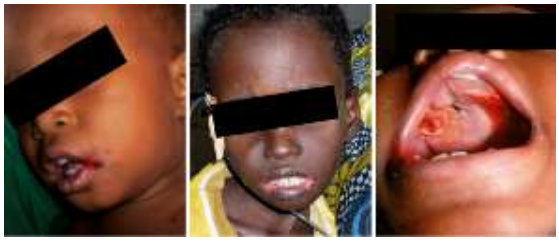
(including location and social context)	
Population description: *(from which study participants are drawn)*	
Research question:	
Methodology:	
Analysis:	
Main findings:	
History:	
Epidemiology:	
Clinical progression:	
Aetiology:	
Treatment regime:	
Mortality rate:	
Risk factors:	

Appendix 4 WHO classified noma stages

*All pictures included are from the WHO noma information booklet [1]

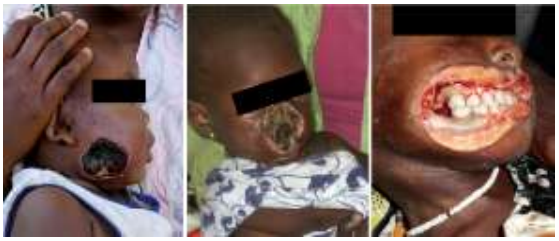
Stage 0: Simple gingivitis

Stage 1: Acute necrotizing gingivitis



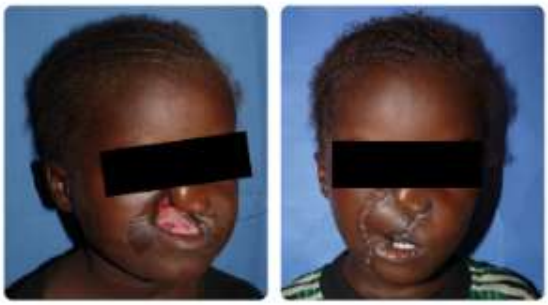
Stage 2: Oedema

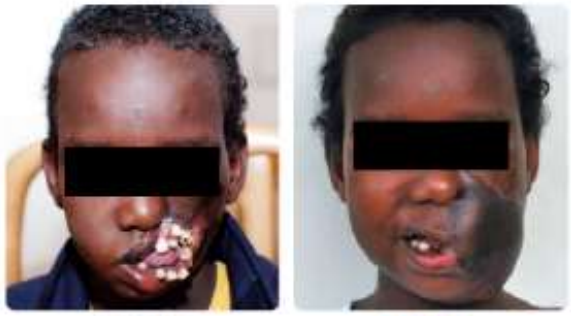
Stage 3: Gangrene



Stage 4: Scarring

Stage 5: Sequela





Appendix 5 Published manuscripts

5.1 Language and beliefs study manuscript

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Language and beliefs in relation to noma: a qualitative study, northwest Nigeria

Elise Farley[1,2]*, Annick Lenglet[3,4], Aisha Abubakar[1], Karla Bil[3], Adolphe Fotso[1], Bukola Oluyide[1], Simba Tirima[1], Ushma Mehta[5], Beverley Stringer[6]

1 Médecins Sans Frontières, Nigeria, **2** Department of Public Health Medicine, University of Cape Town, Cape Town, South Africa, **3** Médecins Sans Frontières, Amsterdam, The Netherlands, **4** Department of Medical Microbiology, Radboud University Medical Center, The Netherlands, **5** Centre for Infectious Disease Epidemiology and Research, School of Public Health and Family Medicine, University of Cape Town, **6** Médecins Sans Frontières, London, United Kingdom

* noma-research@oca.msf.org

OPEN ACCESS

Citation: Farley E, Lenglet A, Abubakar A, Bil K, Fotso A, Oluyide B, et al. (2020) Language and beliefs in relation to noma: a qualitative study, northwest Nigeria. PLoS Negl Trop Dis 14(1): e0007972. https://doi.org/10.1371/journal.pntd.0007972

Editor: Joseph M. Vinetz, University of California San Diego School of Medicine, UNITED STATES

Received: September 12, 2019

Accepted: December 5, 2019

Published: January 23, 2020

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pntd.0007972

Data Availability Statement: MSF has a managed access system for data sharing that respects MSF's legal and ethical obligations to its patients to collect, manage and protect their data

Abstract

Background

Noma is an orofacial gangrene that rapidly disintegrates the tissues of the face. Little is known about noma, as most patients live in underserved and inaccessible regions. We aimed to assess the descriptive language used and beliefs around noma, at the Noma Children's Hospital in Sokoto, Nigeria. Findings will be used to inform prevention programs.

Methods

Five focus group discussions (FGD) were held with caretakers of patients with noma who were admitted to the hospital at the time of interview, and 12 in-depth interviews (IDI) were held with staff at the hospital. Topic guides used for interviews were adapted to encourage the natural flow of conversation. Emergent codes, patterns and themes were deciphered from the data derived from IDI's and FGDs.

Results

Our study uncovered two main themes: names, descriptions and explanations for the disease, and risks and consequences of noma. Naming of the disease differed between caretakers and heath care workers. The general names used for noma illustrate the beliefs and social system used to explain the disease. Beliefs were varied; participant responses demonstrate a wide range of understanding of the disease and its causes. Difficulty in accessing care for patients with noma was evident and the findings suggest a variety of actions taking place before reaching a health center or health worker. Patient caretakers mentioned that barriers to care included a lack of knowledge regarding this medical condition, as well as a lack of trust in seeking medical care. Participants in our study spoke of the mental health strain the disease placed on them, particularly due to the stigma that is associated with noma.

responsibility. Ethical risks include, but are not limited to the nature of MSF operations and target populations being such that data collected often involves highly sensitive data. The dataset supporting the conclusions of this article is available are available on request in accordance with MSF's data sharing policy (available at: http://fieldresearch.msf.org/msf/handle/10144/306501). Requests for access to data should be made to data.sharing@msf.org.

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Conclusions

Caretaker and practitioner perspectives enhance our understanding of the disease in this context and can be used to improve treatment and prevention programs, and to better understand barriers to accessing health care. Differences in disease naming illustrate the difference in beliefs about the disease. This has an impact on health seeking behaviours, which for noma cases has important ramifications on outcomes, due to the rapid progression of the disease.

Author summary

Noma (cancrum oris) is an orofacial gangrene that rapidly disintegrates the hard and soft tissues of the face. Little is known about noma as most cases live in underserved and inaccessible regions. We aimed to assess the language used and beliefs around noma, in northwest Nigeria. Findings will be used to inform prevention programs. Five focus group discussions were held with caretakers of patients with noma admitted to the hospital at the time of interview, and 12 in-depth interviews were held with staff at the hospital. Our study uncovered two main themes: names; descriptions and explanations for the disease, and risks and consequences of noma. Naming of the disease differed between caretakers and heath care workers. Difficulty in accessing care for patients with noma was evident. Barriers to care and lack of knowledge and trust were evident. The impact of noma was not limited to physical presentation; stigmatisation was mentioned as a key difficulty. Differences in disease naming illustrate the difference in beliefs and has an impact on health seeking behaviour, which for noma cases, has severe ramifications due to the rapid progression of the disease.

Introduction

Noma, also known as cancrum oris, is a neglected disease of extreme poverty. It presents as a rapidly progressing gangrenous infection of the oral cavity [1], and mostly affects children aged between two and five years[2]. It has been estimated that without treatment, up to 90% of patients with noma die within two weeks from the onset of symptoms [3], and those who survive have severe facial disfigurements[2]. Treatment in the early stages of disease with antibiotics, wound debridement and nutritional support greatly reduces mortality and morbidity [1,3]. Due to the widespread destruction of the facial structures including the cheek, nose, lips and eyes, patients with noma have multiple physical impairments such as difficulty eating, seeing and breathing, and many suffer from stigmatization in their communities[4]. Noma is thought to be most prevalent in low socio-economic regions in Africa and Asia[4]. The WHO estimate that 140,000 new cases of noma occur annually[5], however this figure is debated due to a lack of robust evidence on the epidemiology of the disease.

Since 2014, Médecins Sans Frontières (MSF) has collaborated with the Nigerian Ministry of Health (MOH) to treat patients with noma identified across the northwest of Nigeria, at the Noma Children's Hospital in Sokoto. This programme provides nutritional, psychosocial, and surgical interventions for patients with noma. Identification of patients with noma relies on active case detection within villages through extensive outreach activities and widespread communication campaigns to raise awareness of the existence of the Noma Children's Hospital.

There is still much to learn about noma as most patients live in difficult to reach areas and the disease often goes undiagnosed and is underreported. Given that many cases occur in underserved areas, few studies have aimed to explore and describe societal and community perceptions of this disease. One study in the literature examined the language used to describe noma in Hausa (the predominant language in northwest Nigeria). A term commonly used for noma was ciwon iska, which translates to 'the disease of the wind'[6]. Language used to describe diseases carry culturally determined associative meanings [7] and have been reported to affect people's conceptions of disease and the health care options they choose[8].

Understanding and using appropriate language is one of the cornerstones of ensuring an effective communication strategy with patients, as well as their families and communities. We conducted this qualitative study to gain an understanding of the locally used descriptive language and concepts of noma. Specifically, we aimed to understand the perspectives of family members of patients with noma and treating practitioners. We anticipated that our findings would inform future interventions and prevention programs.

Methods

Ethics

The MSF Ethics Review Board (1710), Usmanu Danfodiyo University Teaching Hospital Health Research and Ethics Committee in Nigeria (UDUTH/HREC/2017/No.595) and the Ministry of Health in both Sokoto (SKHREC/032/017) and Kebbi (MOH/SUB/4027/Vol.I/14) states approved the study protocol. Informed consent for interviews and audio recordings were sought using an information sheet translated into Hausa stating the purpose of the study and the voluntary nature of participation. All interviewees were over the age of 18 and each participant provided written informed consent (for participants who were illiterate, the consent form was read aloud to them and a thumbprint was then requested). All participants were assured that there was limited risk of harm from participation in this study, and that they were free to withdraw at any point.

Setting

The Noma Children's Hospital in Sokoto, northwest Nigeria, has provided treatment for patients with noma for many years, and, since 2014, MSF has supported noma initiatives at the hospital.

Recruitment and sampling

Five focus group discussions (FGDs) with adult caretakers (predominantly the mothers, grandmothers or fathers of the patient with noma) who were looking after the patients at the hospital and twelve in-depth interviews (IDIs) with healthcare staff were held in June and July 2017. Convenience sampling was paired with multivariate sampling to ensure a wide variety of participants for the five FGD's. The research assistant (AA) selected men and women for the groups separately, due to the social norms of this region, respecting any cultural sensitivities. There were three female groups and two male groups as the majority of caretakers were female. FGD's were composed of not more than eight participants at a time. Vignettes were used to encourage participant reflections [9] on relevant life memories, and current experiences related to noma were explored. Purposeful multivariate sampling [10] was used to recruit healthcare staff members for in-depth interviews in order to ensure rich descriptive data from a diverse group. Twelve staff members at the Noma Children's Hospital were selected by which time data saturation occurred[11]. Three male program management staff, one male

and four female medical team members and three male and one female paramedical staff members were selected (laboratory, mental health, pharmacy, nutrition staff).

Research design

A descriptive qualitative research design was used in which data was gathered from caretakers of patients with noma and staff at the hospital using FGDs and IDIs guided by topic-led questions (see S1 and S2 Texts). Both IDIs and FGDs were carried out using themes relevant to the study aims, adhering to the open ended, qualitative interview procedure. The choice of methods was used to gain a rich understanding of the topic, specifically the patient and practitioner perspectives of the disease[12].

Data collection

Interviews were audio-recorded in quiet, private, locations that were familiar to participants. All FGDs were conducted by AA in Hausa; the Principal Investigator (EF) conducted the IDIs in English. AA transcribed all interviews. AA translated transcriptions of recorded FGDs verbatim from Hausa to English. Confidentiality was enabled for all participants by replacing the names of the respondents and all data referring to them with numerical codes indicating the type of sample (IDI for in-depth interview; FGD for focus group). During the FGD, participants agreed to keep confidential what was discussed during the group session. Both FGD and IDI respondents were reassured that data that could potentially identify a person or location was anonymised using pseudonyms that could not be traced back to them. Electronic data were password protected.

Data validation and analysis

Data validation was conducted through continual checking throughout the IDI's and FGD's; AA and EF would repeat their understanding of what participants were saying throughout the interviews to ensure a correct and clear interpretation.

Data analysis started from the moment data were gathered. Data were initially managed through reading and rereading all transcriptions of recorded conversations allowing for familiarisation and initial coding of data. EF and BS (final author) manually analysed the data by highlighting words, phrases or paragraphs, which then emerged into codes that were constantly compared. Participant responses from IDI's were compared with FGD findings, with common patterns and themes identified. As well as points of agreement, divergent themes were established through this process.

Table 1. Names used by caretakers and Noma Children's Hospital staff (medical, paramedical and program management staff) to describe noma.

	Caretakers	Staff
Danhurawa	X	
Tuareg	X	
Akin	X	
Ciwon iska	X	X
Ciwon daji	X	X
Ciwon/ maci dan wawa	X	X
Zaizayar baki		X
Noma		X
Sakiya		X

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Results

We present two themes that emerged during analysis: naming and explanations for noma (Tables 1 and 2) and risks and consequences of noma (Table 3). We illustrate our findings through quotes from participants.

Naming noma

The most commonly used name among the health care workers was noma. One important finding was that:

Table 2. Naming and explanations of noma with illustrative quotes.

Names	
"Danhurawa" that is the name we called it. Danhurawa that is the name we called our own. Everyone that comes to see it will say yes it is the one. They will say that she is suffering from it.	FGD 1, Female
They called "iska" and another name is "maci dan wawa" which eats the gums that is the names I know iska and maci dan wawa. Maci dan wawa eats the teeth and eats the mouth and make a hole just like this one	FGD 2, Male
They called the disease "Disease of Tuareg" and another name is like akin	FGD 2, Male
They were saying it was ciwon daji (cancer)	FGD 3, Female
The word noma itself in the local language it means farming. So often they mixed it up with farming.	IDI 3, Male, Paramedical
The only name they given to the disease either they say ciwon daji locally which is example like is disease from the bush.	IDI 7, Male, Paramedical
Ciwon daji!	IDI 9, Female, Medical
They always call it noma	IDI 11, Female, Medical
Beliefs and explanations	
This disease is caused by insect, even the measles they did is caused by an insect, insect from the bush.	FGD 1, Female
(I) am sure it is one of the traps of iska (Jinn).	FGD 2, Male
Measles is the cause of the disease.	FGD 3, Female
Some will say it is (caused by) a bird. We told you that if someone get the disease they will say that the bird has catch him, it will make your mouth to swell up until they poke it and it will burst out and destroy the mouth by falling off. It is all happening.	FGD 3, Female
It is God that brings the disease; God gave you the disease	FGD 3, Female
It was henna that is the cause. It was henna that my mother applied on me (henna beautifully designed) then she put me on her back then a witch saw me but then nobody knew that she was a witch. She then said this henna that you put on her is so beautiful! That is all she said! Then people said that my mother should quickly cover my legs. The next day an abscess came out that is the first thing that people saw. After a week then I changed and transformed to what I am today.	FGD 3, Female
The patients believe that it is because of evil cast or evil eye.	IDI 1, Male, Program Staff
I think I have heard someone saying it's like witchcraft.	IDI 3, Male, Paramedical
They (patients and caretakers) have a strong belief that whatever happened is from God.	IDI 3, Male, Paramedical
It is just evil spirit that is responsible for it. They don't believe that it is medical problem.	IDI 6, Female, Paramedical
They always believe it is iska that is the belief; iska they believe is just like a wind or let us say Jinns. This Jinn are something that are in between us but we cannot see them, Jinn can appear in trees and in wind in something, or that is they believe that the Jinns are the ones that came in and cause such kind of problem.	IDI 7, Male, Paramedical

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Table 3. Risks and consequences of noma with illustrative quotes.

Access to Health Care	
After some few days we heard the news of this hospital. They said that they can treat this type of case. Then they prayed and wish us well and success. Then we were told to hurry and go there so that we can confirm that they can really treat the disease. When we arrived, there was a test being carried out and we told that it is possible. Then they show us. All praise be to Almighty Allah he is much better now. We are optimistic that it will be successful.	FGD 4, Male
You will be struggling to get the medicines while the sickness will be spreading. You will be running up and down looking for treatment while disease will be expanding.	FGD 4, Male
I can say that noma is not widely known, and this is the only hospital which is exclusively dedicated for the noma children disease. The one of its kind and then more than 300 patients have benefited from the plastic surgeries, re-constructive surgeries.	IDI 1, Male, Program Staff
We go to all the local government areas in Sokoto, Kebbi and Niger State. We do active case findings that mean trying to find new patients. Also, we do health promotion along the way.	IDI 1, Male, Program Staff
Impact of the Disease	
People run away from whatever you use, just because someone's mouth has cut they will say they will not eat with him.	FGD 2, Male
When you get this disease some people will be discriminating you, some will be running away from you. But you will not be very happy in life.	FGD 3, Female
After some time it will form water then they will poke it (using the traditional hot iron) after that then the mouth will burst out and fall off.	FGD 3, Female
We were collecting traditional medicines. We were given it to him. We were using traditional medicines. Woods, powders and so many different types was given to him.	FGD 4, Male
The issue is that it destroys and eats the gums, destroys someone's mouth, that people is destroyed also; there is no destruction that is more than this.	FGD 2, Male
After some days before a week she changes and transform to this.	FGD 3, Female
What scared us more and makes us to quickly rushed here was that it was itching him and he was scratching it then suddenly I saw his fingers going inside. The mouth area where the disease has affected it cut and falls off.	FGD 4, Male
The success story I would like to share is from a patient that had noma for a long time and she was operated in Lagos without success, she was operated in Ibadan without success. Until somebody saw her (a doctor who has worked at the Noma Children's Hospital before). The doctor saw her covering her face and she wrote a letter for her to come down to Sokoto. So she got surgery about two, three surgeries. She is fine and she is even an employee of this hospital. So it is a good story.	IDI 4, Female, Medical
He is always afraid of people because he stays in the bush. So I have to tell him that these people you are seeing they are just like your friends and your colleagues we are here to help you, we will not do anything to harm you. Before he was discharged he has plenty friends in the ward he will go to this bed he will gist (talk) he will go to that bed jumping from one ward to the other.	IDI 9, Female, Medical

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"The word noma itself in the local language means farming. The word noma, the same spelling, the same pronouncement, so often they (patients) refer to it in the context of farming" (IDI 3).

Several names for the disease were given by the FGD participants:

"In our place we called it ciwon daji" (FGD 4).

Naming of the disease differed between caretakers and heath care workers. Table 1 explores these differences, and suggests only a few overlapping terms; ciwon iska, ciwon daji and ciwon/ maci dan wawa.

Beliefs and explanations

Names form a part of the understanding of the disease in this setting; the broad names used for noma such as ciwon daji are described in association with the beliefs and social system used to explain the disease. Caretakers shared several terms for the disease as well as beliefs about why and how the disease is caused. The three causative categories that were identified were spirits, living creatures (insects and animals), and connections with previous illness.

Spirits including Jinn and God were frequently reported:

"(I) am sure it is one of the traps of Jinn" (FGD2).

"They always believe this thing happens (because) God allows it to be" (IDI7).

Jinn was described as the world of other creatures that we cannot see. The world of Jinn is a spiritual realm all around us filled with normal people leading normal lives. There are good Jinn and bad Jinn, and Jinn can enter human bodies and cause harm:

"Jinn are something that are between us but we cannot see them. Jinn can appear in trees and in wind in something, Jinns are the ones that came in and cause such kind of problem (referring to noma)" (IDI 7).

Some respondents linked the disease to evil spirits or people:

"One of the patients believe that it is because of evil cast or evil eye" (IDI 1).

"It is just evil spirit that is responsible for it" IDI6).

Various animals and insects were also mentioned as the potential cause of noma:

"This disease is caused by insect; insect from the bush" (FGD 1).

Previous infections were also noted as a potential cause:

"Measles is the cause of the disease" (FGD 3).

Whilst beliefs are varied, the participant responses demonstrated a broad range of understandings about the disease and as such, it is thought to exist for multiple reasons.

Risks and consequences: Access to health care

Difficulty in accessing care for patients with noma was evident in the findings, and explored and described in the analytical framework in Fig 1. Caretakers in our study stated they had taken patients to other health centers before being advised to go to the Noma Children's Hospital:

"We took him (to) Binji Town, Binji Hospital, they diagnose him and checked him, then they said go to Noma Hospital, that is the only place you can get treatment for this and that is why we came here" (FGD 2).

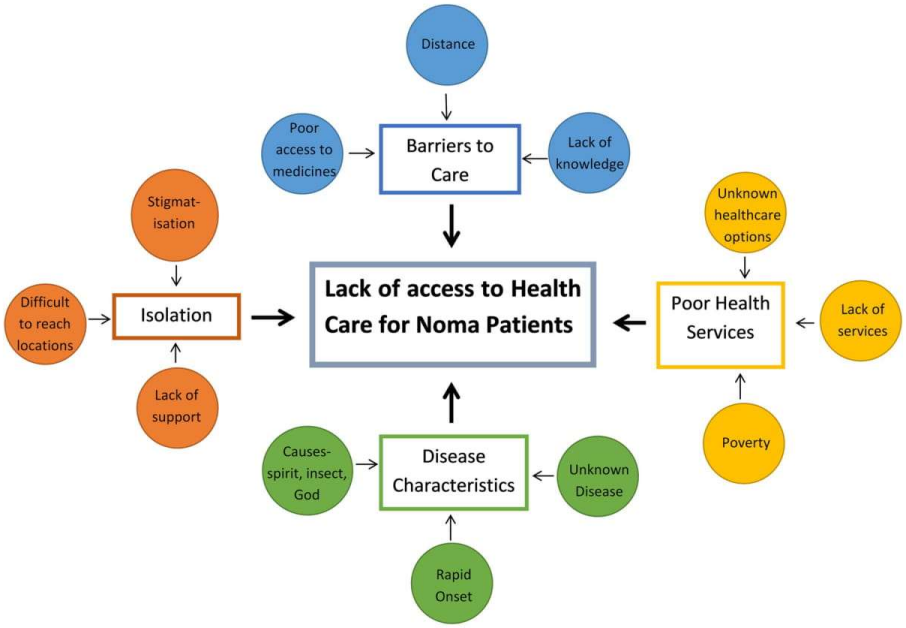

Fig 1. Analytical framework, lack of access to care. Reasons for the difficulties in accessing care for noma patients.

https://doi.org/10.1371/journal.pntd.0007972.g001

Other first points of care were traditional healers, community health centers, and private doctors. Treatment options were varied, some attempted to treat the initial oedema phase of noma:

"After some time it will form water (swelling) then they (traditional healer) will poke it (using the traditional hot iron/ knife) after that the mouth will burst open and fall off" (FGD 3).

Others struggled to find suitable treatment:

"You will be struggling to get the medicines while the sickness will be spreading. You will be running up and down looking for treatment while the disease will be expanding" (FGD 4).

This suggests a combination of actions taking place before reaching a health center or bio-medical health worker. Some participants mentioned barriers to care including a lack of knowledge about the disease and a lack of trust in the health system as well as distance from care:

"People are coming from very far distance; they said that some people are even coming as far as Kaduna (different state) they are coming here" (FGD 1);

Limited access to prescribed medication was also reported:

"You will be struggling to get the medicines while the sickness will be spreading" (FGD 4).

"As we want to come to the hospital, everyone is saying not to go as we will just be wasting our time. Then some people said how can we see this situation of life and death and just give up, we have to try and save a life by seeking treatment?" (FGD 1).

"Back home they will only be trying this and that because they don't know what it is and they don't know anything about it" (FGD 4).

Impact of the disease

The impact of noma is not just limited to the physical presentation; participants in our study spoke of the strain on their mental health that the disease placed on them as caretakers, with stigmatisation highlighted as a key difficulty:

"It cannot allow you to enjoy your life when you are in the company of people. You will not be happy when you are mingling with people. They will not include you in their important discussions. They will not like to sit with you. They will not eat food with you. The only thing is that you will be hiding yourself" FGD 4.

Caretakers spoke of the physical impact of the disease and its rapid progression of the disease along with concomitant infections:

"From the time (the patient had) measles to the time that she started this disease (noma), it was just two weeks" (FGD 1).

The stages of noma were reported as moving rapidly from a swelling of the mouth, to the disintegration of the cheek:

"Her own started with the swelling, then the swelling will go down and again it will swell, after some time then the mouth was destroyed on the lower lip. Then the flesh was coming out and falling off. One day the mouth fell off, it was infected and destroyed, in just a day" (FGD 1).

Health workers spoke of destructive patient interactions and stories were mentioned which indicated the impact stigmatisation and social isolation have on the mental and physical health of patients and caretakers (also highlighted in [13–16]):

"He (patient) is always afraid of people because he stays in the bush. So, I have to tell him that these people (other patients) you are seeing they are just like your friends and your colleagues we are here to help you, we will not do anything to harm you. Before he was discharged he has plenty friends in the ward he will go to this bed he will gist (talk) he will go to that bed jumping from one ward to the other" (IDI 9).

The isolation that caretakers and healthcare professionals reported may influence the ability patients have to access health care and for prevention messaging to reach them. The lack of access to care for patients with noma is explored further in Fig 1.

Discussion

What's in a name?

Our primary emergent theme was the naming of noma in northwest Nigeria. Diseases often have multiple names, and frequently the most common name is only one of multiple reported

for a single disease. Naming of diseases can originate from visible symptoms; work on lymphatic filariasis in Nigeria has reported that local names for the disease include "elephant legs" and "swollen legs", which appropriately describe the visible manifestation of the disease[17]. Other naming options come from expected causes or, quite commonly in biomedicine, diseases are named after the individuals involved in historical descriptions, such as Alzheimer's or Parkinson's[18].

Noma is a Latinised form of a common Greek word, and is a metaphor for the continuing process of a wild fire[6]. This metaphor links conceptually with the rapid progression of the disease, as does the Hausa word ciwon iska, which loosely translates to 'the disease of the wind'[6], this could also refer to the understanding of disease transmission (spirits or animals traveling by the wind). The naming of noma as ciwon daji which loosely translates to cancer in English is also of interest, as this is similar to a biomedical name for the disease which is frequently used, cancrum oris, meaning mouth cancer[6]. Some of the other names for noma used by staff in our study were different to those used by patients. Health care workers in our study most commonly reported using the word noma when discussing the disease; this is expected, as it is the name used most commonly in the biomedical community. Noma, however is not the only name used in this community to describe this disease; other terms include necrotising ulcerative stomatitis and the aforementioned cancrum oris[6]. Our results suggest that the name most commonly used by patients or caretakers to describe noma was ciwon daji. The use of names such as ciwon iska by caretakers shows a naming system more linked to a spiritual conceptualisation of the disease, and limited biomedical understanding of the disease process.

A further novel finding from this work is that the word noma in Hausa means farming. This has the potential to cause confusion during awareness campaigns and should be taken into consideration during the planning phase. The commonly used names for identifying noma should be incorporated into all messaging used in noma prevention and treatment programs. This will help ensure clearer communication between project staff, the community, patients and their caretakers.

Explanations for noma

The way diseases are described and understood can differ between people and groups due to a wide range of perceptions and shared social understanding of the illness, differences in language used[8], understanding of the clinical diagnosis itself[19], and the value judgements placed on these concepts[20]. Producing an explanatory model of disease [21] can provide a significant contribution to effective treatment programs and therefore positive programme outcomes. An explanatory model for noma was formed as the names used for noma were seen to be associated with a social understanding about the disease, which can be shown to impact upon what care is sought or followed by patients.

There is limited literature on the explanatory models around noma in this setting. However, a study on models for health-seeking behaviour for leprosy patients in Adamawa State, central Nigeria has shown that the majority of respondents explained the illness in terms of traditional beliefs and as 'God's wish'[22], as did patients in a further Nigerian study on orofacial clefts [23]. The leprosy and cleft participants in these studies reported seeking help from alternate health sources, for example traditional healers[22,23], as did a study assessing health seeking behaviours for hypertension in Nigeria[24]. Patients were all able to identify what disease they had by name in both the leprosy [22] and hypertension [24] studies, which indicates that these diseases are better understood in the Nigerian context than noma.

Our findings illuminated the notion that noma is linked to the spirit world, this is reiterated in a further study from northern Nigeria[6]. In that work, it was reported that not much was known about noma in those communities, and as such, broad names such as ciwon iska (disease of the wind) were used[6]. During our interviews, the caretakers explained iska as being sent by Jinn, the spirit world. This name links noma to the spirit world and offers insight into the potential explanation for noma in this community. If caretakers believe noma has a spiritual cause, this could explain why many caretakers seek care from traditional healers who typically offer treatment strategies which probe deeply into the psychological, spiritual, and social contexts of illness[25], as well as physical treatment including piercing the cheek with a sharp object and/ or offering herb mixtures to place on the wound or ingest.

Our findings suggest there is no primary explanation within this community for the disease; biomedical beliefs are less dominant, thus suggesting a pluralistic understanding of the disease. The neglected nature of this disease could contribute to and exacerbate this. As so little is known about noma globally, there is limited knowledge to share on prevention. This has an impact on the care that is sought with consequences such as poor linkage to treatment, underreporting and poor outcomes for patients. Our findings suggest that a caretaker's knowledge and explanations for the disease may affect the health seeking treatment decisions (Fig 2). The beliefs people hold about disease have been shown in other studies to impact health seeking behaviours[26–28].

Risk and consequences of noma

Access to health care in this part of Nigeria is difficult, especially in the rainy season, as poor infrastructure makes transportation to health facilities challenging. A lack of access to healthcare has been widely reported as a risk factor for noma development[4,29–35], and our results add weight to these assertions in that caretakers mention the difficulties they experienced accessing care for this disease. The rapid progression of noma, lack of access to care, and the delays caused by caretakers having to progress through several facilities (clinics or traditional healers), means that resulting morbidity and mortality can be severe.

The impact of noma is multifactorial; both caretakers and health workers in our study spoke of the mental health strain the disease placed on both patients and caretakers. The social isolation caused from stigmatisation of diseases is well documented[13–16]. Mental strain caused by social isolation has a wide ranging impact and can negatively affect both the mental and physical health of patients and their families[13–16]. Caretakers described the physical impact of the disease and its rapid progression along with associated links with concomitant diseases. The stages of noma were reported as moving from a swelling of the mouth, to the disintegration of the cheek, which follows clinical descriptions in the literature[31,36].

Names, beliefs, access to health care and the impact of noma are all interlinked, and form a web of issues that compound the ruthlessness of the disease. The strength of this study is that it explored the topic from two perspectives, that of the caretakers of patients, and the staff at the Noma Children's Hospital. There were several limitations including the caretakers being interviewed already being at the hospital. As such, they had likely had education on the disease from hospital staff prior to our interviews, this could have influenced the answers given. This bias could be mitigated by conducting a similar project with community members who do not have a family member affected by the disease. Further research needs to focus on the link with traditional healing, understanding the true burden of the disease and the pathogenic cause. This would enable efficient prevention programs to be formulated.

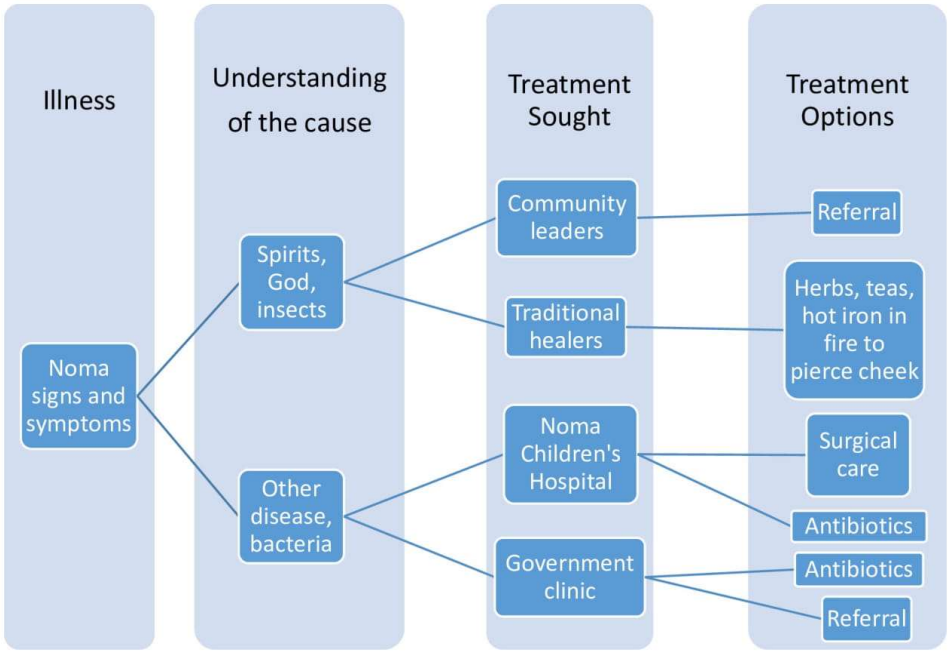

Fig 2. Explanatory model for noma. Knowledge and beliefs about the disease affect health seeking treatment decisions.

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Conclusions

This paper has offered an overview of the naming, explanatory models for and risks and consequences of noma in northwest Nigeria. Caretaker and practitioner perspectives enhance our understanding of the disease in this context and can be used to support case finding, referrals and addressing barriers to care. The impact of the differences noted of the names used between health workers and patients is apparent. Different naming of diseases illustrates the difference in beliefs and has an impact on health seeking behaviour, which for noma cases, has severe ramifications due to the rapid progression of the disease. Other areas where noma is endemic would benefit from similar assessments of patient caretaker and practitioner perspectives to ensure a comprehensive understanding of the contextual issues and explanatory models of the disease. The commonly used names for identifying noma should be incorporated into all messaging used in noma prevention and treatment programs.

Supporting information

S1 Text.
(DOCX)

S2 Text.
(DOCX)

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5.2 Risk factor manuscript

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Risk factors for diagnosed noma in northwest Nigeria: A case-control study, 2017

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Abstract

Background

Noma (cancrum oris), a neglected tropical disease, rapidly disintegrates the hard and soft tissue of the face and leads to severe disfiguration and high mortality. The disease is poorly understood. We aimed to estimate risk factors for diagnosed noma to better guide existing prevention and treatment strategies using a case-control study design.

Methods

Cases were patients admitted between May 2015 and June 2016, who were under 15 years of age at reported onset of the disease. Controls were individuals matched to cases by village, age and sex. Caretakers answered the questionnaires. Risk factors for diagnosed noma were estimated by calculating unadjusted and adjusted odds ratios (ORs) and respective 95% confidence intervals (CI) using conditional logistic regression.

Findings

We included 74 cases and 222 controls (both median age 5 (IQR 3, 15)). Five cases (6.5%) and 36 (16.2%) controls had a vaccination card (p = 0.03). Vaccination coverage for polio and measles was below 7% in both groups. The two main reported water sources were a bore hole in the village (cases n = 27, 35.1%; controls n = 63, 28.4%; p = 0.08), and a well in the compound (cases n = 24, 31.2%; controls n = 102, 45.9%; p = 0.08). The adjusted analysis identified potential risk and protective factors for diagnosed noma which need further exploration. These include the potential risk factor of the child being fed pap every day (OR 9.8; CI 1.5, 62.7); and potential protective factors including the mother being the primary caretaker (OR 0.08; CI 0.01, 0.5); the caretaker being married (OR 0.006; CI 0.0006, 0.5) and colostrum being given to the baby (OR 0.4; CI 0.09, 2.09).

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Competing interests: EF, AL, SvdK, and KB were employed by MSF. All authors have declared that no competing interests exist.

Interpretation

This study suggests that social conditions and infant feeding practices are potentially associated with being a diagnosed noma case in northwest Nigeria; these findings warrant further investigation into these factors.

Author summary

Noma or cancrum oris is an orofacial gangrene that rapidly disintegrates the hard and soft tissue of the face. Little is known about noma as most cases live in underserved, difficult to reach locations. There is a dearth of literature on the risk factors for the development of noma. Médecins Sans Frontières (MSF) in collaboration with the Nigerian Ministry of Health runs projects at the Noma Children's Hospital in Sokoto. A case control study was conducted in northwest Nigeria to explore exposures associated with diagnosed noma using unadjusted and adjusted conditional logistic regression models. Potential risk and protective factors for diagnosed noma were identified and these findings need further exploration. The study identified that feeding pap to the child every day was a potential risk factor for diagnosed noma (possibly a proxy for poor variety in the diet). The following potential protective factors for diagnosed noma were identified: the mother being the primary caretaker, the caretaker being married, and colostrum being given to the baby. Noma is a neglected disease, and current risk factors suggest that intervention efforts could be more effective by focussing on access to health care, the benefits of breastfeeding and a varied diet. However, more research is needed in order to better understand the pathogenesis of this disease in order to improve prevention, early detection and treatment.

Introduction

Noma or cancrum oris, is a poorly understood, rapidly progressing gangrenous infection of the oral cavity, associated with a high mortality rate [1]. It mostly affects children under the age of five years [2]. It is estimated that up to 90% of noma cases die [3], and those who survive have severe facial disfigurements [2]. These can result in multiple physical impairments such as difficulty speaking, swallowing, eating, seeing and breathing which can lead to stigmatization in their communities [4]. Noma is thought to be most prevalent along the noma belt which stretches from Senegal to Ethiopia [4], however noma cases have recently been reported in the United Kingdom [5], United States [6], Afghanistan [7], South Korea [8] and Laos [9]. A northwest Nigerian based study concluded that the incidence of noma is estimated to be 6.4 per 1000 children [10], and the World Health Organization (WHO) estimates that 140 000 children contract noma each year globally [2].

Little is understood about noma as most cases live in underserved, difficult to reach locations, many cases go undiagnosed and the mortality rate is so high. Previous observational studies have suggested that risk factors for development of noma include malnutrition, low birthweight, absence of breastfeeding, poor oral hygiene, co-morbidities, proximity of livestock to area of residence, large family size, access to unsafe drinking water and living in a village with a high prevalence of acute necrotising gingivitis [4,11–13]. Recently, an increased incidence of noma has been reported in higher resource settings in patients with immunosuppressive diseases such as human immunodeficiency virus (HIV) [5,6,8,14,15].

Since 2015, Médecins Sans Frontières (MSF) has collaborated with the Nigerian Ministry of Health (MoH) to treat noma patients identified across the northwest of Nigeria, in Sokoto. The programme provides nutritional, psychosocial (for the patient and their families) and medical care to prepare noma patients for the required surgical interventions at the Noma Children's Hospital. These are conducted by MoH and MSF surgical teams on a routine basis; since August 2015, the programme has treated 227 noma patients. We conducted a case-control study to identify risk factors for diagnosed noma in terms of demographic characteristics, medical history, socio-economic-behavioural aspects and access to health care in order to better guide existing prevention and treatment strategies for this neglected disease.

Methods

Study location

The study was conducted in Sokoto and Kebbi states, which are located in northwest Nigeria.

Study population

Cases were defined as patients with diagnosed noma admitted to the Noma Children's Hospital between May 2015 and June 2016 who were under 15 years of age at self-reported onset of the disease. Controls were individuals matched to cases by village of residence, current age (+/- 2 years) and sex.

Sample size

Our aim was to include all cases enrolled at the Noma Children's Hospital in the year before data collection, and we calculated that with a sample size of 67 cases and 200 controls (three controls per case), we would be able to estimate an odds ratio (OR) of 2.5 for suspected risk factors with a power of 80% and 60% of controls being exposed to that risk factor. Controls were selected from houses neighbouring those in which the cases and their families live.

Data collection

Seventy-eight percent of cases and controls were younger than 18 years of age, their parents or caretakers were asked to participate in the interviews using a structured questionnaire. The questionnaire covered the sociodemographic characteristics of the cases and controls (age, gender, education, employment, total household members), their current living conditions (water source, proximity to livestock, material of houses) and their vaccination history (read on vaccination card if available). Additionally, parents and/or caretakers were asked to respond to questions pertaining to the duration of breastfeeding after the cases and controls were born and other nutrition-related practices during the neonatal period and current practices. The health status, access to health care and healthcare seeking behaviour for the case or control in the previous 12 months were also assessed. Finally, all cases and controls aged less than five years at the time of interview had a mid-upper arm circumference (MUAC) measurement taken at the time of the interview.

The questionnaire was formatted in Kobo Collect (http://www.kobotoolbox.org/) and uploaded to tablets for mobile data collection purposes. Completed questionnaires were uploaded daily to a secure MSF server through an internet connection. The study coordinator verified all completed questionnaires on a daily basis for data consistency and quality.

Data analysis

We calculated the frequencies and respective proportions for all categorical variables and used chi-square tests for comparison of these variables between cases and controls. For continuous variables, we calculated means with standard deviation or medians and interquartile ranges (depending if approximately Normally distributed) for cases and controls separately, and used t-tests to compare Normally distributed variables, and Kruskal Wallis tests for non-Normally distributed variables.

Food variables for current feeding practices were categorised as animal products (meat, milk, egg), grains (fura, mashed rice, millet, corn, bread) and vegetables (sweet potato, beans, bean cake, moringa leaf with ground nut cake, cassava). Respondents could answer with 'Yes', 'No' and 'Don't know'. We grouped all responses for 'No' and 'Don't know' into a single category. To investigate the impact of this grouping, we conducted a sensitivity analysis for each of these variables. As the results showed that the direction of association remained the same, we retained this grouping as the reference category.

We estimated risk factors for being a diagnosed noma patient by comparing odds of exposure in cases and controls using unadjusted and adjusted conditional logistic regression to calculate Odds Ratios (ORs) and their respective 95% confidence intervals (CI) and p-values. The adjusted conditional logistic regression model was constructed using all risk factors that had a p-value of <0.2 in the unadjusted analysis and sufficient outcomes in each category. Variables were eliminated from the adjusted model using a manual backwards stepwise approach [16], and adjusted models were compared using the likelihood ratio test, any variable with a p-value under 0.2 was kept in the model. All data analyses were conducted with Stata 14 (StataCorp, College Station, TX, USA).

Ethics

The MSF Ethical Review Board approved the study protocol (study 1710), as did the Usmanu Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee in Nigeria (UDUTH/HREC/2017/No.595) and the Ministry of Health in both Sokoto (SKHREC/032/017) and Kebbi (MOH/SUB/4027/Vol.1/14) states. All interviewees were over the age of 18 and written informed consent was provided by each participant (for participants who were illiterate, the consent form was read aloud to them and a thumb print was then requested). All participants were assured that there was limited risk of harm from participation in this study, and that they were free to withdraw at any point.

Results

General findings

Out of the 112 noma patients who had sought care in the programme between May 2015 and June 2016, we identified 87 who lived in Kebbi and Sokoto states and were eligible for inclusion in the study. Of these, 10 could not be located, and we managed to interview 77 cases (88.5%). We were unable to reach the village of three identified cases for logistical reasons. Thus, the final analysis included 74 noma cases and 222 controls. Six of the cases had passed away in the time between discharge and the interview; the interviews were still conducted with their caretakers. At the time of first admission to the hospital, 17 of these cases had acute noma, 57 had inactive noma, two had trismus and one had no diagnosis noted at time of admission to the hospital. Twenty one cases were hospitalized at the time of interview and the remaining 56 were interviewed in their home villages.

Table 1. Sociodemographic characteristics of cases and controls (p values from chi squared, t test or kwallis).

		Controls (N = 233)	*Cases (N = 77)*	*P-value*
Child age at time of interview, Median (IQR)		5.0 (3.0, 15.0)	5.0 (3.0, 15.0)	0.91
Caretaker sex (female)		113 (50.9%)	37 (48.1%)	0.67
Caretaker age	18–35	147 (68.7%)	37 (48.7%)	0.002
	35–90	67 (31.3%)	39 (51.3%)	
	Missing	8	1	
Child first born		33 (14.9%)	13 (16.9%)	0.67
Family size, Mean (SD)		11.5 (8.8)	15.8 (13.8)	0.0018
Number of wives, Mean (SD)		2.0 (1.6)	1.6 (0.7)	0.64
Main caretaker	Mother	132 (59.5%)	25 (32.5%)	<0.001
	Other	36 (16.2%)	28 (36.4%)	
	NA	54 (24.3%)	24 (31.2%)	
Caretaker employed	No	76 (43.2%)	33 (51.6%)	0.39
	Yes	92 (54.8%)	31 (48.4%)	
	Missing/ NA	54	13	
Caretaker education	None	66 (29.7%)	28 (43.8%)	0.34
	Educated	102 (46.0%)	36 (56.3%)	
Number of houses in compound, Mean (SD)		3.8 (2.8)	4.5 (3.5)	0.008
Main materials of house walls	Wood, mud, bamboo	175 (78.8%)	41 (53.3%)	<0.001
	Stone, brick, cement	45 (20.3%)	12 (15.6%)	
	Other	2 (0.9%)	24 (31.2%)	

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As expected, there were no significant differences in matching variables (sex and age of child) between cases and controls. The control group differed from the case group in that caretakers were younger, their family sizes were smaller (and houses in the compound fewer) and most of their houses were made of mud (which might be a proxy for higher socio-economic status) (Table 1). Also, the respondents for the control group were more frequently the mother of the child (Table 1). The self reported median age of onset of noma amongst cases was 2.0 (IQR 2.0, 3.0).

Cases between 6 months and 5 years old had lower mean MUAC measurements (mean 134; SD 20) than controls (mean 142; SD 11; p = 0.002. Six percent of cases (n = 5) had a vaccination card available at the time of interview, compared with 16% (n = 36; p = 0.03) of controls. The vaccination status (based on the vaccination card was) for polio (cases n = 3, 3.9%; controls n = 13, 5.9%; p = 0.07) and measles (cases n = 2, 2.6%; controls n = 15, 6.8%; p = 0.1) was very low for both cases and controls. Parents and caretakers reported that most cases (n = 63, 81.8%) and controls (n = 158, 71.2%; p = 0.22) had been breastfed between one to two years after birth. With respect to the main source of drinking water, parents reported that the two main water sources were a bore hole in the village (cases n = 27, 35.1%; controls n = 63, 28.4%; p = 0.08) and a well in the family compound (cases n = 24, 31.2%; controls n = 102, 46.0%; p = 0.08). In terms of animal ownership, the proportion of case and control families reporting owning donkeys, dogs, sheep, goats and chickens were similar. Case families, however, were less likely to have cows in their compound compared with controls (cases n = 36, 46.8%; controls n = 128, 57.7%; p = 0.09).

Risk factor analysis

The unadjusted analysis suggested that the likelihood of being a diagnosed noma case increased when the household was large (>10 people), the child was heavy at birth (self-

reported weight), breastfeeding occurred for >1 year, first solid food was given after the age of 12 months, the child ate pap (type of porridge staple made from maize, sorghum, or millet), and grains each day. Protective factors against acquiring noma included: the mother being the primary caretaker, the caretaker being married, having a well in the compound, colostrum being given to the child, child first given water over the age of 7 months, all children in the household being alive and the child having taken medication (traditional or biomedicine) in the year preceding the interview (Table 2).

Due to collinearity, the following variables were not included in the adjusted analysis: the food group variable "Grains" (fura, mashed rice, millet, corn, bread), material the walls of the house was made out of, wealth score, measles, polio, one or more vaccination being reported on a vaccination card. In the adjusted analysis, eating pap every day remained strongly associated with being a risk factor for diagnosed noma (OR 9.8; CI 1.5, 62.7; p = 0.02) as did a later age of first solid food (>12 months) (OR 5.07; CI 0.9, 26.08; p = 0.07). Variables that were protective against being a case included the mother being the primary caretaker (OR 0.08; CI 0.01, 0.5; p = 0.007), the caretaker being married (OR 0.006; CI 0.0006, 0.5; p = <0.001) and colostrum being given to the baby (OR 0.4; CI 0.09, 2.09; p = 0.07) (Table 2).

Discussion

This study has highlighted potential risk and protective factors associated with being a diagnosed noma case in northwest Nigeria, including caretaker demographics and infant feeding practices. This identification aims to shed light on potential useful areas for further investigation. Similar risk factors have been suggested including the absence of breastfeeding [12], dietary habits [17], unsafe drinking water, limited access to high quality health care, high infant mortality [4], and food security [11]. A 2017 review noted that measles vaccination was a protective factor for noma [11], but we were unable to corroborate this as the estimated vaccination coverage in both cases and controls was too low for a relevant comparison to be conducted. Our adjusted analysis did not identify an association between noma and household size or water source as reported elsewhere [9,12,18], however, the unadjusted analysis suggested a possible association between these exposures and diagnosed noma and therefore warrants further investigation. We were also unable to confirm other reported risk factors for noma including high numbers of previous pregnancies in the mother, [12] pre-existing illness, malnutrition [17], poor oral hygiene practices [1,2,4,9–11,18–23], proximity of livestock to the area of residence and low birthweight [2,4,7,12,18,20,23,24], these require further exploration.

One novel observation of the study was some weak evidence for the possible protective nature of colostrum. There are inherent health benefits associated with colostrum as it is rich in antibodies that confer passive immunity and growth factors which have been shown in recent studies to assist in the treatment of autoimmune disorders and gastrointestinal conditions [25]. Recent case reports have highlighted the global problem of noma and in some cases a relation to concomitant infections including HIV-positive patients in London [5] and in the United States [6], and a Korean child with Crohn's disease [8]. These reports offer insight into the disease and strongly suggest that immunosuppression plays a role in the causal pathway of noma development which supports the finding of the protective nature of colostrum. However, it should be noted that these are clinical case reports and not analytical epidemiological studies. It is also possible that mothers who give their children colostrum are also more likely to follow other health messaging. Both aspects would have a favourable impact on the overall health status of an infant and therefore render the child to be at a lower risk of noma development. Our findings on this point were not definitive but this could be a useful point for future research.

Table 2. Unadjusted and adjusted risk factors for being a noma case from conditional logistic regression, Sokoto and Kebbi States, Nigeria 2017.

		Controls (N = 232)	Cases (N = 77)	Unadjusted			Adjusted		
		n (%)	n (%)	OR	95% CI	P-Value	OR	95% CI	P-Value
Primary Caretaker is mother		152 (69%)	25 (32%)	0.2	0.1, 0.5	<0.001	0.05	0.01, 0.5	0.007
Caretaker married		158 (71%)	14 (18%)	0.08	0.01, 0.09	<0.001	0.006	0.0006, 0.5	<0.001
Child first born		33 (15%)	13 (17%)	1.2	0.6, 2.5	0.6			
Caretaker Educated		102 (46%)	36 (47%)	1	0.6, 1.8	1			
Caretaker Employed		92 (41%)	31 (40%)	0.9	0.5, 1.7	0.9			
Total household members	1–9	113 (51%)	29 (38%)		Reference				
	10 or above	109 (49%)	48 (62%)	1.8	1.006, 3.08	0.05	2.06	0.8, 5.3	0.1
COMPOUND LIFE									
Water Source	Other	120 (54%)	53 (69%)		Reference				
	Well in compound	102 (46%)	24 (31%)	0.5	0.2, 0.9	0.03			
Water treated		73 (33%)	24 (31%)	0.9	0.5, 1.6	0.8			
Electricity	Yes	77 (35%)	25 (32%)	0.5	0.2, 1.4	0.2	0.2	0.04, 1.5	0.1
Livestock in compound	1–3	100 (45%)	40 (52%)		Reference				
	4 or more animal species	123 (55%)	37 (48%)	0.8	0.4, 1.4	0.4			
NUTRITION									
Colostrum	No	19 (9%)	19 (25%)		Reference			Reference	
	Yes	149 (67%)	44 (57%)	0.3	0.2, 0.7	0.002	0.4	0.09, 2.09	0.07
	Don't know	54 (24%)	14 (18%)	0.07	0.005, 0.4		0.001	3.3e-06, 0.5	
Breastfed length	7–12 month, other	64 (29%)	14 (18%)		Reference				
	>1 year and <2 years	158 (71%)	63 (82%)	16.9	2.1, 134.5	0.008			
Age child first given water	0–6	126 (57%)	53 (69%)		Reference				
	7 or above months	26 (12%)	6 (8%)	0.4	0.2, 1.2	0.03			
	Don't know	70 (32%)	18 (23%)	0.2	0.07, 0.8				
Age first given solid food	0–11	113 (51%)	44 (57%)		Reference			Reference	
	12 months or after	38 (17%)	16 (21%)	1.2	0.6, 2.3	0.03	5.07	0.9, 26.08	0.07
	Don't know	72 (33%)	17 (22%)	0.2	0.08, 0.7		0.2	0.01, 2.9	
Pap every day (Y)		124 (56%)	55 (71%)	3.3	1.5, 8.2	0.004	9.8	1.5, 62.7	0.02
Food eaten at least once a day (Y) (ref = no/ don't know)									
Animal products		28 (13%)	10 (13%)	0.9	0.4, 2.1	0.9			
Grains		165 (74%)	62 (81%)	5.9	1.2, 29.7	0.03			
Vegetable		57 (26%)	21 (27%)	1	0.5, 1.9	1			
Drinks		94 (42%)	36 (47%)	1.2	0.7, 2.2	0.6			
Child, family eat same meals (Y)		165 (74%)	61 (79%)	3.4	0.8, 13.6	0.09			
HEALTH									
Births in total	0–5	99 (46%)	30 (39%)		Reference				
	6 or more	69 (31%)	34 (44%)	1.4	0.8, 2.6	0.5			
	Don't know	54 (24%)	13 (17%)	3.80E-08	0, -				
Births Alive	Some Died	64 (29%)	43 (56%)		Reference				
	All still alive	103 (46%)	20 (26%)	0.4	0.2, 0.6	0.003			
	Don't know	55 (25%)	14 (18%)	3.90E-08	0, -				
Birthweight	Light	27 (12%)	9 (12%)		Reference				
	Heavy	78 (35%)	39 (51%)	1.6	0.7, 3.7	0.03			
	Don't know	117 (53%)	29 (38%)	0.7	0.3, 1.7				
Meds in previous year(Y)		127 (57%)	32 (42%)	0.4	0.2, 0.7	0.006	0.3	0.07, 1.6	0.2

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The finding in the unadjusted analysis that having taken medication in the year prior to the study was a protective factor could indicate that having access to health care plays a role in noma development. This could be due to health care proximity or possibly due to improved socio economic status which would allow the families to pay for transport to get to health care and/or healthcare provision. Those who develop noma would possibly have fewer possibilities to seek care for other diseases or the beginning stages of noma, and as such are at higher risk of developing the disease.

The finding that eating pap every day is a risk factor for diagnosed noma development, could be due to the fact that pap is the food usually used for weaning in Nigeria, it has a low nutrient density and has been reported to be at risk of unhygienic handling [26]. Two microbiological analyses of foods commonly used in weaning (including pap) in Nigeria, showed bacterial contamination at higher levels than international guidelines recommend [27,28]. All of these factors mean that during the weaning period, the use of pap can predispose infants to infections and subsequently high mortality rates [26]. Possible solutions to reduce this exposure, would be to strengthen education about hygienic food preparation [27], the benefits of alternate practices such as fermentation which enhances nutritive value of the food [26] or encouraging variety in the diet. Improving feeding during the weaning time is crucial to decrease child malnutrition, mortality rates and to enhance development [28].

The findings showed that in both the case and control groups there was a high proportion of child morbidity and that families where the majority of infants born to the same mother survived, were less likely to have a noma case. This finding might strengthen the role that socio-demographic characteristics of families and households play in the disease dynamics of diagnosed noma. If more children die in households where noma cases are detected, it could indicate that children in these households are also more exposed to unsafe water, poorer standards of living and reduced access to care, as all of these exposures are known to be associated with higher infant mortality [29–34].

The proportion of vaccination coverage in the study population is below the standards recommended by the Nigerian Ministry of Health [35] and WHO [36]. There is evidence that the occurrence of vaccine preventable diseases and malnutrition precede the onset of noma [4,6,9,18–20]. The low coverage of vaccination not only increases the risk of morbidity and mortality from vaccine preventable diseases, but is a contributing factor in immunosuppression which is thought to play a key role in the sequence of events for noma development.

Our study is unique because available evidence around noma manifestation and risk factors for the development of the disease is based on a handful of primary studies [13,12,37], case reports [5,7–9] and reviews [2,4,19]. These studies were methodologically different from ours which could offer reasons for the differing findings. A case control study conducted in Niger came closest to the current study design, although this study had an intake period of 6 years and the controls were not matched on sex [12]. Our results also differ from those of a further Niger-based study [13], which included four villages in the study population and focused on the link between noma and acute necrotising gingivitis. In comparison, our study was conducted over a relatively short time period and was retrospective in nature. Furthermore, our cases and controls were matched on sex in addition to village of residence and age, which might have eliminated some bias that could have been present in the previously mentioned studies. Finally, our study included diagnosed noma cases who were resident across 80 villages in two states of northwest Nigeria, so they represent a much wider geographical area than the previous studies, which might have contributed to the differences in risk factors identified [13].

We attempted to interview all patients cared for at the hospital in the year before data collection, however this was not possible due to several constraints. Even though we managed to

exceed our minimum sample size, we identified strong associations between only a minority of the explored risk factors and diagnosed noma. It is likely that the risks associated with individual exposures for noma are weaker than we assumed in the original sample size calculation.

A further limitation is that our risk factor analysis only represents those cases who sought care at the Noma Children's Hospital in Sokoto. Due to the reported 90% mortality rate [3] and rapid progression of noma, this likely means that the results of the current study are only applicable to the subset of noma cases who experienced the least severe complications from the disease.

Finally, we included all cases who were under the age of 15 at the time of self-reported disease onset. Therefore some cases (and thus controls) were under 15 at the age of onset but were currently >= 18 (13 cases) therefore leading us to interview them personally and not their caretaker. This might have introduced some bias into the study as certain questions around infant feeding practices etc. would only have been possible to be answered by their caretakers, thus leading to missing information on these questions. We tried to mitigate this by conducting sensitivity analyses for these variables which resulted in similar findings.

Conclusions and recommendations

In conclusion, our case control study suggests that infant and current feeding behaviours as well as caretaker demographics may affect the risk of developing noma. Malnutrition and low vaccination coverage, high morbidity of infectious diseases along with low access to health care are all likely contributing factors.

We recommend that further research is implemented to determine the true burden of noma, and that prospective studies are implemented to better understand the sequence of events contributing to the development of noma. Only with these sets of indicators will it be possible to better formulate and target prevention programmes.

Supporting information

S1 Checklist. STROBE Checklist.
(DOCX)

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5.3 Outcomes manuscript

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Outcomes at 18 mo of 37 noma (cancrum oris) cases surgically treated at the Noma Children's Hospital, Sokoto, Nigeria

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Background: Noma is a rapidly progressing infection of the oral cavity frequently resulting in severe facial disfigurement. We present a case series of noma patients surgically treated in northwest Nigeria.

Methods: A retrospective analysis of routinely collected data (demographics, diagnosis and surgical procedures undergone) and in-person follow-up assessments (anthropometry, mouth opening and quality of life measurements) were conducted with patients who had surgery >6 mo prior to data collection.

Results: Of the 37 patients included, 21 (56.8%) were male and 22 (62.9%) were aged >6 y. The median number of months between last surgery and follow-up was 18 (IQR 13, 25) mo. At admission, the most severely affected anatomical area was the outer cheek (n = 9; 36.0% of patients had lost between 26% and 50%). The most frequent surgical procedures were the deltopectoral flap (n = 16; 43.2%) and trismus release (n = 12; 32.4%). For the eight trismus-release patients where mouth opening was documented at admission, all had a mouth opening of 0–20 mm at follow-up. All patients reported that the surgery had improved their quality of life.

Conclusions: Following their last surgical intervention, noma patients do experience some improvements in their quality of life, but debilitating long-term sequelae persist.

Keywords: cancrum oris, noma, outcomes

Introduction

Noma (cancrum oris) is a poorly understood, rapidly progressing infection of the oral cavity with a reported 90% mortality rate within 2 wk from the onset of symptoms if untreated.[1] Noma begins as a mouth ulcer and, within days, progresses to oedema of the cheek followed by necrosis and the rapid destruction of the hard and soft tissues of the face.[2] Treatment with antibiotics, wound debridement and nutritional support in the early reversible stages of the disease greatly reduce mortality and morbidity.[3] Noma is thought to be multifactorial in nature.[3] The aetiology of noma is currently debated; organisms such as *Fusobacterium necrophorum* and *Prevotella intermedia*[4,5] have been identified but not consistently.[3]

If the patient survives the acute stages, the disease can become inactive, after which patients often need complex surgical reconstruction to restore function and improve aesthetics.[2] Reconstruction often entails rebuilding the lips and cheeks and, in some cases, the eyelids and nose.[6,7] However, each noma case is unique and, as such, the surgical procedures used to treat noma differ.[6]

Long-term physical sequelae of noma include displacement of the teeth and intense scarring and bony fusion between the maxilla and mandible.[2,3,6,8–10] Sequelae around daily functioning may include difficulty eating, seeing, talking and breathing.[2,10,11] The social isolation and mental health sequelae of noma patients have not been documented in the literature but should not be underestimated.

Trismus (restriction of mouth opening) is one of the most disabling sequelae of noma[12] and can lead to complications such as aspiration pneumonia, malnutrition, poor oral hygiene, speech deficits, airway compromise and pain.[13] Trismus associated with noma can be caused by scarring around the temporomandibular joint capsule (extra-articular ankylosis) or by destruction and scarring of the temporomandibular joint itself (intra-articular ankylosis).[12,14–17]

Reported surgical techniques to address the spectrum of noma defects include pedicled supraclavicular flaps for the treatment of large unilateral facial defects,[18] abbe, estlander and fan flaps for the reconstruction of the lips and corner of the mouth,[6,19] forehead, deltopectoral, radial forearm and free flaps for the reconstruction of the cheek[6,15] and abbe, radial forearm, free, medial forehead and local turnover flaps for the reconstruction of central defects (upper lip and nose).[6,8,15] Mouth opening is improved by performing bone-bridge excision, sometimes associated with contralateral coronoidectomy.[15]

Outcomes of treatment are difficult to ascertain due to inconsistent patient follow-up often due to the remote locations of the home villages of patients. One of the few studies on long-term outcomes of trismus release on 36 noma patients was based in northwest Nigeria and showed that, after a mean follow-up time of 43 mo, results were poor with only 39% of patients showing an improvement in mouth opening.[12]

The Noma Children's Hospital (NCH), northwest Nigeria, run by the Nigerian Ministry of Health and supported by Médecins Sans Frontières (MSF), offers care to noma patients including reconstructive surgical interventions. We present a description of the follow-up of a series of patients treated surgically at the NCH to inform ongoing clinical treatment.

Our study adds to the existing noma literature and is unique as we have followed up with the patients over a longer period (18 mo) in comparison with other studies, which had follow-up periods of 2–6 wk.[8,20,21]

Materials and methods

We conducted a case series study with patients who had been surgically treated for noma at the NCH more than 6 mo before data collection and who lived in Sokoto or Kebbi states, northwest Nigeria. Data collection took place from April to June 2018.

Data collection

Data collection was performed in two stages. The first stage was based on data collected at admission and for the duration of patients' stay at the NCH (routine data). The second stage of data collection occurred during in-person follow-up visits conducted in the home villages of the patients.

Routine data

The routinely collected data were stored in a bespoke database at the NCH. Information gathered on each of the patients included demographics, diagnosis upon admission (chronic is defined as the absence of ongoing acute infection) and nutritional status.

The NOITULP (nose, outer and inner cheek lining, upper and lower lip) classification system[14] was used by a surgeon with experience in the treatment of noma to grade patients upon admission. This classification system delineates the extent of orofacial damage and related functional compromise, according to fractional loss of anatomical units ranging from no loss to 100% loss. Trismus categories range from normal mouth opening (>40 mm) to no mouth opening.[14]

Surgical data collected included the number and type of surgical procedures and surgical complications (infection, dehiscence, flap necrosis, flap failure). American Society of Anaesthesiologists (ASA) scores were assigned to patients prior to surgery (indicating the fitness of patients before surgery): ASA I, a normal healthy patient; ASA II, a patient with mild systemic disease; ASA III, a patient with severe systemic disease; ASA IV, a patient with severe systemic disease that is a constant threat to life; ASA V, a moribund patient who is not expected to survive without the operation; and ASA VI, a declared brain-dead patient whose organs are being removed for donor purposes. Anaesthesia complications during and after surgery were recorded (difficult airway, hypothermia, equipment failure).

Follow-up data

Data collected included the consenting patients' weight (kg), height (cm), age (y), middle upper arm circumference (MUAC; for children aged 6 mo to 5 y) and maximum mouth opening (mm).

Height was measured using a height board for those aged ≤5 y and a tape measure for those aged >5 y. A manual floor scale was used for weighing all participants. Age estimated to the closest year was self-reported by either the patient (if ≥18 y) or their caregiver. Mouth opening was measured by trained research assistants using a ruler. The maximum mouth-opening measurements were recorded as the mouth wide open minus the mouth closed (incisor-to-incisor where possible or alveolar ridge to alveolar ridge).

We asked questions related to the ability of each patient to eat and drink, their self-reported changes in appearance and how they currently experienced social inclusion in their community. These questions were based on tools used in prior reconstructive surgical studies.[22–26] Quality of life questions were asked to adult respondents directly and to child respondents if they felt comfortable discussing these issues with the interviewer. If children were aged <7 y or felt uncomfortable talking with the interviewers, the children's caregivers were asked the questions. As part of this quality of life assessment, open-ended qualitative questions were asked to participants about how and if the surgery had changed their lives. These responses were analysed thematically.

Data analysis

Data analysis routine data

A descriptive analysis was conducted. Median and interquartile range (IQR) were reported for non-normally distributed continuous values; means and standard deviations (SD) were reported for values with normal distributions.

For children aged 6 mo to 5 y, MUAC measurements were used to classify the nutritional status of children upon admission as having severe (SAM; MUAC<115 mm), moderate (MAM;

MUAC≥115–<125 mm) or global (GAM; MUAC<125 mm) acute malnutrition.[27]

For children aged 6–15 y, body mass index (BMI) was calculated and gender-specific World Health Organisation (WHO) BMI charts were used to categorise children according to BMI for age. Children were classified as either underweight (BMI<5th percentile), normal (6th–84th percentile), overweight (85th–95th percentile) or obese (>95th percentile).[28]

For each individual aged ≥16 y, weight and height were used to classify their BMI range as either underweight <18.5 kg/m^2, normal 18.5–25 kg/m^2, overweight 25–30 kg/m^2 or obese >30 kg/m^2.[29]

Data analysis follow-up

Nutritional status at follow-up was assessed by the same means as at admission: SAM, MAM, GAM and BMI were calculated.

Mouth-opening measurements were used to grade patients according to the NOITULP scale trismus categories at follow-up by the research team in conjunction with a consultant-level surgeon.

All analyses were conducted in Stata 15 (StataCorp LP, College Station, TX, USA).

Results

Demographics

We included 37 (82.2%) of the 45 eligible patients. The other eight patients could not be located either due to inaccessible roads or because the individual had moved from the listed village of residence. All patients were alive at follow-up. Of these 37 patients, 21 (56.8%) were male, 34 (91.9%) were from Sokoto state and 12 (34.3%) were aged >15 y at admission, as were 17 (46.0%) at follow-up (the patients age range was between 4–50 y at follow-up). The majority of patients (n = 35, 94.6%) were diagnosed as having chronic noma upon admission. The main reported reasons for seeking care were cosmetic (n = 25; 67.6%) and the related stigmatisation (n = 24; 64.9%) (Table 1). The median number of months between last surgery and follow-up was 18 (IQR 13, 25) mo.

NOITULP classification at admission

At admission, the most severely affected anatomical area was the outer cheek (n = 9; 36.0% of patients had lost between 26% and 50%) (Table 1).

Surgical procedures

Of the 37 patients included in our study, 12 (32.4%) had one surgery, 15 (40.5%) had two to three surgeries and the other 10 (27.0%) had four or more surgeries. In total, 92 surgeries were conducted, during which 125 procedures were performed. The mean duration of each surgery was 90 (SD 49) min. The most frequently used surgical procedure was a deltopectoral flap (n = 16 patients; 43.2%) followed by trismus release (n = 12 patients; 32.4%) (Table 1). No blood transfusions were required for any patients during their surgeries.

Eight surgical complications were noted in seven patients (18.9%); one patient had a superficial infection and an abscess. Complete dehiscence was reported in two patients (5.4%). One (2.7%) of each of the following complications were reported: flap failure, flap necrosis, flap detachment, neck pain needing physiotherapy and an infection on a corner of the mouth. There were no donor site complications and no deaths.

Anaesthesia information

All patients who had data available on the type of anaesthesia received (n = 35) had undergone general anaesthesia. ASA scores were assigned for the 87 surgeries for these 35 patients: 69 (79.3%) surgeries had an ASA score of I, 17 surgeries (19.5%) had a score of II and one surgery (1.15%) had a score of III. Four (10.8%) patients had anaesthesia complications noted during five surgeries. Three surgeries had unanticipated difficult airways (difficulty with facemask ventilation, difficulty with endotracheal intubation); there was one case of hypothermia and one case of anaesthesia equipment failure.

Nutritional status

Of the 37 patients included in the study, 5 (13.5%) had an improved nutritional status at follow-up and the nutritional status of 4 (10.8%) had deteriorated. The other patients had an unchanged nutritional status.

Of the three patients aged between 6 mo and <5 y at admission, two patients (66.7%) were classified as having SAM and one (33.3%) was classified as having GAM. At follow-up, all three patients (100%) were within the normal range, indicating that these three children had an improved nutritional status at follow-up.

In the 6–15 y age group (n = 17), 12 children (70.6%) were categorised as normal weight at admission, 4 (23.5%) of these children were underweight at follow-up and the others (47.1%) were normal. Two patients (11.8%) were underweight at admission: one (5.9%) was classified as normal and the other was still underweight (5.9%) at follow-up. One patient (5.9%) was overweight at admission and normal at follow-up.

For those aged ≥16 y (n = 17), mean BMI was 19.0 (SD 3.3) upon admission and 18.7 (SD 3.5) at follow-up. The difference between these points is minimal and both measurements fall within the WHO-classified normal range.

Trismus

There were 17 trismus-release procedures conducted on 12 patients (8 patients =1 procedure, 3 patients =2 procedures and 1 patient =3 procedures). At follow-up, the median maximum mouth opening for those aged ≤15 y (n = 7) was 15.3 mm (IQR 7, 18 mm) and 10 mm (IQR 2, 20 mm) for those aged ≥16 y (n = 5).

Although we had mouth-opening measurements at follow-up that could be translated into the NOITULP mouth-opening score for all patients, at admission we only had the allocated NOITULP score and not the actual mouth-opening measurements for

Table 1. Respondent characteristics at admission, surgical procedures performed, self-reported quality of life responses and NOITULP scores upon admission, noma case series, n = 37

		n (37)	%
Gender	Female	16	43.2
	Male	21	56.8
State	Kebbi state	3	8.1
	Sokoto state	34	91.9
Patient age upon admission (y)	0–5	13	37.1
	6–15	10	28.6
	>15	12	34.3
Patient education	None	1	2.8
	Arabic studies	34	94.4
	Primary school	1	2.8
	Missing	1	
Noma diagnosis on admission	Acute noma	2	5.4
	Chronic noma	35	94.6
Had treatment for noma prior to coming to NCH	No	22	59.5
	Yes	15	40.5
Kinds of previous noma treatment	Antibiotics	11	73.3
	Traditional	4	26.7
Self-reported comorbidities reported upon admission at the NCH	Malaria	10	27.0
	HIV	0	0.0
	TB	0	0.0
	Measles	14	37.8
Any vaccination before hospital admission	No	17	46.0
	Yes	20	54.1
Healthcare-seeking reason	Cosmetic	25	67.6
	Stigmatisation	24	64.9
	Functional disability	14	37.8
NOITULP classification upon admission			
Nose	0: no loss	12	50.0
	1: 25% lost	5	20.8
	2: 26–50% lost	5	20.8
	3: 51–75% lost	1	4.2
	4: 76–100% lost	1	4.2
	Missing	13	
Outer cheek lining	0: no loss	5	20.0
	1: 25% lost	5	20.0
	2: 26–50% lost	9	36.0
	3: 51–75% lost	6	24.0
	4: 76–100% lost	0	0.0
	Missing	12	
Inner cheek lining	0: no loss	6	24.0
	1: 25% lost	5	20.0
	2: 26–50% lost	8	32.0
	3: 51–75% lost	6	24.0
	4: 76–100% lost	0	0.0
	Missing	12	
Upper lip	0: no loss	8	36.4
	1: 25% lost	4	18.2
	2: 26–50% lost	5	22.7
	3: 51–75% lost	2	9.1
	4: 76–100% lost	3	13.6
	Missing	15	

Table 1. Continued

		n (37)	%
Lower lip	0: no loss	10	47.6
	1: 25% lost	8	38.1
	2: 26–50% lost	1	4.8
	3: 51–75% lost	1	4.8
	4: 76–100% lost	1	4.8
	Missing	16	
Trismus	Normal mouth opening (>40 mm)	12	54.6
	Mouth opening 21–39 mm	3	13.6
	Mouth opening 0–20 mm	2	9.1
	No mouth opening	5	22.7
	Missing	15	
Surgical procedures performed on study cohort	Deltopectoral flap	16	43.2
	Release of trismus	12	32.4
	Commissuroplasty and lip reconstruction	11	29.7
	Estlander flap	10	27.0
	Forehead flap	6	16.2
	Nasal reconstruction	5	13.5
	Fan flap	5	13.5
	Cheek rotation flap	2	5.4
	Abbe flap	1	2.7
	Submentalisland flap	1	2.7
	Other procedures	12	32.4
Self-reported quality of life assessment at long-term follow-up	At this point in time, go to school	23	62.2
	At this point in time, I have friends	34	91.9
	I am now included in the community	32	86.5
	I can now get married	7	18.9
	I can eat more easily than before the surgery	32	86.5
	I can drink more easily than before the surgery	31	83.8
	People can now understand what I am saying more easily than before the surgery	32	86.5
	I feel more happy with the way I look than before the surgery	32	86.5

eight patients. As such, a comparison of the preoperative and postoperative mouth-opening NOITULP classification for these eight patients is provided in Table 2. No patient had a normal mouth-opening status at the follow-up visit (all classified as T2, 0–20 mm) (Table 2).

Quality of life at follow-up

All respondents reported that the surgery had improved their quality of life in one way or another. Respondents reported that the surgery led to decreased social isolation (having friends, n = 34, 91.1%; being included in communal activities, n = 32, 86.5%) and functional improvements (eating more easily, n = 32, 86.5%; improvements in speaking, n = 32, 86.5%).

At the follow-up visits, patients and caregivers were asked if and how the surgery had changed their lives. Some feedback from patient caregivers was negative and they did not want any further care:

> *The surgery was not successful and I do not want to come back to the hospital* (8-y-old patient).

Other caregivers reported difficulties with restricted mouth opening and related functional issues:

> *The opening of the mouth is very small making it difficult to eat or drink* (29-y-old patient).

There was some mixed feedback, showing improvements in quality of life but continued difficulty with mouth opening:

> *The mouth opening is a bit difficult because the side stitches are tight. However, she can eat and talk well* (28-y-old patient).

And some other patients reported positive functional changes and social acceptance:

Table 2. Mouth-opening categories upon admission and follow-up by age group

Patient	Age at follow-up, y	NOITULP score admission	Maximum mouth opening at follow-up, mm	NOITULP score at follow-up
1	7	T2	13	T2
2	7	T3	7	T2
3	8	T1	18	T2
4	8	T0	15	T2
5	10	T3	5	T2
6	18	T3	20	T2
7	20	T3	2	T2
8	22	T2	10	T2

T0, normal mouth opening: >40 mm; T1, mouth opening: 20–40 mm; T2, mouth opening: 0–20 mm; T3, no mouth opening.

He was shy and angry before the surgery and he is now able to eat and go to school. He used to not be audible but now he talks loud and clear (10-y-old patient).

He is very happy to have the treatment and he can meet different people since the wound is closed and healed (10-y-old patient).

Discussion

Our findings suggest that surgical care for noma patients improved their quality of life, despite minimal evidence that trismus had improved. This corroborates findings from an Ethiopian study, which showed that post-operative follow-up revealed significant improvement in the lives of noma patients[30]. Most of the patients had more than one surgery, and the most commonly used procedure in our cohort was the deltopectoral flap, which is utilised in the reconstruction of the cheek, the most severely affected anatomical area.

Our study confirms the complexity and unique manifestation of noma and the need for numerous surgical procedures to obtain an acceptable functional result. The most commonly performed procedures were the deltopectoral flap, release of trismus, commissuroplasty and lip reconstruction, estlander flap, forehead flap and nasal reconstruction. The procedures performed rely on regional flaps and local tissue and are in line with other reported surgical techniques used to treat noma.[6,8,15,18,19,31,32] Other providers have described the use of free flaps[33,34] however, given the technical and resource demands of microsurgery, these techniques are not currently utilised at the NCH. The surgical programme instead enlists older but reliable reconstructive techniques that are less risky in this context.

Noma cases are at a high risk of developing trismus resulting in difficulties in speech, chewing, and maintaining healthy oral hygiene practices.[12] This study has highlighted that despite surgical intervention, none of the patients in this cohort regained a normal mouth opening. Respondents reported ongoing concerns with their restricted mouth opening and the impact this restriction had upon their lives. Similar studies with noma patients noted that the results of trismus release in noma patients was extremely poor.[12,16] A northwest Nigerian study reported that 43 mo after surgery, the mean mouth opening of 36 patients was 10 mm.[12] A similar study with 95 patients from Niger and Burkina Faso reported that after 3 y, the mean mouth opening was 21 mm.[15] Our results were similar to these studies and showed that all patients had a mouth opening of between 0–20 mm at follow-up (median mouth opening of our cohort: 15 mm for those aged ≤15 y; 10 mm for those aged >16 y).

This outcome is not unique to noma. The overall success rates in curing trismus in inflammatory processes other than noma (oral submucous fibrosis, chronic non-bacterial osteomyelitis) in the paediatric population can be low.[35,36] In the majority of noma patients (as well as in patients with other inflammatory causes of trismus), the trismus is extra-articular.[15] Noma can disrupt the peri-articular bony tissues of the subcondylar area, which is the location of the growth plate of the mandible. Other researchers in mandibular trauma have also reported that this disruption of the growth plate has resulted in increased fibrosis and trismus,[13,36–38] and we can hypothesise that this is also a contributory factor in noma. Similarly, this area of the mandible can be disrupted by surgery to correct trismus (such as gap- or inter-positional arthroplasty).[20,35] This disruption is mitigated by delaying trismus release until the mid-teen years, to avoid, or at least decrease, the need for revision trismus surgery. Delaying trismus-release surgery until skeletal maturity is likely to be effective for noma patients, to reduce the postsurgical reduction in mouth opening. This delay should only occur if a child with noma can drink and consume sufficient calories to continue to grow and gain weight. While there are no specific rules or recommendations for trismus release and ankylosis repair in the literature, in studies and meta-analyses demonstrating high success rates for inflammatory causes, the patients are typically in their teenage years.[35] The success rates for paediatric trismus surgery are far higher in congenital and traumatic cases, where the surrounding capsule and other structures are unaffected.[35] A further step that has been shown to maintain adequate mouth opening and resulting quality of life after trismus-release surgery is longer term postoperative physiotherapy which can enable patients to have

an improved mouth opening.[15,35] We do not have physiotherapy treatment or uptake information for this study; however; the NCH program currently includes rigorous physiotherapy following trismus release while at the hospital, patients are also provided with an exercise list to complete when at home after discharge and they are assessed by the physiotherapist at the follow-up appointments at the hospital.

Our study has illuminated three potential changes for program planning and potential interventions. Firstly, as the anaesthesia complications were notable, it is important that surgical teams should include anaesthesia professionals who have specialised in difficult airway management. Secondly, as some patients remained malnourished, it is important to conduct nutritional follow-up with all patients. Lastly, vaccine preventable diseases and a lack of vaccines are a risk factor for the development of noma[3]. The inadequate vaccination status of the patients included in this study shows that these populations should be the target for public health interventions, which could reduce the number of noma cases along with a host of other diseases.

There were several limitations to this study. Most patients reported improvements in their quality of life; however, these questions were only asked at follow-up. To improve our assessment of quality of life changes, it would be beneficial to use a standardised, validated assessment tool at admission and follow-up.[39] Social desirability bias could have influenced these answers, changing our understanding of patient-reported outcomes. The addition of preoperative and postoperative photographs to this study would have been beneficial. Furthermore, the retrospective review of routinely collected data limited the type and quality of data available for analysis. We have implemented a prospective study to assess the outcomes of patients that will address many of the weaknesses of the current study.

Following their last surgical intervention, noma patients do experience some improvements in their quality of life, but debilitating long-term sequelae persist. Reconstructive surgery does appear to restore form and function in some patients. However, noma is a preventable condition that, if detected early, can be effectively treated with antibiotics before the devastating consequences described in this cohort of patients occur. Therefore, public health interventions should prioritise strategies which address known risk factors for noma through a community-based health systems approach that targets prevention, early detection and the rapid treatment of acute noma.

Authors' contributions: EF, MA, AL and KB were responsible for the study concept and design. LT conducted the retrospective chart review with assistance from EF and MJO. EF and MJO collected the remaining data. EF conducted the statistical analysis. EF, MA, RW, AOT and AL interpreted the findings. EF, MA, RW, AOT and AL drafted the manuscript. All authors critically reviewed the manuscript.

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Ethical approval: The MSF, Usmanu Danfodiyo University Teaching Hospital and Sokoto and Kebbi State Ministries of Health Ethics Review Boards approved the study protocol. All participants were treated in accordance with the ethical principles of the Helsinki Declaration. Adult participants and caregivers of children participants provided written consent for participation in the study, and children aged between 7 and 18 years provided written assent. For illiterate individuals, a thumbprint was requested.

Data availability: MSF has a managed access system for data sharing that respects MSF's legal and ethical obligations to its patients to collect, manage and protect their data responsibility. Ethical risks include, but are not limited to, the nature of MSF operations and target populations, being such that data collected often involve highly sensitive data. The dataset supporting the conclusions of this article is available on request in accordance with MSF's data-sharing policy (available at: http://fieldresearch.msf.org/msf/handle/10144/306501). Requests for access to data should be made to data.sharing@msf.org.

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5.4 Traditional healer study manuscript

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'I treat it but I don't know what this disease is': a qualitative study on noma (cancrum oris) and traditional healing in northwest Nigeria

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Background: Noma, a neglected disease mostly affecting children, with a 90% mortality rate if untreated, is an orofacial gangrene that disintegrates the tissues of the face in <1 wk. Noma can become inactive with early stage antibiotic treatment. Traditional healers, known as mai maganin gargajiya in Hausa, play an important role in the health system and provide care to noma patients.

Methods: We conducted 12 in-depth interviews with caretakers who were looking after noma patients admitted at the Noma Children's Hospital and 15 traditional healers in their home villages in Sokoto state, northwest Nigeria. We explored perceptions of noma, relationship dynamics, healthcare practices and intervention opportunities. Interviews were audiorecorded, transcribed and translated. Manual coding and thematic analysis were utilised.

Results: Traditional healers offered specialised forms of care for specific conditions and referral guidance. They viewed the stages of noma as different conditions with individualised remedies and were willing to refer noma patients. Caretakers trusted traditional healers.

Conclusions: Traditional healers could play a crucial role in the early detection of noma and the health seeking decision-making process of patients. Intervention programmes should include traditional healers through training and referral partnerships. This collaboration could save lives and reduce the severity of noma complications.

Keywords: cancrum oris, noma, operational research, traditional healers, traditional healing

Introduction

Noma (cancrum oris) is a rapidly progressing gangrenous infection of the oral cavity, which mostly affects children aged 2–5 y. If left untreated, it is associated with a reported 90% mortality rate.[1] Those who survive have severe facial disfigurements and multiple physical impairments, including difficulties in eating, seeing and breathing.[2] Noma manifests in stages categorised by the World Health Organisation (WHO) as simple gingivitis, acute necrotising gingivitis (accompanied by fetid breath), oedema, gangrene (hard and soft tissue destruction), scarring and sequelae.[3] The total destruction of the cheek can take place in less than 1 wk.[3] During the early stages of noma, infections can become inactive if treated with antibiotics, wound cleaning and nutritional support, decreasing morbidity and mortality.[1] In

many cases, however, patients live in remote locations and access to healthcare takes considerable time.

Primary research on noma is limited, and as such, knowledge sharing about the disease is impeded. The most commonly reported risk factors are malnutrition, poverty, immunosuppression, coinfections, poor vaccination coverage, lack of access to quality healthcare, not receiving colostrum at birth and caretakers (also known as caregivers) being someone other than the mother.[2–6] No primary studies on noma prevalence exist, but it is thought to be most prevalent along the noma belt, which stretches from Senegal to Ethiopia.[2] Cases have recently been reported in other countries, including Laos,[7] Afghanistan,[8] the UK[9] and the USA.[10] The WHO estimate there are 140 000 new noma cases each year.[1]

The Nigerian Ministry of Health supported by Médecins Sans Frontieres (MSF) implements prevention and treatment programmes for noma at the Noma Children's Hospital (NCH) in Sokoto, northwest Nigeria. The programme includes a strong outreach component focusing on finding early stage cases and raising awareness about noma with community members and health workers.

The health system in Nigeria is comprised of three levels: primary (local government), secondary (state government) and tertiary (federal government).[12] These levels of the health system operate in tandem alongside traditional medicine. *Mai maganin gargajiya* (the Hausa name for traditional healers) play an important role in healthcare globally[13] and in Nigeria, with an estimated 80% of the population exclusively using this form of care.[14] A Nigerian study showed that close to 10% of rural dwellers and 4% of urban dwellers in Nigeria were traditional healers, proportions which are much higher than those trained in biomedicine.[15] Patronage of traditional healing has previously waned due to restrictions and the introduction of biomedicine, but recently there has been an increase in seeking this form of care due to the ability of traditional healers to provide physical, psychological and spiritual care.[16] Traditional healers are said to either reside in the villages within which they serve or to move around from village to village providing care as they go,[17] by utilising remedies including plants and trees,[18–20] piercing and cuts[21] and prayer.[22]

As prevention and early detection are the most important strategies in reducing the impact of noma, it is crucial to take into consideration the role that traditional healers play in the pathway to care for noma patients. We interviewed caretakers of noma patients and traditional healers to explore their perceptions of noma, the relationship dynamics between the two, traditional healers' healthcare practices for the different stages of noma and the feasibility of creating referral partnerships with traditional healers. The information generated through this research will be used to guide noma outreach strategies.

Methods

Setting

Interviews with caretakers of noma patients were conducted at NCH and interviews with traditional healers were conducted in their home villages in Sokoto state, northwest Nigeria. From January to December 2018, 110 noma patients were admitted to NCH, 53 (48.2%) with early stage noma, 50 (45.5%) of whom were female and 58 (52.7%) from Sokoto state. The median age of self-reported onset was 3 y (IQR 1–7 y) and 40 (36.4%) patients had sought care for the noma patient from traditional healers before coming to NCH.

Study design

A descriptive, qualitative study was conducted between April and June 2018. Semistructured interview guides with open-ended questions were used, and the course of the interviews were left open so that any new themes which emerged could be fully explored.

Recruitment and sampling

In-depth interviews were conducted with 12 caretakers (looking after child patients admitted to the NCH at the time of data collection), who were recruited using convenience sampling. The interviews were carried out by HMB, a first language Hausa speaker who was thoroughly trained before data collection commenced and who has experience working with noma patients, accompanied by the Principal Investigator (PI), EF. The researchers interviewed caretakers who were present at NCH during the data collection period. The head matron of NCH invited caretakers to participate in the study. As the caretakers were at NCH for extended periods of times (up to 6 mo), they were known to the head matron. We met with the head matron and requested that she invited caretakers from both rural and urban locations to increase the variety of potential participants. Fifteen traditional healers (people in the community who have taken on the role of providing non-biomedical healthcare and have not received biomedical training) were recruited through purposive sampling. The outreach team at NCH compiled a list of traditional healers working in Sokoto state, where MSF's programme was based (between a 30-min and 3-h drive from NCH). Traditional healers were then contacted from this list by telephone. If they could not be reached by telephone, the research team visited their villages and invited them to participate.

All participants were informed of the aims of the study prior to the interviews taking place. The researchers conducted interviews until data saturation occurred, saturation being the point at which no new information emerged from the interviews.[23]

Data collection

Interview guides were developed in English, translated into Hausa by HMB and then back-translated by a further Hausa speaker to ensure accurate translation. Any inconsistencies were rectified and the final version was used for pilot interviews, after which additional adjustments were made and the guides were then finalised. Interviews were conducted in Hausa and audiorecorded in quiet, private locations. During the interviews, photographs of the five different stages of noma were shown to traditional healers to help interviewees discuss their knowledge and healthcare practices for the various stages of the disease.

Interviews lasted approximately 30–45 min. No one else besides the researchers and participants were present during the interviews.

Data analysis

Audiorecorded interviews were transcribed into Hausa and then translated verbatim into English by HMB and checked by EF. Data saturation was discussed between investigators and once this occurred, data collection ended. Transcripts were manually coded by EF. EV and EF read the translated transcripts several times, and then codes that emerged were highlighted. The codes were then discussed within the research team, first between HMB and EF, and then with three other members of the research team (EV, JGC and BS).[24] Thematic analysis was undertaken to identify patterns in the data with attributed codes.[25]

Ethics

The MSF Ethics Review Board (1824), Usmanu Danfodiyo University Teaching Hospital Health Research and Ethics Committee in Nigeria (UDUTH/HREC/2018/No.670) and the Ministry of Health in Sokoto State (SKHREC/039/018) approved the study protocol. The procedures followed were in accordance with the ethical standards of the Helsinki Declaration. Written informed consent for interviews and audiorecordings were obtained in Hausa. For participants who were illiterate, the consent form was read aloud to them and a thumbprint was then requested in place of a signature.

Results

We interviewed 12 caretakers of noma patients and 15 traditional healers. Caretakers were predominantly the mothers of patients (10/12); one was the grandmother of a patient and the other was the father of a patient. The median age of caretakers was 38 y and ranged from 22 to 55 y. Traditional healers were mostly male (13/15). The two female traditional healers were 35 and 40 y of age, and had worked as traditional healers for 2 and 3 y, respectively. The median age of male traditional healers was 55 y, ranging from 35 to 80 y, and they reported practising traditional medicine for a median number of 30 y, ranging from 2 to 50 y.

Three main themes emerged during data analysis: (1) the role and experiences of traditional healers, particularly in the management of noma cases; (2) relationship dynamics between caretakers and traditional healers; and (3) knowledge and perceptions of noma and treatment healthcare practices for the different stages of the disease.

The role and experiences of traditional healers in Sokoto, northwest Nigeria

Traditional healers reported that they played specific roles in the community, were well known and believed that their healing skills were understood and appreciated in the areas where they lived and worked:

> Everybody in this village small or big…knows that it is my work (*Traditional Healer 8*).

Even though the traditional healers resided in the communities within which they worked, some were well known in a wider geographical region and reported that patients visited them from hundreds of kilometres away, some even travelling across borders:

> Based on my ability, people are coming [from] everywhere [even] all the way [from] Tawa [in Niger]. They are all coming to search for help from me (*TH 15*).

Traditional healers' specialisations

Traditional healers reported learning their craft in different ways, including inheriting the knowledge from family members and others through dreams and spirits:

> I inherited [traditional healing knowledge] from my grandfather (*TH 3*).

> This craft, I got it from a spirit. In my dreams I am told what [treatments] to get and so I go and get them and then I will mix it (*TH 9*).

Many traditional healers stated that they had specialisations and only treated specific diseases. One traditional healer reported treating an array of diseases, whereas others noted one or two. None of the traditional healers specifically mentioned noma, although some of them mentioned treating elements of it (such as *ciwon daji* [cancer] and *iska* [spirit]):

> We have remedies for *gudawa* (*dysentery*), *shawara* (*typhoid*) and for *basur* (*haemorrhoids*) (*TH 1*).

> I sell remedies for *ciwon baya* (*back pain*) and *zufan jiki* (*general swelling of the body*) (*TH 4*).

Treatment practices

These diseases were reportedly treated by the traditional healers with a variety of methods. Most of the remedies offered were obtained from sources surrounding their villages, such as trees and plants. Remedies included giving patients dried herbs, grinded plants 'to soak' and then to drink, ointments to rub onto the skin and piercing of the skin to create '*bleeding marks*'. In conjunction with other aspects of their healing, traditional healers used spiritual beliefs, including reciting the Qur'an to their patients.

Relationship dynamics between caretakers and traditional healers

Caretakers' perceptions about traditional healers

Caretakers of noma patients reported seeking care from a range of health services in the community, including hospitals,

pharmacists (informal care providers who sell medication) and traditional healers:

> I prefer going to the hospital because they care most about a person's health (Caretaker 7).

> I like going to the pharmacist because you can go very quickly and buy the medication (C 4).

Caretakers had differing perceptions of traditional healing: some said they made use of traditional healers' healthcare services because they were effective or accessible and some because they were affordable:

> If we go, we get better (C 9).

> Some people prefer visiting traditional healers if they are ill as they will quickly get treatment [in comparison] to [the time it would take at the] hospital (C 10).

> I went there [to a traditional healer]. I find it much better, very much better, as there is less cost (C 6).

Other interviewees said that they had heard positive things about the services offered but had not personally visited a traditional healer before. One caretaker said:

> My neighbours used to go and they are happy about it and told me to try it but I did not try it (C 1).

Trust and confidence

Caretakers who had visited traditional healers for general health issues noted a positive relationship with them and described the type of care offered as efficient:

> When we went he immediately said what it was, he then gathered the remedies and gave them to me. He said 'Do as I say, do it like that'. By His grace when we did it like that [the treatment] worked (C 9).

The same positive relationship was noted by traditional healers:

> A lot of people are buying and drinking [our remedies] and feel good about it (TH 1).

Trust in the relationship between caretaker and traditional healer was mentioned by both parties:

> I am trusted by people. Honestly, a lot of babies that are weaned that could not stop crying or choked while taking the breast are brought to me and are [treated] successfully (TH 1).

> Ah, honestly we trust them because the healer is like our father (C5).

This trust was paired with accountability as partial payments were made upon care provision and the remaining payments were only made after the care provided was seen to be successful:

> [We] make a payment agreement that [the caretaker] will not [pay all] now. If I treat and he gets healed after [you can pay me]. If you did not heal, I do not want your money (TH 8).

Knowledge and perceptions of noma and healthcare practices for the disease

Knowledge about noma

Many caretakers and traditional healers referred to noma as *ciwon daji* or *daude*, which, when translated from Hausa to English, refers to a general cancer that can occur anywhere in the body:

> We conclude that it was *ciwon daji* (C 2).

Some caretakers believed that noma was the 'disease of *iska*' (spirit) and that it was 'brought by God'. Views differed about the causes of noma, with some caretakers believing that measles 'started' noma in their child. There were also traditional healers who believed that noma was caused by mumps:

> This work is that of mumps. Mumps make the teeth have inflammation. This [is] the same as [the] remedy for mumps. If it affects a person it will destroy their mouth and the mouth will smell (TH 12).

Some traditional healers reported never having seen or treated the disease, even when shown photographs of it during interviews:

> I never saw it honestly…I have not done a matter like this (TH 2).

> I do not know anything about this disease (TH 3).

Noma stages and healthcare options

Caretakers reported seeking care at a variety of biomedical institutions, including pharmacies, community health centres, clinics and hospitals, as well as from traditional healers, before coming to NCH. The pathway to care was at times complex and time-consuming:

> So it was the starting point of the disease, we saw that her face was getting chubby and then we went to collect traditional treatment. We were mixing it and giving it to her to drink. We saw the cheek getting bigger so we took her to the hospital where they dressed the wound and closed the affected area. After 2 d he opened it and the area was spoiled and so we took her to [the big town] *(C 4)*.

> Before we came here we went to one hospital where he was given three injections. They referred us to the general hospital, and they referred us to a medical centre where we spent 11 d. Someone who works at the other hospital came and saw the disease and asked the medical centre to refer us to Sokoto *(C 5)*.

Some caretakers mentioned delays in accessing care; the main reasons were not having money to pay for transport and problems with finding childcare for their other children.

A variety of symptoms for the different stages of noma were described by caretakers and traditional healers. Many of the caretakers who were interviewed reported the first signs and symptoms of noma as a '*fever*', '*skin rash like a single grain of millet*' and swelling:

> At first her eyes swelled. The following morning everywhere had swollen up; you cannot even see the eye *(C 8)*.

When traditional healers were asked about their knowledge of the different stages of noma, the majority saw them as separate diseases and treated them as such. Healers most often reported treating the earlier stages of noma (gingivitis and oedema) and referring children with the later stages of the disease to other forms of care. One traditional healer noted that '*[he] does not know noma disease*', but for the swelling stage of the disease he said '*there is remedy for it*', and for the necrosis stage he stated he '*does not know*' the remedy, showing that noma was not seen as a single disease, but as multiple conditions.

Two commonly reported stages treated were gingivitis and swelling of the cheek. Gingivitis was usually treated with an ointment that was rubbed directly onto the gums:

> If the teeth are bleeding, I give a remedy. If a person puts it inside the mouth and [swills] it around the mouth, the [bleeding] will stop *(TH 8)*.

Some traditional healers diagnosed the stage of noma associated with swelling of the cheek as *ciwon daji* or *ciwon iska* and offered care to the patients accordingly. Caretakers also reported being given this diagnosis and relevant remedies:

> [We are] taught it is *ciwon daji*. They find a branch of a tree and soak it to drink and to rub. That is what we were taught to do if the cheeks become big *(C 7)*.

> I will mix [the bark from three trees locally known as] tsada, tamarind and kaiwa and grind them and sieve them to drink in the morning and in the evening. [I use] the madarar tunwahiya (ground herbs), mix them all together and pour them onto the swollen area *(TH 9)*.

Some traditional healers noted uncertainty about the stages of the disease and whether the stages were related, but had treated the swollen cheek stage, which had a known remedy:

> I treat it but I do not know what the disease is unless I understand it is swelling. If it is swelling I can understand it and give treatment remedy *(TH 3)*.

Traditional treatment options for a swollen cheek included piercing the cheek with a hot blade (initially placed in a fire) to decrease the swelling:

> If the remedy is drunk, it will go down or it will swell up to do piercing or it will burst *(TH 8)*.

Caretakers also reported visiting traditional healers for assistance with piercing the swollen cheek:

> I visited…this piercer, the piercing was done, the following morning the [swelling] did not stop we came here [NCH] *(C 10)*.

Traditional healers did not commonly report seeing patients in the necrosis stage of the disease, and as such, this stage was not widely known, although some were able to recognise it. One traditional healer described this stage as '*burnt meat*'.

Caretakers reported being offered various remedies from traditional healers when visiting them with a child later diagnosed at NCH as having noma. The remedies offered included '*ground herbs or tree branches…for drinking, rubbing and bathing*' and '*to be mixed with pap* (a type of porridge staple made from maize, sorghum or millet) *to drink*'.

Caretakers reported mixed efficacy of these remedies:

> Last year when he was sick I took him [to the traditional healer] so this year when it came back I thought it is the same with the last one and I took him there, then I collected that remedy and it did not work so I took him to hospital *(C 6)*.

> I collected [the remedy] but I did not see any improvement *(C 7)*.

Knowledge transfer and referrals

Traditional healers reported utilising referral to hospitals and doctors for unknown ailments, or conditions they felt would be best treated elsewhere.

> For the [diseases I] cannot [treat], I will send them to a doctor who can treat them *(TH 5)*.

> [I]f I see that [the disease] is much and beyond me and I cannot do the work I will refer him to the hospital. If it is too much [for me] I can only send a person to hospital *(TH 9)*.

Referring to all stages of noma treatment, one traditional healer stated that, '*For that disease, it is a doctor that gives help*'. Other traditional healers reported not knowing where to refer noma patients.

One caretaker reported being referred to NCH by a traditional healer, who stated, '*This disease is beyond my power but some kids are taken to Sokoto (NCH)*'.

And some traditional healers reported that now that they knew about NCH, they would begin to refer any noma cases:

> As from today that we started the relationship, your issue [noma] is not a playing one as from today if I hear a person having it if I know your place I will take him (*TH 13*).

When asked whether they would be interested in attending a training course on noma, which would involve learning about the different stages of the disease, some traditional healers noted they were too old to travel, but most said they would be willing to attend and were enthusiastic about learning more about noma.

Discussion

Traditional healers play a role in the health system of northwest Nigeria; our findings showed that they are trustworthy, accessible, affordable care providers who offer specialised forms of care for specific conditions and offer guidance on referral options. Traditional healers viewed the stages of noma as different conditions with individualised remedies rather than as one disease, which is similar to the biomedical approach in that each stage of noma has a specific treatment protocol.[1] Traditional healers reported referring people to other providers when they were unable to treat a specific condition, and the majority stated that they would be willing to refer noma patients to NCH and attend a training course on the disease.

There is no other literature looking at how traditional healers diagnose and treat noma, making comparisons with other findings challenging, with only one study suggesting that qualitative research methodologies are useful in understanding craniofacial conditions such as noma.[25] The naming of noma as *aiwan dajî*, which loosely translates to cancer in English, is also of interest, as this is similar to a biomedical name for the disease that is frequently used, cancrum oris, meaning mouth cancer.[26]

A third of caretakers at NCH visited traditional healers before coming to NCH. Our study corroborates other research findings which show that traditional healers are the first point of care for many people, especially those living in rural areas with little access to biomedical health facilities,[7,9] and that the first line of treatment for 60% of children living in Nigeria who have a high fever from malaria would be traditional medicine.[26] The pluralistic nature of the Nigerian health system, where biomedical and traditional care are offered together in a dynamic system, is not unique to this setting and has been seen in other contexts, including Ghana,[29] Nepal[18] and South Africa.[30]

Our study showed that caretakers trusted traditional healing methods and that care was sought from traditional healers due to the belief in its quality, as also seen in a study from Cameroon.[31] Treatments offered by the traditional healers in our study, such as ointments and piercings/bleeding marks, were similar to those offered by healers in other studies,[21,31] as were the diversity of the diseases treated.[19,20,32–34]

Due to the rapid evolution of noma,[2] it is imperative that patients are detected early and receive the appropriate treatment (antibiotics, wound cleaning and nutritional support) during the reversible stages of the disease. Some traditional healers reported recognising and treating the earlier stages of noma, and this, along with the fact that caretakers reported seeking care at traditional healers first, reinforces the importance of ensuring that traditional healers are able to detect cases of noma early and refer them to the appropriate healthcare facilities. Not many traditional healers reported treating the later stages of the disease, possibly indicating that caretakers seek care elsewhere for these stages, or that, due to the rapid progression of the disease, the patients die before seeking care.

Partnering with traditional healers in order to set up robust referral networks for diseases has been implemented in a variety of settings.[27,35,36] A South African study noted that referrals by traditional healers were affected by the attitudes, perceived subjective norms and perceived behavioural controls as influences on behaviour, which would need to be studied at a more in-depth level in our setting.[37]

The willingness of traditional healers to be a part of referral networks and take part in a training course, caretakers' positive views of traditional healing and their geographical proximity to patients provides a unique opportunity to build such partnerships. This could increase the frequency with which noma patients are detected at a community level and the speed with which they are referred, thus leading to efficient access to treatment in the crucial early, reversible stages of the disease. Future studies on the effectiveness and efficiency of referrals are needed as well as research assessing biomedical healthcare worker knowledge on noma as this could greatly impact the effectiveness of referral partnerships.

Study limitations include interviewing the caretakers of patients already accessing biomedical care, which raises a potential social desirability bias as there could have been a reluctance to offer a wide range of opinions about traditional healers,[38] and not locating traditional healers who had provided care for patients in the later stages of noma.

Conclusion

Our research has identified several different actors involved along the pathway to care of noma patients, including traditional healers, who need to be included in intervention activities. These findings show that traditional healers would be willing to attend training on the disease and be a part of referral partnerships for noma patients. This collaboration could expedite care provision from the community level, which would ultimately save lives and reduce the severity of the complications associated with noma.

Authors' contributions: FF contributed a substantial amount to conceptualisation of the project, including protocol development, and also to data collection, data analysis and writing up of the results in conjunction with the coauthors. HMB contributed a substantial amount to data collection, data transcription and translation, and also to data analysis and writing up of the results. AI and EV provided supervision for all aspects of the project. AL, JGC and EV contributed to conceptualisation of the project, protocol development, formulation of the analysis plan, interpretation of data, writing up of the results and manuscript content. UM, AcU, KB, BO, AF and BS contributed to conceptualisation of the project, as well as reviewing the writing up of the results and offering advice on manuscript content. NA and JS contributed to data collection during the project, as well as reviewing the writing up of the results and offering advice on manuscript content. All authors provided final approval of the version to be published and agree to be accountable for all aspects of the work.

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Availability of data and materials: MSF has a managed access system for data sharing that respects MSF's legal and ethical obligations to its patients to collect, manage and protect their data responsibly. Ethical risks include, but are not limited to, the nature of MSF operations and target populations being such that data collected often involves highly sensitive data. The dataset supporting the conclusions of this article is available on request in accordance with MSF's data sharing policy (available at: http://fieldresearch.msf.org/msf/handle/10144/306501). Requests for access to data should be made to data.sharing@msf.org.

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5.5 Prevalence manuscript

Original research

BMJ Global Health

The prevalence of noma in northwest Nigeria

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ABSTRACT

Background Noma, a rapidly progressing infection of the oral cavity, mainly affects children. The true burden is unknown. This study reports estimated noma prevalence in children in northwest Nigeria.

Methods Oral screening was performed on all ≤15 year olds, with caretaker consent, in selected households during this cross-sectional survey. Noma stages were classified using WHO criteria and caretakers answered survey questions. The prevalence of noma was estimated stratified by age group (0–5 and 6–15 years). Factors associated with noma were estimated using logistic regression.

Results A total of 177 clusters, 3499 households and 7122 children were included. In this sample, 4239 (59.8%) were 0–5 years and 3692 (52.1%) were female. Simple gingivitis was identified in 3.1% (n=181; 95% CI 2.6 to 3.8), acute necrotising gingivitis in 0.1% (n=10; CI 0.1 to 0.3) and oedema in 0.05% (n=3; CI 0.02 to 0.2). No cases of late-stage noma were detected. Multivariable analysis in the group aged 0–5 years showed having a well as the drinking water source (adjusted odds ratio (aOR) 2.1; CI 1.2 to 3.6) and being aged 3–5 years (aOR 3.9; CI 2.1 to 7.8) was associated with being a noma case. In 6–15 year olds, being male (aOR 1.5; CI 1.0 to 2.2) was associated with being a noma case and preparing pap once or more per week (aOR 0.4; CI 0.2 to 0.8) was associated with not having noma. We estimated that 129120 (CI 105294 to 152 947) individuals <15 years of age would have any stage of noma at the time of the survey within the two states. Most of these cases (93%; n=120 082) would be children with simple gingivitis.

Conclusions Our study identified a high prevalence of children at risk of developing advanced noma. This disease is important but neglected and therefore merits inclusion in the WHO neglected tropical diseases list.

Key questions

What is already known?

- Our understanding of the current disease burden and epidemiology is limited; the WHO estimates 770 000 people are currently living with noma globally.
- Three Nigerian studies estimated the burden of disease ranging from 7 cases per 1000 children aged between 1 and 16 years (2003) to 6.4 per 1000 children (2003) to 1.6 per 100 000 population at risk (2010–2018).

What are the new findings?

- The prevalence of any stage of noma was identified in 3.3% of sampled children.
- Having a well as a drinking water source, being aged between 3 and 5 years and preparing pap less than once a week were associated with higher noma prevalence.

What do the new findings imply?

- Noma is a disease with considerable burden in northwest Nigeria.
- Resource allocation to improve health systems to prevent, detect and treat noma is required and this could be enhanced if noma were added to WHO's list of neglected tropical diseases.

INTRODUCTION

Noma, also known as cancrum oris, is a poorly understood, rapidly progressing infection of the oral cavity, with a reported 90% mortality rate.[1] If untreated, death usually occurs within 2 weeks after the onset of acute necrotising ulcerative gingivitis (stage 1 noma).[1 2] Treatment with antibiotics, wound debridement and nutritional support in the early reversible stages of the disease greatly reduce mortality and morbidity.[2] Noma mostly affects children aged 2–5 years, and those who survive have severe facial disfigurements and multiple functional impairments including difficulties eating, seeing and breathing, contributing towards stigmatisation.[2] Noma starts as an inflammation of the gums leading to the rapid destruction of the hard and soft tissues of the face usually within 1 week.[3] The WHO has classified noma into stages[1]: stage 0, simple gingivitis; stage 1, acute necrotising ulcerative

gingivitis; stage 2, oedema; stage 3, gangrene; stage 4, scarring; stage 5, sequelae. It is unknown what proportion of simple gingivitis cases progress to the later stages of noma, but it is thought to be a small fraction.[1] In the majority of cases, infection causes the destruction of the cheek, while destruction of the jaw, lip, nose and eye have also been reported.[4] Noma can become inactive with, and sometimes without, treatment. Once this occurs, patients can survive into adulthood but often require extensive reconstructive surgery and physiotherapy to correct the resulting defects and improve function.[1] The aetiology of noma is unknown but thought to be multifactorial.[2] Noma typifies the complex interactions between extreme poverty, malnutrition, poor oral hygiene, poor access to routine childhood vaccinations, limited access to quality healthcare and immunosuppression resulting from comorbidities such as HIV.[2]

In the 1800s, noma was widely reported in Europe[5] but is currently thought to be most prevalent in low-resource settings in Africa and Asia.[6] Based on expert opinion, the WHO estimates that 770000 people are currently living with noma globally; however, it is unclear what stages of noma are included in this estimate.[7] The oldest estimate of the burden of this disease that we could locate was from Edinburgh, UK, which indicated that noma was diagnosed once out of every 5000 cases of children with an illness between 1860 and 1871.[8] Two recent Nigerian studies estimated the burden of disease ranged from 7 cases per 1000 children aged between 1 and 16 years (2003)[9] to 6.4 per 1000 children (2003).[10] A study from 2019 estimated the period prevalence of noma from 2010 to 2018 was 1.6 per 100 000 population at risk in Nigeria.[11] These estimates are based on expert opinion, number of hospital admissions and retrospectively collected data, and it is unclear which stages of noma were included.[12] Our understanding of the current disease burden and epidemiology thus remain limited. There are few studies not only on the burden of disease but also on the pathogenesis and mortality rate. Although these aspects highlight the neglected nature of the disease, noma is not currently on the WHO neglected tropical diseases list.

Noma cases are frequently reported in Nigeria.[9 13–15] The Nigerian Centre for Disease Control recorded 37 646 noma cases from 2011 to 2017.[16] However, these records may underestimate the true burden of cases, given limited surveillance data and the potential for under-reporting (low rates of diagnosis, patients not accessing healthcare, reported high and rapid mortality).[16] The majority of noma cases are reported from the northwest and northeast of the country.[17] At the 2018 National Noma Day Workshop, the Nigerian Ministry of Health confirmed that noma was a national public health priority, and highlighted the urgent need to generate robust evidence on the country's disease burden for programmatic planning.[18] This study contributes towards this need by estimating the prevalence of noma in northwest Nigeria.

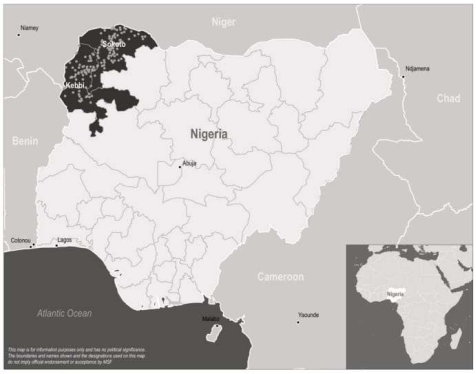

Figure 1 Map of Africa (inset) and Nigeria (main panel). Main panel, grey lines represent state boundaries. Sokoto and Kebbi states, locations for this study, are shaded dark. Pale grey dots within Sokoto and Kebbi states indicate the clusters where data collection occurred during the survey.

METHODS

Study design and setting

A two-stage cluster-based cross-sectional survey was conducted in Sokoto and Kebbi States in northwest Nigeria (figure 1).

Sampling

Sokoto and Kebbi States have estimated populations of 4 798 979 and 4 203 978, respectively.[19] Sample size calculations indicated the need for inclusion of 3615 households across 181 clusters with 20 households per cluster in order to estimate noma prevalence with precision of 0.4%. This calculation was based on the following assumptions: prior prevalence estimate, 1%[10]; design effect, 2; 1.98 children per household in the group aged 0 to 4years[20]; average household size, 6[21]; and a 10% non-response rate.

The number of villages (clusters) per ward was selected proportional to the population size of each administrative ward. A sampling frame of villages was created by ward in Sokoto and Kebbi using geosampling remote sensing methods. The OpenStreetMap database was compared against freely available satellite imagery to identify and verify village geolocations and add new village geolocations to the list. Villages were each assigned a number and a random selection was conducted.

Study participants

All children aged ≤15 years who lived in a selected household in sampled clusters were included in the study.

Data collection

Five research teams, each with five team members, of whom one was a nurse or doctor, and one the team leader, carried out data collection. Teams were trained for 1 week prior to the commencement of data collection. Teams followed directions to selected clusters

using a mobile mapping application (OsmAnd) on data collection tablets (electronic mobile devices). Random household selection at cluster level was done using the adapted WHO Expanded Programme on Immunisation method.[22]

In selected households, consenting caretakers answered a structured questionnaire, collected on tablets using KoBoCollect (KoboToolBox), which covered sociodemographic characteristics, living conditions, child's vaccination status, oral hygiene practices, food preparation, feeding practices and access to healthcare in the 12 months preceding the interview. For the questions around feeding practices, pap was defined in this context as a type of porridge staple made from maize, sorghum or millet. Interviews were conducted in Hausa, and answers were coded automatically on the KoBoCollect tool into English.

In the sampled households, all eligible children underwent oral screening, which involved visual examination by a medical team member for any noma stage, based on the WHO classification.[1] The caretakers of children with simple gingivitis were advised to follow a strict oral health regimen (gargle with salt water or use water to clean mouth twice or more a day) as were acute necrotising gingivitis cases who were also referred to the closest health centre. If children were identified as having any later stage of noma, they were referred directly to the Noma Children's Hospital for care.

To assess the malnutrition status in children aged 6 months to 5 years, mid-upper arm circumference (MUAC) measurements were conducted using a flexible MUAC device with a precision of 1 mm.

Medical data (oral screening and MUAC) were collected on paper and later entered into a password-protected database by the study team.

Collected data were screened daily by the research team supervisors to identify inconsistencies and missing items, and immediate feedback was given to the data collection teams.

Statistical analysis

We performed descriptive analyses of household characteristics in the study sample. Categorical variables are reported as frequencies and percentages. Continuous variables are summarised using medians and IQR. Missing data numbers are recorded in each table.

Wealth scores were calculated by assigning a value of one to each of the following items owned by the family: a mobile phone, motorbike, tractor and camel (these items were chosen based on consultation with local researchers, knowledgeable about the context). The minimum wealth score was zero and the maximum was four.

Weighted prevalence and 95% CI for all WHO noma stages were estimated and stratified by age group (0–5 years and 6–15 years). The number of individuals with noma in Sokoto and Kebbi States was calculated by extrapolating the percentage prevalence from our study results to the total population in the group aged 0–15 years for these states. This calculation took into consideration the cluster survey design and population age distribution of the two states. Using MUAC measurements, we estimated the weighted prevalence of severe acute malnutrition (SAM, MUAC <115 mm), moderate acute malnutrition (MAM, between MUAC ≥115 and <125 mm) and global acute malnutrition (GAM, MUAC <125 mm) in children aged 6 months to 5 years. The SEs of the estimates were adjusted using the linearisation method (svyset suite of Stata commands) to reflect the two-stage clustered design of the survey.[23] The estimates and SEs were weighted to account for the actual population distribution of the two states, as our survey sample was observed to have under-represented participants aged 6–15 years, when we compared our sample's age distribution with the population age distribution. The design effect (DEFF) was calculated to assess the ratio of variance under the sampling method used, in comparison to the variance of a simple random sample. This reflects the impact of the cluster sampling strategy. DEFF is reported for each prevalence and malnutrition estimate.

Univariable analysis with logistic regression was conducted to identify factors associated with noma stages 1 and 2 in the total study sample, where the number of noma cases were too small to allow for multivariable analysis.

Univariable and multivariable analyses were conducted using logistic regression to estimate factors associated with any noma stage (stage 0–2); stratified by age group (0–5 and 6–15 years). Variables chosen for inclusion in the multivariable analysis were those with 10 or more cases[24] and a univariable strength of association equivalent to a $p<0.2$, after assessing collinearity among variables. To further understand the association with age, an age covariate with finer age categories (0–2 years, and 3–5 years, in the younger age group model; and 6–10 years, and 11–15 years, in the older age group model, respectively) were included in the univariable analyses for both age group models, and in the 0–5 year old multivariable model.

All data analysis was conducted with Stata V.15 (StataCorp LP, College Station, Texas, USA).

Patient and public involvement

Patients and the public were involved in the framing of the study questionnaire and data collection. Dissemination of results to patients and the public will take place through outreach activities from the NCH.

Ethical considerations

Written informed consent was obtained from all literate caretakers; caretakers with insufficient literacy provided a thumbprint and a signature from a literate witness. For individuals aged 8–17 years, the child provided assent and a caretaker provided written consent.

RESULTS

The survey was conducted from 17 September to 5 November 2018, and included 3499 households in 177

clusters, 92 clusters from Sokoto and 85 from Kebbi (four clusters were not accessible because of security issues), with 7164 children aged <15 years. As 42 children did not have oral examinations, they were excluded from the analysis and the remaining 7122 were included. The median caretaker age was 30 years (IQR 25–35); 3423 caretakers (97.8%) were female; 2194 (30.8%) were employed or self-employed, and the median household size was five people (IQR 4–7). Most children (n=4239; 59.5%) were aged 0–5 years, 3692 (52.1%) were female, 5875 (83.0%) had no education, and 6686 (94.4%) had a primary caretaker that was the mother (table 1).

Prevalence

Table 2 reports the prevalence of all stages of noma in the study population overall and by age group. Any stage of noma was identified in 3.3% of sampled children (n=194; CI 2.7 to 4.0). Stage 0 noma was identified in 3.1% (n=181; CI 2.6 to 3.8), stage 1 in 0.1% (n=10; CI 0.1 to 0.3) and stage 2 in 0.05% (n=3; CI 0.02 to 0.2). No children with stages 3–5 noma were detected in our study population (table 2). Based on these results, 3300 out of every 100 000 children in the group aged 0–15 years would have any stage of noma and 150 out of every 100 000 children would have stage 1 or 2 noma in the study area.

The prevalence of SAM in children aged 6 months to 5 years (n=3993) was 3.7% (n=149; CI 3.2 to 4.4) and MAM 7.7% (n=309; CI 6.7 to 8.7) (table 2).

Factors associated with noma

Table 3 describes univariable analysis of risk factors for stage 1 and 2 noma regardless of age category. This analysis showed that having eaten pap in the last 24 hours (OR 0.2; CI 0.1 to 0.9); the child eating pap once or more per week (OR 0.4; CI 0.1 to 0.9) and the caretaker preparing pap once or more per week compared with less frequent preparation of pap (OR 0.3; CI 0.1 to 0.8) were associated with not having stage 1 and 2 noma. The child experiencing an illness in the 12 months prior to the interview was associated with being a stage 1 or 2 noma case (OR 8.8; CI 1.1 to 69.5) (table 3).

The risk factors associated with any stage of noma for the group aged 0–5 years are shown in table 4. The multivariable analysis shows that two factors remained associated with being a noma case in the group aged 0–5 years, namely, having a well as the source of drinking water (adjusted odds ratio (aOR) 2.09; CI 1.22 to 3.60) and being aged 3–5 years (aOR 3.90; CI 2.04 to 7.47) (table 4).

In the group aged 6–15 years, the risk factors associated with any stage of noma are shown in table 5. Multivariable analysis showed that males were more likely to be noma cases (aOR 1.52; CI 1.04 to 2.22), and that the caretaker preparing pap once or more per week was associated with not having noma (aOR 0.36; CI 0.16 to 0.82) in the group aged 6–15 years (table 5).

Vaccination coverage rates in both age groups were low (21% of 0–5 year olds and 12% of 6–15 year olds had any immunisations noted on the vaccination card seen by the interviewer). No association between vaccination status and noma was seen in our study.

DISCUSSION

We have shown that the prevalence of any stage of noma in Kebbi and Sokoto States is 3.3%. Based on the study results, we therefore estimate that 129 120 (CI 105 294 to 152 947) individuals <15 years of age would have any stage of noma at the time of the survey within the two states. Most of these cases (n=120 082, 94% of all cases) would be children with simple gingivitis (ie, stage 0) and approximately 7101 (4% of all cases) and 1937 (2% of all cases) of children would have stage 1 and 2 noma, respectively. Our estimates exceeded those from Bello *et al* 2010–2018 period prevalence estimates (1.6 per 100 000)[11] and Fieger *et al*. in 2003 (6.4 per 1000 children).[10] Differences between the estimates could be due to geographical differences (Bello *et al* is north central Nigeria vs our northwest Nigeria), or due to methodological differences (Bello *et al* used patient record review of patients presenting at hospital and Fieger *et al* based their estimates on the number of clefts and mathematical modelling vs our community-based cross-sectional survey). It was unclear which stages of noma were included in these estimates.

Despite only covering two states of one country, our prevalence estimates would account for 17% of the current global WHO prevalence estimates.[7] Even though direct comparisons between the WHO and current study estimates are difficult as the stages included in the WHO estimates were not reported, our findings do suggest that the true burden of noma worldwide may be higher than previously thought.

Results from this study highlight the under-reported and overlooked nature of noma. Even though oral diseases, such as noma, are largely preventable, they impact over 3.5 billion people worldwide (untreated dental caries are the most prevalent of these oral health issues), disproportionally affecting marginalised groups.[25] Oral diseases are frequently more neglected than other diseases in low-income and middle-income countries, which may be linked to the fact that modern dentistry focuses on high-technology solutions, which are unaffordable and not currently feasible in low-resource settings.[26] This overarching neglect of oral diseases is magnified in the case of noma, as patients live in underserved, often rural locations.[27] Many cases will never seek care, and, even if they do, noma is unknown to many healthcare workers in endemic areas.[28] The condition may thus go undiagnosed, and rapid detection with opportunities for early treatment through improved oral hygiene, nutritional support and antibiotics, may be missed.

Strong surveillance systems have been the cornerstone of many successful neglected tropical disease control

Table 1 Demographic characteristics of households and children in the noma prevalence survey population

Households			**n=3499 (%)**
Caretaker age, years median (IQR)			30 (25–35)
Caretaker sex			
Female			3423 (97.8%)
Male			76 (2.2%)
Caretaker income source			
Employed or self-employed			2194 (30.8%)
Unemployed or other*			4927 (69.2%)
Total household members median (IQR)			5 (4–7)
Drinking water source			
Bore hole in the village			644 (18.4%)
River			91 (2.6%)
Tap (running water)			578 (16.2%)
Well in the compound			1512 (43.2%)
Other			674 (19.3%)
Treat water before drinking (yes)			1026 (29.3%)
Type of sanitation facility			
Flushing toilet			224 (6.4%)
Pit latrine (with slab)			650 (18.6%)
Pit latrine (no slab)			1168 (33.4%)
Other†			1457 (41.6%)
Children	**Total n=7122 (%)‡**	**0–5 year olds n n=4239 (%)**	**6–15 year olds n n=2841 (%)**
Age groups (years)			
0–5	4239 (59.8%)		
6–15	2841 (40.1%)		
Missing	42		
State			
Kebbi	3291 (46.5%)	2045 (48.2%)	1246 (43.9%)
Sokoto	3789 (53.5%)	2194 (51.8%)	1595 (56.1%)
Missing	42	0	0
Child sex			
Female	3692 (52.1%)	2119 (49.9%)	1573 (55.4%)
Male	3388 (47.9%)	2120 (50.0%)	1268 (44.6%)
Missing	42	0	0
Education of child			
None	5875 (83.0%)	3850 (90.8%)	2025 (71.3%)
Any education	1204 (17.0%)	388 (9.2%)	816 (28.7%)
Missing	42	1	0
Primary caretaker of the child interviewed			
Mother	6686 (94.4%)	4061 (95.8%)	2625 (92.4%)
Other (father, grandmother, grandfather)	394 (5.6%)	178 (4.2%)	216 (7.6%)
Missing	42	0	0

*Other caretaker income source includes being a housewife or student.
†Other sanitation facility includes neighbours house, the bush, river.
‡n=42 missing age category.

programmes.[29 30] The WHO has stated that robust surveillance helps to better understand the burden and distribution of disease, and to identify high-risk populations so that evidence-based decision-making can be used to target interventions in resource-constrained contexts.[31] A further benefit of robust surveillance is an increase in

Table 2 Noma stage and malnutrition prevalence (overall and by age group)

	Total (n=7122)*			0–5 year olds n=4239 *			6–15 year olds n=2841 *			
	n (%)	CI	DEFF	n (%)	CI	DEFF	n (%)	CI	DEFF	P value (age comparison)
Any noma	194 (3.3%)	2.7 to 4.0	1.9	63 (1.5%)	1.1 to 2.0	1.3	129 (4.4%)	3.6 to 5.4	1.6	<0.001
Noma stages										
None	6928 (96.6%)	95.9 to 97.2	1.9	4176 (98.5%)	98.0 to 98.9	1.3	2712 (95.6%)	94.6 to 96.4	1.6	<0.001
Stage 0: Simple gingivitis	181 (3.1%)	2.6 to 3.8	1.8	56 (1.3%)	1.0 to 1.8	1.3	123 (4.2%)	3.4 to 5.2	1.5	
Stage 1: Acute necrotising gingivitis	10 (0.1%)	0.1 to 0.3	1.2	6 (0.1%)	0.07 to 0.3	1	4 (0.1%)	0.04 to 0.4	1.5	
Stage 2: Oedema	3 (0.05%)	0.02 to 0.2	1	1 (0.02%)	0.0 to 0.2	1	2 (0.1%)	0.02 to 0.3	1	
Stage 3: Gangrene	0 (0%)	NA	NA	0 (0%)	NA	NA	0 (0%)	NA	NA	
Stage 4: Scarring	0 (0%)	NA	NA	0 (0%)	NA	NA	0 (0%)	NA	NA	
Stage 5: Sequela	0 (0%)	NA	NA	0 (0%)	NA	NA	0 (0%)	NA	NA	
Malnutrition				6 month–5 year olds (n=3993)						
Moderate acute malnutrition	NA	NA	NA	309 (7.7%)	6.7% to 8.7%	1.5				
Severe acute malnutrition	NA	NA	NA	149 (3.7%)	3.2% to 4.4%	1				

P value comparing age groups.
*44 missing age category
DEFF, design effect.

Table 3 Univariable analysis for stage 1 and 2 noma

	Study population		Univariable analysis		
	Proportion of all respondents; n=7122; %(n/N*)	Proportion respondents with stage 1 and 2 noma; n=13; % (n/N*)	OR	CI	P value
Primary caretaker					
Other	5.6% (394/7080)	7.7% (1/13)		Ref	0.561
Mother	94.4% (6686/7080)	92.3% (12/13)	0.5	0.07 to 4.18	
Pap eaten in the 24 hours before interview					
No	32.1% (2271/7080)	53.8% (7/13)		Ref	0.030
Yes	67.9% (4809/7080)	46.2% (6/13)	0.2	0.07 to 0.87	
Frequency of the child eating pap per week					
<1 or never	30.4% (2151/7080)	46.2% (6/13)		Ref	0.049
one or more	69.6% (4929/7080)	53.8% (7/13)	0.4	0.13 to 0.99	
Frequency of the caretaker preparing pap per week					
<1 or never	29.9% (2116/7080)	53.8% (7/13)		Ref	0.018
one or more	70.1% (4964/7080)	46.2% (6/13)	0.3	0.11 to 0.81	
Duration of breastfeeding at time of interview (months)					
12+	89.4% (6310/7061)	84.6% (11/13)		Ref	0.782
0–12	10.6% (751/7061)	15.4% (2/13)	1.2	0.27 to 5.63	
Colostrum given to the child at birth					
No	12.0% (843/7047)	15.4% (2/13)		Ref	0.366
Yes	88.0% (6204/7047)	84.6% (11/13)	0.5	0.10 to 2.32	
Child sick during last 12 months					
No	30.0% (2,131/7,080)	7.7% (1/13)		Ref	0.041
Yes	70.0% (4949/7080)	92.3% (12/13)	8.8	1.11 to 69.49	
Did you seek healthcare for this child in the last year?					
No	48.4% (3428/7080)	23.1% (3/13)		Ref	0.221
Yes	51.6% (3652/7080)	76.9% (10/13)	2.5	0.58 to 10.51	
Vegetables eaten in the 24 hours before interview					
No	68.2% (4829/7080)	76.9% (10/13)		Ref	0.461
Yes	31.8% (2251/7080)	23.1% (3/13)	0.6	0.13 to 2.50	
Wealth score (mobile phone, motorbike, tractor, camel)					
0–1	63.5% (4522/7122)	84.6% (11/13)		Ref	0.106
2–4	36.5% (2600/7122)	15.4% (2/13)	0.3	0.08 to 1.27	

Analysis adjusted for the survey design.
P value from logistic regression model.
*n=total number of respondents who answered the question (excluding missing).

the number of cases identified, diagnosed and treated.[32] Due to the neglected nature of noma, surveillance activities for active noma cases are hampered and it is unlikely that current surveillance mechanisms adequately identify deaths from noma at a community level. The mortality rate associated with noma is unknown, but estimated to be as high as 90% if the disease is left untreated.[1] Deaths may be primarily due to starvation, aspiration pneumonia, respiratory insufficiency or sepsis,[33 34] and not be attributed to noma, further reducing the potential for accurate reporting of disease burden. Our findings suggest that improved efforts to enumerate the burden of disease are necessary.

This study highlights the need for a single classification system for the differential diagnosis of each stage of noma, which would be beneficial in standardising reporting of noma globally by the clinical and research noma community. In published work, noma is often classified into two stages (acute and chronic noma[35 36]) or with the Montandon system (classifies noma according to the location of the defect).[37] The lack of standardisation complicates comparison between different studies. The

Table 4 Univariable and multivariable analyses of associations with any noma cases (stage 0 to 5), 0–5 years

	Study population		Univariable analysis			Multivariable analysis		
	Proportion of all respondents; n=4239; %(n/N*)	Proportion respondents with any noma stage; n=63; % (n/N*)	OR	CI	P value	aOR	CI	P value
Child demographics								
Child age (years)								
0–2	46.2% (1957/4239)	17.5% (11/63)		Ref	<0.001		Ref	<0.001
3–5	53.8% (2282/4239)	82.5% (52/63)	4.1	2.20 to 7.62		3.9	2.04 to 7.47	
Birth order								
1–2	39.9% (1691/4239)	30.2% (19/63)		Ref	0.174		Ref	0.398
3 or more	60.1% (2548/4239)	69.8% (44/63)	1.5	0.83 to 2.88		1.36	0.67 to 2.79	
Feeding practices								
Duration of breastfeeding								
12+ months	84.4% (3565/4226)	95.2% (60/63)		Ref	0.02			
0–12 months	15.6% (661/4226)	4.8% (3/63)	0.3	0.09 to 0.81				
Colostrum given to baby								
No	11.9% (502/4221)	11.1% (7/63)		Ref	0.899			
Yes	88.1% (3719/4221)	88.9% (56/63)	1.1	0.37 to 3.09				
Frequency of the child eating pap per week								
<1 or never	31.6% (1340/4239)	34.9% (22/63)		Ref	0.597			
1 or more	68.4% (2899/4239)	65.1% (41/63)	0.9	0.47 to 1.54				
Frequency of the caretaker preparing pap per week								
<1 or never	30.8% (1307/4239)	34.9% (22/63)		Ref	0.505			
1 or more	69.2% (2932/4239)	65.1% (41/63)	0.8	0.46 to 1.46				
Animal products eaten in the 24 hours before interview								
No	91.5% (3879/4239)	95.2% (60/63)		Ref	0.274			
Yes	8.5% (360/4239)	4.8% (3/63)	0.5	0.16 to 1.67				
Grains eaten in the 24 hours before interview								
No	19.3% (819/4239)	22.2% (14/63)		Ref	0.607			
Yes	80.7% (3420/4239)	77.8% (49/63)	0.8	0.45 to 1.59				
Vegetables eaten in the 24 hours before interview								
No	69.6% (2952/4239)	69.8% (44/63)		Ref	0.963			
Yes	30.4% (1287/4239)	30.2% (19/63)	1	0.56 to 1.73				
Health								
Are the teeth ever cleaned (self-reported)								
No	13.8% (508/3679)	9.7% (6/62)		Ref	0.3			
Yes	86.2% (3171/3679)	90.3% (56/62)	1.5	0.69 to 3.39				
Teeth cleaning frequency per day (self-reported)								
Once or twice	85.1% (3132/3679)	88.7% (55/62)		Ref	0.37			
Less than once	14.9% (547/3679)	11.3% (7/62)	0.7	0.34 to 1.50				
SAM, MAM								
Normal	88.5% (3535/3993)	91.1% (51/56)		Ref	0.199			
SAM	3.7% (149/3993)	7.1% (4/56)	1	0.55 to 6.85				
MAM	7.7% (309/3993)	1.8% (1/56)	0.2	0.03 to 1.71				
GAM								
Normal	88.5% (3535/3993)	91.1% (51/56)		Ref	0.666			
GAM	11.5% (458/3993)	8.9% (5/56)	0.8	0.26 to 2.36				

Continued

Table 4 Continued

	Study population		Univariable analysis			Multivariable analysis		
	Proportion of all respondents; n=4239; %(n/N*)	Proportion respondents with any noma stage; n=63; % (n/N*)	OR	CI	P value	aOR	CI	P value
Was the child vaccinated (self-report)								
No	27.5% (1165/4239)	23.8% (15/63)		Ref	0.516			
Yes	72.5% (3074/4239)	76.2% (48/63)	1.2	0.67 to 2.20				
Vaccinations listed on vaccination card								
Diphtheria								
No	71.1% (635/893)	75.0% (12/16)		Ref	0.688			
Yes	28.9% (258/893)	25.0% (4/16)	0.8	0.21 to 2.81				
Pertussis								
No	73.7% (658/893)	75.0% (12/16)		Ref	0.84			
Yes	26.3% (235/893)	25.0% (4/16)	0.9	0.24 to 3.21				
Tetanus								
No	82.1% (733/893)	75.0% (12/16)		Ref	0.584			
Yes	17.9% (160/893)	25.0% (4/16)	1.4	0.40 to 5.11				
Hepatitis A								
No	93.4% (834/893)	93.8% (15/16)		Ref	0.9			
Yes	6.6% (59/893)	6.3% (1/16)	0.9	0.11 to 6.86				
Hepatitis B								
No	77.4% (691/893)	68.8% (11/16)		Ref	0.415			
Yes	22.6% (202/893)	31.3% (5/16)	1.6	0.52 to 4.84				
Measles								
No	38.0% (339/893)	31.3% (5/16)		Ref	0.628			
Yes	62.0% (554/893)	68.8% (11/16)	1.3	0.43 to 4.11				
Pneumococcal disease								
No	69.4% (620/893)	75.0% (12/16)		Ref	0.686			
Yes	30.6% (273/893)	25.0% (4/16)	0.8	0.19 to 2.96				
Yellow fever								
No	64.7% (578/893)	68.8% (11/16)		Ref	0.745			
Yes	35.3% (315/893)	31.3% (5/16)	0.8	0.24 to 2.75				
Meningitis								
No	87.6% (782/893)	75.0% (12/16)		Ref	0.15			
Yes	12.4% (111/893)	25.0% (4/16)	2.3	0.74 to 7.26				
Polio								
No	21.8% (195/893)	12.5% (2/16)		Ref	0.351			
Yes	78.2% (698/893)	87.5% (14/16)	2	0.48 to 8.12				
Any vaccination listed on vaccination card								
No	79.2% (3356/4239)	74.6% (47/63)		Ref	0.415			
Yes	20.8% (883/4239)	25.4% (16/63)	1.3	0.70 to 2.40				
Child sick during last 12 months								
No	29.7% (1260/4239)	23.8% (15/63)		Ref	0.235			
Yes	70.3% (2979/4239)	76.2% (48/63)	1.4	0.82 to 2.28				
How often child was sick, last 12 months								
0–1	50.9% (2156/4239)	50.8% (32/63)		Ref	0.994			
2 or more	49.1% (2083/4239)	49.2% (31/63)	1	0.60 to 1.68				

Continued

Table 4 Continued

	Study population		Univariable analysis			Multivariable analysis		
	Proportion of all respondents; n=4239; %(n/N*)	Proportion respondents with any noma stage; n=63; % (n/N*)	OR	CI	P value	aOR	CI	P value
Did you seek healthcare for this child in the last year?								
No	47.3% (2006/4239)	50.8% (32/63)		Ref	0.634			
Yes	52.7% (2233/4239)	49.2% (31/63)	0.9	0.50 to 1.53				
Difficulties accessing healthcare (cost, time, distance)								
Didn't seek care	47.3% (2006/4239)	50.8% (32/63)		Ref	0.765			
No difficulties	46.0% (1949/4239)	44.4% (28/63)	0.9	0.51 to 1.60				
Yes, there were difficulties	6.7% (284/4239)	4.8% (3/63)	0.7	0.20 to 2.08				
Caretaker and household information								
Caretaker age (years)								
Under 30	49.8% (2109/4239)	34.9% (22/63)		Ref	0.01		Ref	0.251
30 or older	50.2% (2130/4239)	65.1% (41/63)	1.8	1.16 to 2.94		1.38	0.80 to 2.39	
Primary caretaker of the child interviewed								
Other	4.2% (178/4239)	7.9% (5/63)		Ref	0.166			
Mother	95.8% (4061/4239)	92.1% (58/63)	0.5	0.18 to 1.34				
Total number of household members								
0–6	71.7% (3039/4239)	74.6% (47/63)		Ref	0.591			
Above 6	28.3% (1200/4239)	25.4% (16/63)	0.9	0.48 to 1.51				
Drinking water source								
Other (borehole, river, tap)	54.9% (2326/4239)	36.5% (23/63)		Ref	0.007		Ref	0.008
Well	45.1% (1913/4239)	63.5% (40/63)	2.1	1.24 to 3.66		2.09	1.22 to 3.60	
Water treatment								
No	71.2% (3020/4239)	73.0% (46/63)		Ref	0.759			
Yes (strain through cloth, let stand and settle, boil)	28.8% (1219/4239)	27.0% (17/63)	0.9	0.54 to 1.57				
Wealth score (mobile phone, motorbike, tractor, camel)								
0–1	63.5% (2693/4239)	65.1% (41/63)		Ref	0.81			
2–4	36.5% (1546/4239)	34.9% (22/63)	0.9	0.55 to 1.60				

Analysis adjusted for the survey design.
Variables with 10 or more cases and a p<0.2 in the univariable analysis included in the multivariable model (child age, birth order, caretaker age, drinking water source).
P value from logistic regression model.
aOR, adjusted odds ratio.

WHO noma staging system[1] is the most comprehensive to date and includes an early-stage noma definition which is useful as it identifies those at risk of progressing to later stage noma. However, it lacks specificity as it overlaps with commonly seen ailments such as simple gingivitis and acute necrotising gingivitis and therefore may overestimate the burden of disease. It is currently unknown what the risk factors are for progression of noma, nor the proportion of patients who progress to the later stages of disease. Explicit reference to which WHO stages of noma are included in prevalence and incidence estimates as well as improved detail of the method employed in these estimations would greatly improve our ability to compare findings across studies. The lack of consistency of approach to assessing the incidence and prevalence of noma in the literature and the lack of real investment in assessing the true incidence and prevalence of this condition particularly in regions that bear the highest global burden contribute to the ongoing neglect of this disease and the populations it affects.

Study findings indicate that children aged between 3 and 5 years had a higher prevalence of noma in comparison to those aged 2 years or less, a finding corroborated by other studies.[38–41] We hypothesise that this finding is likely due to the relationship between child feeding practices in Nigeria and malnutrition as a risk factor for noma. Our study did not identify an association between acute malnutrition and having noma. However, other

Table 5 Univariable and multivariable analyses of associations with any noma cases (stage 0 to 5), 6–15 years

	Study population		Univariable analysis			Multivariable analysis		
	Proportion of all respondents; n=2841; %(n/N*)	Proportion respondents with any noma stage; n=129; % (n/N*)	OR	CI	P value	aOR	CI	P value
Demographics								
Child age (years)								
6–10	74.9% (2127/2841)	76.0% (98/129)		Ref	0.722			
11–15	25.1% (714/2841)	24.0% (31/129)	0.93	0.64 to 1.36				
Child gender								
Female	55.4% (1573/2841)	45.7% (59/129)		Ref	0.036		Ref	0.031
Male	44.6% (1268/2841)	54.3% (70/129)	1.5	1.03 to 2.20		1.52	1.04 to 2.22	
Birth order								
1–2	50.2% (1426/2841)	55.8% (72/129)		Ref	0.186		Ref	0.613
3 or more	49.8% (1415/2841)	44.2% (57/129)	0.79	0.56 to 1.12		0.9	0.61 to 1.34	
Feeding practices								
Colostrum given to baby								
No	12.1% (341/2826)	11.7% (15/128)		Ref	0.856			
Yes	87.9% (2485/2826)	88.3% (113/128)	1.06	0.57 to 1.98				
Frequency of the child eating pap per week								
<1 or never	28.5% (811/2841)	36.4% (47/129)		Ref	0.042		Ref	0.136
1 or more	71.5% (2030/2841)	63.6% (82/129)	0.68	0.47 to 0.98		1.87	0.83 to 4.21	
Frequency of the caretaker preparing pap per week								
<1 or never	28.5% (809/2841)	38.8% (50/129)		Ref	0.011		Ref	0.015
1 or more	71.5% (2032/2841)	61.2% (79/129)	0.61	0.42 to 0.89		0.36	0.16 to 0.82	
Animal products eaten in the 24 hours before the interview								
No	91.0% (2585/2841)	94.6% (122/129)		Ref	0.265			
Yes	9.0% (256/2841)	5.4% (7/129)	0.57	0.22 to 1.52				
Grains eaten in the 24 hours before the interview								
No	18.2% (516/2841)	15.5% (20/129)		Ref	0.455			
Yes	81.8% (2325/2841)	84.5% (109/129)	1.22	0.73 to 2.04				
Vegetables eaten in the 24 hours before the interview								
No	66.1% (1877/2841)	71.3% (92/129)		Ref	0.293			
Yes	33.9% (964/2841)	28.7% (37/129)	0.78	0.50 to 1.23				
Health								
Are the teeth ever cleaned (self-reported)								
No	3.1% (88/2823)	4.7% (6/128)		Ref	0.372			
Yes	96.9% (2735/2823)	95.3% (122/128)	0.63	0.23 to 1.73				
Teeth cleaning method (self-reported)								
Toothbrush	23.8% (677/2841)	18.6% (24/129)		Ref	0.654			
Ash or cloth	1.9% (55/2841)	2.3% (3/129)	1.54	0.45 to 5.32				
Salt and water or stick	16.4% (466/2841)	15.5% (20/129)	1.26	0.68 to 2.32				
None or other	57.8% (1643/2841)	63.6% (82/129)	1.44	0.82 to 2.52				
Teeth cleaning frequency per day (self-reported)								
Once or twice	95.2% (2687/2823)	93.0% (119/128)		Ref	0.275			
Less than once	4.8% (136/2823)	7.0% (9/128)	1.53	0.72 to 3.26				
Any vaccinations listed on vaccination card								
No	88.5% (2513/2841)	86.0% (111/129)		Ref	0.451			
Yes	11.5% (328/2841)	14.0% (18/129)	1.24	0.71 to 2.17				

Continued

Table 5 Continued

	Study population		Univariable analysis			Multivariable analysis		
	Proportion of all respondents; n=2841; %(n/N*)	Proportion respondents with any noma stage; n=129; % (n/N*)	OR	CI	P value	aOR	CI	P value
Polio vaccination (self-report)								
No	29.8% (846/2841)	24.0% (31/129)		Ref	0.131		Ref	0.113
Yes	70.2% (1995/2841)	76.0% (98/129)	1.36	0.91 to 2.01		1.4	0.92 to 2.13	
Child sick last 12 months								
No	30.7% (871/2841)	24.0% (31/129)		Ref	0.148		Ref	0.138
Yes	69.3% (1970/2841)	76.0% (98/129)	1.39	0.89 to 2.18		1.51	0.88 to 2.60	
How many times was child sick during last 12 months								
0–1	51.1% (1451/2841)	46.5% (60/129)		Ref	0.379			
2 or more	48.9% (1390/2841)	53.5% (69/129)	1.19	0.81 to 1.74				
Did you seek healthcare for this child in the last year?								
No	50.1% (1422/2841)	47.3% (61/129)		Ref	0.62			
Yes	49.9% (1419/2841)	52.7% (68/129)	1.1	0.75 to 1.63				
Difficulties accessing healthcare (cost, time, distance)								
Didn't seek care	50.1% (1422/2841)	47.3% (61/129)		Ref	0.068		Ref	0.259
No difficulties	43.9% (1247/2841)	41.9% (54/129)	0.99	0.63 to 1.55		0.78	0.45 to 1.36	
Yes, there were difficulties	6.1% (172/2841)	10.9% (14/129)	1.98	1.12 to 3.51		1.44	0.73 to 2.85	
Caretaker and household information								
Caretaker age (years)								
Under 30	21.5% (611/2841)	20.2% (26/129)		Ref	0.731			
30 or older	78.5% (2230/2841)	79.8% (103/129)	1.08	0.69 to 1.69				
Caretaker gender								
Female	97.5% (2770/2841)	99.2% (128/129)		Ref	0.271			
Male	2.5% (71/2841)	0.8% (1/129)	0.32	0.04 to 2.40				
Primary caretaker of the child interviewed								
Other	7.6% (216/2841)	8.5% (11/129)		Ref	0.712			
Mother	92.4% (2625/2841)	91.5% (118/129)	0.87	0.43 to 1.78				
Total number of household members								
0–6	58.1% (1650/2841)	67.4% (87/129)		Ref	0.025		Ref	0.145
Above 6	41.9% (1191/2841)	32.6% (42/129)	0.66	0.46 to 0.95		0.74	0.49 to 1.11	
Drinking water source								
Other (borehole, river, tap)	57.8% (1641/2841)	54.3% (70/129)		Ref	0.498			
Well	42.2% (1200/2841)	45.7% (59/129)	1.16	0.79 to 1.87				
Water treatment								
No	69.1% (1964/2841)	65.1% (84/129)		Ref	0.376			
Yes (strain through cloth, let stand and settle, boil)	30.9% (877/2841)	34.9% (45/129)	1.21	0.79 to 1.87				
Wealth score (mobile phone, motorbike, tractor, camel)								
0–1	62.9% (1787/2841)	70.5% (91/129)		Ref	0.063		Ref	0.19
2–4	37.1% (1054/2841)	29.5% (38/129)	0.7	0.48 to 1.02		0.77	0.52 to 1.14	

Analysis adjusted for the survey design.
Variables with 10 or more cases and a p<0.2 in the univariable analysis included in the multivariable model (child gender, birth order, frequency of the child eating pap per week, frequency of the caretaker preparing pap per week, polio vaccination, child sick last 12 months, difficulties accessing health carehealthcare, total number of household members, wealth score.
P value from logistic regression model.
aOR, adjusted odds ratio; p, p value from logistic regression model.

studies have shown that rural Nigerian children typically breastfeed until 24 months of age[42] and then transition to a limited diet.[43] This has shown to result in higher levels of malnutrition and stunting[43] and therefore, a potentially higher risk of developing noma. This discrepancy in our findings in comparison to other studies could be due to the fact that our population had early stage noma, whereas other studies could have identified the association between malnutrition and late stage noma. It is also possible that late stage noma could cause malnutrition if the child was having difficulties eating due to the noma infection.

Our findings showed that older (aged 6–15 years) male children were more likely to have noma in comparison to older female children. We do not know what would explain this finding as we would not expect an inherent difference in gender in noma development. This finding warrants further research.

We showed that various factors relating to pap preparation and consumption were linked to not having stage 1 and 2 noma among the whole study sample and of any stage noma in the group aged 6–15 years old. It is difficult to explain this finding as it could be due to a lack of access to food or that pap made more frequently has less chance of becoming contaminated (thus causing less disease) as it is stored for shorter periods of time. A Nigerian study showed that when mothers prepared food far in advance, contamination was more likely to occur.[44] A further Nigerian study in Kebbi State showed that pap was contaminated with high levels of Salmonella in comparison to other commonly eaten foods.[45] This finding affected children in the older age group which may be because they are more reliant on this food source in comparison to the younger children.

This study further indicated that having a well as the main water source in comparison to other water sources such as a borehole, river or tap, was associated with having noma in the group aged 0–5 years. Well water has a high risk of contamination from nearby pit latrines or livestock,[46] and the consumption of contaminated well water is a risk factor for diarrhoea,[47] which in turn is an identified comorbidity for children with noma.[48]

Vaccination coverage in all eligible children included in the study was low. Even though this result prevented us from exploring whether vaccination is associated with noma prevention, it does confirm findings from other studies in rural Sokoto State, where up to 70% of children were not vaccinated against measles and other common childhood diseases.[35] Low immunisation coverage is an important indicator of struggling societal systems in need of multisectoral improvements, including access to quality timely healthcare, access to safe drinking water, improved nutrition and security. Prevention efforts should also include early detection training with healthcare workers, and setting up effective referral pathways. These initiatives are resource-intensive and require large-scale investment of time, money and human resources.

This study had a large sample size and robust approach to sampling and analysis, and we are confident that prevalence estimates are broadly representative of the study area. However, a few limitations should be considered. This cross-sectional study was conducted on a disease with an extremely rapid clinical progression with onset to death taking as little as 2 weeks.[1] Thus, it is possible that Neyman bias was present and we only identified a fraction of noma cases that occur. The research team did come across stage five noma patients in study villages, but not in households included in the study. These patients were referred to the NCH for care. It is possible that a study with a larger sample size could have identified children with the later stages of disease. Some of the answers were self-reported by caretakers, which could have introduced social desirability bias that either inflated or deflated the risk factor associations found in the study. This aspect was mitigated by anonymising the survey and trying to phrase questions in contextually acceptable ways. Data on some risk factors, such as comorbidities, water quality and malnutrition in older children were not collected, limiting our ability to identify associations with these factors. It is difficult to interpret the results of questions asking about consumption of any food and specific foodstuffs in the 24 hours prior to the interview and associations with noma as respondents with noma could have difficulty eating in general and would thus have been less likely to report eating at all. Finally, the challenging security situation limited the areas the research teams could access. This may have introduced selection bias, and an underestimation of noma and malnutrition prevalence, as we did not visit the hardest to reach communities who were likely most vulnerable to noma infection. Future research on the burden of noma should be combined with existing surveillance systems for other disease and research activities such as malnutrition and vaccination surveys.

Noma meets the criteria of a neglected tropical disease as defined by the WHO: it is a preventable disease that affects children in low-resource contexts; children that survive will have life-long physical and mental health sequelae; and there is poor understanding of the disease, its pathogenesis and global burden.[49] This study has shown that the prevalence of any stage of noma is higher than previous estimates. While we did not find any later stages of the disease, the high rates of simple gingivitis and the presence of known risk factors for noma (low vaccination rates, malnutrition and poor access to healthcare) suggest the need for improved coverage of preventative interventions and access to care in northwest Nigeria. Our prevalence estimates are greater than those for snakebite in Nigeria (497 per 100 000 people), which the WHO recently recognised as a neglected tropical disease.[50] Noma prevention and control will require a concerted health systems approach. Adding noma to WHO's list of neglected tropical diseases will facilitate global attention for noma and the allocation of much-needed resources to those countries where noma continues to be a public health problem.

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Appendix 6 Questionnaires or question guides

6.1 Language and beliefs question guides

6.1.1 In-depth interview guide

Background: The key informant interviews will be conducted in a setting that minimises the influence of the researcher and encourages the interviewee to discuss noma, and their role in the project.

Introduction (5 mins max): • Thank the participant for agreeing to take part in this research.

- Introductions - explain who you are and share some of your experience.
- Create a relaxed atmosphere; offer the participant something to drink when this is possible.
- Tell each participant:

  "I (We) would like to talk to you about your experiences of noma and your role at the hospital. We would like to hear your stories, what you think about the disease, what works well for treatment and the challenges you face. This interview will contribute to a better understanding of noma and the work occurring at the Noma Children's Hospital in Sokoto. The interview will take approximately 30 minutes and can be stopped by you at any time without any consequences. If you would like to continue there is a form we have to complete to check that you have all the information you need before we start. Would you like to continue? Would you be happy for us to record this conversation for our records?
- Make sure the participant has been informed and has consented verbally to participate in the research study.

NOTE: Turn on the recorder and test it is recording.

Questions should be adapted where necessary, but can follow the below themes:

1. Discuss patient flow thorough the noma surgical program.
2. What noma stage patients are at when they are included in to the program?
3. How long on average after onset do patients come to hospital?
4. What would the best terms be to use in the questionnaire to describe noma, as there is no official Hausa word for noma?
5. What beliefs staff have about noma?
6. What beliefs have staff heard from patients?

6.1.2 Focus group discussion question guide

Introduction (5 mins max):

- Thank the participants for agreeing to take part in this research.
- Introduce yourself.
- Create a relaxed atmosphere; offer the participants something to drink when this is possible.
- Tell the group:

  "I (We) would like to talk to you about noma, your beliefs about this disease and the words you use to describe it. This discussion will contribute to a better understanding of how people living with noma experience the disease.

  The interview will take approximately 45 - 60 minutes with anyone in the group deciding to leave at any time if they no longer want to contribute at any time without any consequences".
- Make sure the group participants have been informed about the study and have consented to participate in the research.

****TURN ON the recorder and test it is recording****

Topic	**Specific Questions**	**Prompts and Notes**
Introduction	- Study aim - Why invited to participate - Consent and respect within the group	Answer any questions group has about study
Language used to describe noma	- Show picture of noma patient and ask group - if this person was walking in your village, what name would you use to describe the disease they had? - Ask what their community would call the disease? - What the names mean? - Where the names come from?	Specific names, ask about origins of names, ask each group member what name it is called in their village, try and see if there are variations
Perception of noma	- Ask caretakers what other people say about this disease? - What do community members know about disease? - Is it a common disease?	Ask about community and personal perceptions of the disease.
Beliefs	- Where does the disease come from? - What causes the disease? - Risk factors for disease? - How best to treat disease?	Omen, spell, come from the wind, withchcraft

6.2 Risk factors questionnaire

Study Number: _____

Date : _____

INTERVIEWER PLEASE READ INTRODUCTION:

- Thank you for agreeing to participate in this study!
- **This study is important as it will help us to develop programmes to prevent noma in Nigeria.**
- I will ask you questions about yourself, your lifestyle, and about the child of interest (case).
- All of your responses are confidential, and I will not write your name on this form.
- There are no right or wrong answers.
- This interview will take about 45 minutes.
- Please answer all questions honestly.
- Do you have any questions before we begin?

A. SOCIODEMOGRAPHIC CHARACTERISTICS	
1. How old is your child (the case)?	_____ years OR _____ months
2. How old are you (parent/guardian)?	_____ years
3. Relationship to the case:	a) Mother b) Father c) Grandmother d) Grandfather e) Aunt f) Uncle g) Guardian h) Other, please specify: _____
4. How many wives do you have (if husband)? (Skip to 6) How many wives does your husband have (if wife)?	_____ (number)
5, What number wife are you?	a) 1st b) 2nd c) 3rd d) 4th e) Other, please specify: _____
6. What is the highest level of education you have completed?	a) None b) Arabic studies c) Primary school

	d) Secondary school e) University f) Other, please specify: _____
7. What is your primary business/money making activity?	a) Livestock (own cattle, sheep, goats etc.) b) Agriculture (grow and sell food products from own land) c) Trading/shop (owner of business) d) Seasonal labour/daily e) Regular work (work in shop, drive bus, regular job etc.) f) No business/housewife g) Student h) Don's know i) Other, please specify: _____
8. What is your husband's/wife's primary business/money making activity?	a) Livestock (own cattle, sheep, goats etc.) b) Agriculture (grow and sell food products from own land) c) Trading/shop (owner of business) d) Seasonal labour/daily e) Regular work (work in shop, drive bus, regular job etc.) f) No business/housewife g) Student h) Don's know i) Other, please specify: _____
9. Does any member of your compound own: (circle all appropriate)	a) A watch b) A motorbike c) A radio d) A phone e) A generator to make electricity f) A car
10. What level of education has your child completed (the case)?	a) None b) Arabic studies c) Primary school d) Secondary school
11. Who normally takes care of the child in question?	a) Mother b) Father c) Grandmother d) Grandfather e) Aunt

	f) Uncle g) Guardian h) Other, please specify: _____			
B. LIVING CONDITIONS				
12. How many people live in your compound and of what sex?		**Male**	**Female**	**Total**
	Children 0-4 yrs			
	Children 5-17 yrs			
	Adults 18 & older			
	Total			
13. How many houses are there in your Compound?	_____ (number)			
14. What is the main material of the external walls of your house?	a) Improvised/temporary (e.g. plastic) b) Wood, mud, bamboo c) Stone, brick, cement d) Other, please specify: _____			
15. Do you have running water (a tap) in your compound?	a) Yes b) No			
16. Where do you get your drinking water from?	a) Bore hole in the village b) Well in the compound c) Tap (running water) d) River/stream e) Other, please specify: _____			
17. Do you treat your drinking water?	a) Yes b) No			
18. If you do treat your drinking water, how do you treat it?	a) Boil b) Add bleach/chlorine tabs c) Add floculant and strain through a cloth d) Strain it through a cloth e) Use water filter (ceramic/sand) f) Let it stand and settle g) Other, please specify: _____ h) Don't know			
19. Does your compound have electricity?	a) Yes b) No			
20. Do you have cows living in your compound?	a) Yes b) No			

21. Do you have donkeys living in your compound?	a) Yes b) No
22. Do you have dogs living in your compound	a) Yes b) No
23. Do you have sheep living in your compound?	a) Yes b) No
24. Do you have goats living in your compound?	a) Yes b) No
25. Do you have chickens living in your compound?	a) Yes b) No
26. Do you have any other animals living in your compound?	a) Yes b) No. What kind: _____
27. How many meals did the family eat yesterday (at the hospital)?	_____ (number)
28. How many meals does your family eat when you are in your village	_____ (number)
29. Does your child eat cassava every day when you are living in the village?	a) Yes b) No
30. Does your child eat pap every day when you are living in the village?	a) Yes b) No
31. What food does your child normally eat in the day? (Please list contents of all meals)	Breakfast: _____ _____ Lunch: _____ _____ Dinner: _____ _____ Other: _____
32. What food does your family normally eat in the day? (Please list contents of all meals if different from above)	a) Same as child (above) b) Different from child (details below) Breakfast: _____ _____ Lunch: _____ _____ Dinner: _____ _____ Other: _____

C. VACCINATION		
33. Does your child have a health card?	a) Yes b) No	
34. Was your child vaccinated?	a) Yes b) No	
35. Do you have a child's vaccination book here?	a) Yes b) No	
36. Interviewer: Ask to see vaccination card, if the caretaker has one, circle all vaccinations that are recorded in the book. **Add number of doses based on dates recorded in the vaccination card if possible**	**Vaccination**	**Number of doses**
	a) Diphtheria	
	b) Hepatitis A	
	c) Hepatitis B	
	d) Poliomyelitis	
	e) Measles	
	f) Mumps	
	g) Pertussis	
	h) Pneumococcal	
	i) Rotavirus	
	j) Rubella	
	k) Tetanus	
	l) Typhoid	
	m) Yellow fever	
	n) Meningococcal meningitis	
	o) Rabies	
	p) Chicken pox	
37. Self-reported vaccines. Ask caretaker which vaccinations child received.	**Vaccination**	**Self-reported (tick)**
	a) Diphtheria	
	b) Hepatitis A	
	c) Hepatitis B	
	d) Poliomyelitis	
	e) Measles	
	f) Mumps	
	g) Pertussis	
	h) Pneumococcal	
	i) Rotavirus	
	j) Rubella	
	k) Tetanus	
	l) Typhoid	
	m) Yellow fever	
	n) Meningococcal meningitis	
	o) Rabies	
	p) Chicken pox	

D. BREASTFEEDING PRATICES AND CHILDREN	
38. How many children did you/your wife give birth to?	_____ (number)
39. How many of these children are still alive?	_____ (number)
40. How many boy children do you have (including those who died)?	_____ (number)
41. How many girl children do you have (including those who died)?	_____ (number)
42. What number in the birth order of your children, is the case?	_____ (number)
43. How much did your child (case) weigh when they were born?	a) Light b) Heavy
44. Birthweight in grams (if known)	_____ (grams)
45. How long did you breast feed for the child/case?	a) Less than 2 months b) 3-6 months c) 7-12 months d) 1-2 years e) Other, please specify: _____
46. Did you give colostrum (first mild) to the case?	a) Yes b) No c) Don't know
47. Do you give the baby/case breast milk and other food simultaneously?	a) Yes. What type of food _____ b) No
48. When did you first begin giving the case water when they were a baby?	a) _____ (age in months/years) b) Don't know
49. When did you first begin giving the baby/case solid foods?	a) _____ (age in months/years) b) Don't know
50 What are the first foods you gave the baby/case?	_____ _____ (list items)
51. Does your child have any traditional marking cuts in their face?	a) Yes b) No

52. If yes, what was used to make the cuts?	_____
53. What age were the markings made?	_____

E. CHILD HEALTH AND ACCESS TO CARE 12 MONTHS BEFORE INTERVIEW

54. Has your child been sick (in addition to noma) in the last 12 months before the interview?	a) Yes b) No
55. If yes, how many times during the last 12 months?	_____ (number)

Disease	Symptoms	Disease diagnosed by health professional (select from below list)	Month of disease	How long did the disease last for	Did the child eat more or less during the sickness
1					
2					
3					
4					
5					

List of diseases to choose from

- *Malaria*
- *Measles*
- *HIV*
- *Bronchial infections*
- *Other (specify)*
- *Respiratory infections*
- *Intestinal infections*
- *Rash*
- *Diarrhoea*

56. Has your child taken medication in the last 12 months?	a) Yes b) No If yes, what medicine _____

F. ACCESS TO CARE - GENERAL

57. For any of the times that your child was sick in the last 12 months (apart from the noma), did you seek some form of health care?	a) Yes b) No c) Don't know

58. Which of the following health care facilities did you access: (Circle all that apply)	a) Hospital b) Clinic c) Traditional healer d) Village elder e) Other, please specify: _____
59. Did the doctor/nurse ever do a home visit when your child was sick?	a) Yes b) No

60. Where would you go when your child is sick in general? (tick the appropriate one)

	Hospital	**Clinic**	**Traditional healer**	**Street pharmacy**	**Shop pharmacy**
a) 1st place I would visit					
b) 2nd place I would visit					
c) 3rd place I would visit					
d) 4th place I would visit					

61. How do you get to the point of care?

	Hospital	**Clinic**	**Traditional healer**	**Street pharmacy**	**Shop pharmacy**
a) Taxi					
b) Bus					
c) Walking					
d) Bicycle taxi					
e) Hitchhiking					
f) Motorbike					
g) Other, please specify? _____					

62. How long does it take to get to the point of care

	Hospital	**Clinic**	**Traditional healer**	**Street pharmacy**	**Shop pharmacy**
a) 0-14 minutes					
b) 15-44 minutes					
c) 45 minutes - 1.5 hours					
d) 1.5 hours - 2.5 hours					
e) Half a day					
f) Full day					
g) 2 days					
h) Other, please specify? _____					

G. CHILD ORAL HEALTH	
63. Does your child brush their teeth?	a) Yes b) No
64. If yes, how many times a day?	_____ (number)
65. Can I see your child's toothbrush and toothpaste?	a) Yes (interviewer visually confirms toothbrush + toothpaste) b) Yes (interviewer visually confirms only toothbrush) c) Yes (interviewer visually confirms only toothpaste) d) No (interviewer does not have visual confirmation)
H. MUAC MEASUREMENT AT THE TIME OF THE INTERVIEW	
66. INTERVIEWER to test nutritional status by using mid upper arm circumference (MUAC) tool	Colour of MAUC measurement: i. Green ii. Yellow iii. Red a) Number of MAUC measurements: _____ b) Nutritional status upon admission from medical file: _____
I. OPEN ENDED INTRODUCTORY NOMA QUESTIONS	
67. What disease do you believe your child has?	
68. What do you think caused this problem?	
69. What do you think is the best way to fix it?	
70. Are there any beliefs in your culture about this disease?	
J. NOMA DISEASE IN THE CHILD	
71. What do you call this disease before you came to the hospital (show picture of noma)?	a) Gaude b) Ciwon Daji c) Zizaya baki d) Cancer e) Noma f) Other _____

72. What do you now call this disease?	a) Gaude b) Ciwon Daji c) Zizaya baki d) Cancer e) Noma f) Other _____
73. What do you believe causes this disease?	a) Iska (wind) b) Witchcraft c) Bad water d) Bad food e) Animal
74. What do you think is the best way to fix it?	a) Traditional medicine - herbs/powder to drink b) Traditional medicine - to put on wound c) Cutting cheek with sharp blade (after placing blade in fire) d) Medicine from hospital e) Operation f) Other _____
75. When did you first notice the signs and symptoms of Noma?	a) Rainy season (May - September) b) Dry season (Harmattan, October - April)
76. How long from first signs and symptoms (mouth ulcer/bleeding gums) did it take for the noma to develop to Stage 2? (Swelling of cheek)? (Show picture)	a) 1 day b) 2-3 days c) 4-7 days d) 1-2 weeks e) 3-4 weeks f) More than one month
77. How long from first signs and symptoms (mouth ulcer/ble3eding gums) did it take for noma to develop to Stage 3? (Skin on cheek/nose falling off)? (Show picture)	a) 1 day b) 2-3 days c) 4-7 days d) 1-2 weeks e) 3-4 weeks f) More than one month
78. What age was the child when they developed noma?	_____ (years/months)
79. What were the initial signs and symptoms of the disease?	a) Mouth ulcer b) Soft tissue damage c) Problems feeding d) Problems breathing e) Other, please specify: _____

80. Which symptoms did you seed care for?	a) Mouth ulcer b) Soft tissue damage c) Problems feeding d) Problems breathing e) Other, please specify: _____
81. Why did you seek care for your child?	a) Cosmetic reasons b) Soft tissue damage c) Problems feeding d) Problems breathing e) Other, please specify: _____
82. Do you feel your child/you has been stigmatised in any way due to the disease?	a) Yes b) No (skip to 85)
83. If yes, how? (choose all that apply)	a) Not allowed to go to school b) Gets teased by community members c) I am not allowed to socialise with other parents d) My family has disowned me e) My husband/wife left me f) I cannot go to pray g) My friends no longer talk to me h) My village elders told me to leave my village i) My community members said I had a spell on me j) Other, please specify: _____
84. If yes, how often is the child/caretaker affected by the stigmatisation?	a) Every day b) Three times a week c) Once a week d) Once every 2 weeks e) Once a month f) Once every 6 months g) Once a year h) Less than once a year

85. Where did you seed care for your child?

	Hospital	**Clinic**	**Traditional healer**	**Street pharmacy**	**Shop pharmacy**	**Other, specify**
a) 1st place visited						
b) 2nd place visited						
c) 3rd place visited						

d) 4th place visited						

86. How did you get to the point of care?

	1st place visited	2nd place visited	3rd place visited	4th place visited
a) Taxi				
b) Bus				
c) Walking				
d) Bicycle taxi				
e) Hitchhiking				
f) Motorbike				
g) Other, please specify				

87. How long did it take to get to the point of care?

	1st place visited	2nd place visited	3rd place visited	4th place visited
a) 0-14 minutes				
b) 15-44 minutes				
c) 45 minutes - 1.5 hours				
d) 1.5 hours - 2.5 hours				
e) Half a day				
f) Full day				
g) 2 days				
h) Other, please specify				

88. How much did it cost to get to the point of care (in Naira)?

	Amount
a) 1st place visited	
b) 2nd place visited	
c) 3rd place visited	
d) 4th place visited	

89. How long after you noticed the initial symptoms, did you seek care?	a) Same day b) 1 day c) 2-5 days d) 1 week e) 1-2 weeks f) Other, please specify: _____
90. Did any of the healthcare providers that you visited know what was wrong with your child?	a) Yes b) No Who: _____ What was the diagnosis: _____

91. Were the healthcare providers able to offer treatment quickly?	a) Yes b) No
92. What care did the healthcare provider provide?	a) Traditional herbs/powder b) Traditional tea c) Traditional cutting cheek instrument/ advice d) Operation e) Antibiotics f) Traditional treatment g) Lab tests h) None i) Other, please specify: _____
93. Did the healthcare provider do any lab tests?	a) Yes b) No
94. If yes, do you know what tests they were and what the results were?	_____
95. Have you had previous surgeries for noma?	a) Yes. How many: _____ b) No
96. In your own words, can you describe to me what noma is?	
97. What impact has noma had on your child's life? (prompts: school, eating, breathing)	
98. What impact has noma had on your life?	
99. Do you have any questions about noma?	

END OF SURVEY

Thank you very much for your time and for agreeing to participate in our study. Do you have any questions for me?

6.3 Outcomes questionnaire

Patient hospital ID		
Date of assessment		
Date of patient's final surgery		
Assessment	6 months	12 months
Name of assessor		

Is the patient still alive	Yes	No
** *If No, complete Verbal Autopsy Form Consent and if given, Verbal Autopsy Form* **		

Metrics (to measure WHZ, weight for height and weight for age)	
Weight	(kg)
Height	(cm)
Age	(round to closest year)

MUAC (for those under 5 years)	(mm)	
Colour	Red	
	Orange	
	Yellow	
	Green	

Maximum mouth opening		
Mouth open	(mm)	
Mouth closed	(mm)	
Maximum Mouth Opening	(mm)	
Mouth opening comments (Note here if measurement was taken from alveolar ridges and not incisors)		
Has the surgery improved your quality of life?	Yes	No
In what way:		
I can go to school now	Yes	No
I have friends now	Yes	No
I am included in the community	Yes	No
I am now getting married	Yes	No
I can eat more easily	Yes	No
I can drink more easily	Yes	No
People can now understand what I am saying more easily than before	Yes	No
I feel more happy with the way I look than before the surgery	Yes	No

6.4 Traditional healer study question guides

6.4.1 Interview guide caretakers

Introduction (5 mins max):

- Thank the participant for agreeing to take part in this research.
- Introduce yourself.
- Create a relaxed atmosphere; find a quiet, private place to sit, offer the participant something to drink when this is possible.
- Make sure the interviewee have been informed about the study and has consented to participate in the research.
- Tell the participant:

  "*I would like to talk to you about your perceptions of traditional healing, your relationship with traditional healers and the experiences you may have had visiting them. This discussion will contribute to a better understanding of how people interact with traditional healers, especially in regards to seeking treatment for noma.*

  The interview will take approximately 30 - 60 minutes and you can decide to end the interview at any time without any consequences".

****DO NOT RECORD****

Topic	**Specific questions**
Demographic characteristics	- Age - Gender - Profession - Village - Family setting (married etc.) - Relationship between caretaker and patient (mother, grandmother, uncle) - Number of children

Introduction	- Study aim - Why invited to participate - Consent - Answer any questions participant has about study

**** TURN ON the recorder and test it is recording****

Topic	**Specific questions**	**Prompts/Probe**
Caretakers perceptions of traditional healing	Can you tell me about the different health care options available to you in your village?	**Probes:** Clinic, Hospital, Traditional Healer, Mobile health such as vaccination campaigns
	Which of these health options do you usually prefer and why?	**Probe:** Any negative views on any kind of health care, or vaccinations? Different health care options for different diseases?
	Can you tell me what you have heard about traditional healing in your community? How do your neighbours/village members view community healing?	**Probe**: If person is not able to discuss their own experiences, ask them to discuss if their neighbours/local community members consult healers. Probe for what kind of healers and services are offered. Trust? Scared?
	Have you ever visited a traditional healer? If yes, can you describe this experience to me? Can you describe how long you stayed with the healer and what the experience was like?	P**robes:** Ask about non-noma experiences. Why did you go, what kind of care was provided, who accompanied you, treatment received, how many times you visited?
	Can you explain to me why you decided to visit the traditional healer?	**Probes:** Trust, knowledge of the healer, recommendation, cost, proximity, type of illness visited for.
	Can you describe what your relationship is like with the traditional healer?	

	Can you tell me about the kind of treatment you received from the healer? How did you feel about it?	**Probes:** Understanding of disease and treatment, satisfaction, consulted someone else after?
	Can you tell me about how long after the first symptoms started, you decided to access care? Were there any reasons you waited to access care?	**Probes:** Too far, cost, prefer traditional healer, others in my family told me not to, child was too ill to travel
Noma specific diagnoses and care provided by the traditional healers	I'd now like to ask you some questions related to noma [use Hausa terms]. How long ago did the disease begin?	Can be a month, or season
	Can you tell me what has happened since you first noticed the symptoms of the disease? Were there any issues along the way? How did you come to the decision to seek health care? How long did it take to make this decision? Can you explain why it took that length of time? Can you describe who made the decision and how the decision was made?	**Describe:** Pathway to care. Link to measles.
	Did you receive any diagnosis or treatment before coming to the Noma Hospital?	**Probes:** Consulted other healthcare facilities/traditional healer
	What kind of diagnosis were you given?	**Probes:** Previous mention of noma, names of other diseases (measles)/conditions diagnosed, difference in diagnosis from different people

	If you saw a traditional healer, what did they say about noma? Please be as specific as you can, even if you can't remember all the details.	
	What kind of treatment did the traditional healer offer you?	**Probes:** Did they offer more than one treatment option? Which ones? Link to measles?
	Which kind of treatment was given to your child? Can you tell me why this kind of treatment was given?	**Probe:** Choice: did the caretaker feel there was a choice in the treatment, who is part of the decision-making process
	If you did not visit a traditional healer for noma, can you tell me why? Who did you go to for treatment	

6.4.2 Interview guide - traditional healers

Introduction (5 mins max):

- Thank the participant for agreeing to take part in this research.
- Introduce yourself, and tell the participant you are not there as a health provider.
- Create a relaxed atmosphere; offer the participant something to drink when this is possible.
- Make sure the interviewee has been informed about the study and has consented to participate in the research.
- Tell the participant:

  "*I would like to talk to you about your perceptions of noma, your relationship with community members and your experiences of the disease. This discussion will contribute to a better understanding of how people interact with traditional healers in regards to seeking treatment for noma.*

  The interview will take approximately 30 - 45 minutes and you can decide to end the interview at any time without any consequences".

****DO NOT RECORD****

Topic	**Specific Questions**
Demographic Characteristics	- Age - Village - Length of time being a traditional healer - Type of healer (broad overview of role)
Introduction	- Study aim - Why invited to participate - Consent - Answer any questions participant has about study

**** TURN ON the recorder and test it is recording****

Topic	Specific Questions	Prompts and Notes
Relationship between traditional healer and caretakers	Can you tell me more about the role you play in the community? What does your work involve?	Why do people come to you? When do people come to you? Trust What kind of treatments do you prescribe? Do you ever offer multiple treatments for one ailment? Can you provide an example?
	Could you tell me how you learned your craft?	How do you keep your knowledge up to date? How would you feel about attending a training on noma?
	What are some of the most common things people come to see you for?	For common illnesses For prevention Other reasons?
	Can you describe the kind of relationship you have with your patients?	**Probes:** Trust, any issues, status in community
Traditional healer perceptions of noma and noma treatment?	Show picture of different noma stages and ask: What do you know about this disease? What treatment would you prescribe for the different stages of the disease?	Is it a common disease? Do you have a name for it? Where does the disease come from? What causes the disease? Any way that can be prevented? How best to treat disease? When best to treat disease? Link with measles?
	Have you ever treated a case of this disease? If yes: Can you tell me more about what happened while treating this disease?	Who brought the patient? How long after first symptoms did patient come? (Can show pictures of different stages of the disease) Had they visited other health providers before coming to you? What symptoms did the patient have? What treatment regimen did you suggest? Did you have any follow up visits? If so, what happened?

	How do you feel about the disease?	Where does it come from? Do others in the village know about it? Do people in the village fear it? Stigma?
	What other forms of health care are there in your community?	Vaccination Campaigns Clinic Hospital Home
	What do you think about other forms of health care?	Trust Barriers to care
	How do you feel about referring patients to other forms of health care?	Trust Barriers to care
	Would you refer a noma patient to the NCH? Can you explain why/why not?	If so, when would you refer a noma patient? Do/could you think of the clinic as a partner for helping treat noma?

6.5 Prevalence questionnaire

Family ID: _____

Date of Interview : _____

Name of interviewer: _____

HOUSEHOLD QUESTIONS ANSWERED BY CARETAKER

Do you have running water (a tap) in your compound?	Yes No
Where do you get your drinking water from?	a) Bore hole in the village b) Well in the compound c) Tap (running water) d) River/stream e) Other, please specify: _____
Do you treat your drinking water?	Yes No
If you do treat your drinking water, how do you treat it?	a) Boil b) Add bleach/chlorine tabs c) Strain it through a cloth d) Use water filter (ceramic/sand) e) Let it stand and settle f) Other, please specify: _____ g) Don't know
How old are you (parent/ guardian)? (years)	_____ (years)
Respondents/ caretakers relationship to children:	a) Mother b) Father c) Grandmother d) Grandfather e) Aunt f) Uncle g) Guardian h) Other, please specify: _____

CHILD SPECIFIC QUESTIONS

	Child 1	Child 2	Child 3	Child 4	Child 5	Child 6
How old is your child? (round to closest year, can use events calendar)						
What number is this child in the bird order of your family?						
Does your child have any teeth?						
If yes, how many teeth?						
Does your child brush or clean their teeth?						
If yes, what do they use to brush/ clean their teeth?	a) Toothbrush b) Stick c) Cloth d) Ash e) Salt and water Other: ________________	a) Toothbrush b) Stick c) Cloth d) Ash e) Salt and water Other: ________________	a) Toothbrush b) Stick c) Cloth d) Ash e) Salt and water Other: ________________	a) Toothbrush b) Stick c) Cloth d) Ash e) Salt and water Other: ________________	a) Toothbrush b) Stick c) Cloth d) Ash e) Salt and water Other: ________________	a) Toothbrush b) Stick c) Cloth d) Ash e) Salt and water Other: ________________
If yes, how often do they brush their teeth?						
If child has rotten teeth, what do you use to clean?						
Has your child eaten pap in the last 24 hours (day)?	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No
How often does your child eat pap?	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week

How often do you prepare the pap	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week	a) >once a day b) 4–6 days/wk c) 2-3 days/wk d) < once a week
Did you give colostrum (first milk) to the child?	Yes No Don't know	Yes No Don't know	Yes No Don't know	Yes No Don't know	Yes No Don't know	Yes No Don't know
What is your most used sanitation facility	a) Flushing toilet b) Latrine with slab c) Pit latrine no slab Other: _____	a) Flushing toilet b) Latrine with slab c) Pit latrine no slab Other: _____	a) Flushing toilet b) Latrine with slab c) Pit latrine no slab Other: _____	a) Flushing toilet b) Latrine with slab c) Pit latrine no slab Other: _____	a) Flushing toilet b) Latrine with slab c) Pit latrine no slab Other: _____	a) Flushing toilet b) Latrine with slab c) Pit latrine no slab Other: _____
Was your child vaccinated	Yes No Don't know	Yes No Don't know	Yes No Don't know	Yes No Don't know	Yes No Don't know	Yes No Don't know
Do you have your child's vaccination book here?	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No
Interviewer: Ask to see vaccination card, if the caretaker has one, write all vaccinations that are recorded in book (date and name of vaccination)						
Has your child been sick in the last 12 months before this interview?	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No

If yes, how many times during the last 12 months? (put number)						
For any of the times that your child was sick in the last 12 months, did you seek some form of health care?	Yes No Don't know	Yes No Don't know	Yes No Don't know	Yes No Don't know	Yes No Don't know	Yes No Don't know
Which of the following health care facilities did you access?	a) Hospital b) Clinic c) Traditional healer Other: _____	a) Hospital b) Clinic c) Traditional healer Other: _____	a) Hospital b) Clinic c) Traditional healer Other: _____	a) Hospital b) Clinic c) Traditional healer Other: _____	a) Hospital b) Clinic c) Traditional healer Other: _____	a) Hospital b) Clinic c) Traditional healer Other: _____

PHYSICAL EXAMINATIONS (BY NURSE OR CLINICIAN)

Weight in kg						
Height in cm						
MUAC mm						
MUAC colour	a) Green b) Yellow c) Orange d) Red	a) Green b) Yellow c) Orange d) Red	a) Green b) Yellow c) Orange d) Red	a) Green b) Yellow c) Orange d) Red	a) Green b) Yellow c) Orange d) Red	a) Green b) Yellow c) Orange d) Red
Anaemia eye test	a) Anaemic b) Not anaemic	a) Anaemic b) Not anaemic	a) Anaemic b) Not anaemic	a) Anaemic b) Not anaemic	a) Anaemic b) Not anaemic	a) Anaemic b) Not anaemic

Noma Stage (as per below)	a) None b) 0 c) 1 d) 2 e) 3 f) 4 g) 5	a) None b) 0 c) 1 d) 2 e) 3 f) 4 g) 5	a) None b) 0 c) 1 d) 2 e) 3 f) 4 g) 5	a) None b) 0 c) 1 d) 2 e) 3 f) 4 g) 5	a) None b) 0 c) 1 d) 2 e) 3 f) 4 g) 5	a) None b) 0 c) 1 d) 2 e) 3 f) 4 g) 5
If yes to any stage of noma, how many days ago did the child first show any signs of this disease?	Number:	Number:	Number:	Number:	Number:	Number:

NOMA STAGES:

None

Stage 0: Simple Gingivitis

Stage 1: Haemorrhagic or Necrotizing Gingivitis/ Stomatitis

Stage 2: Oedema (early acute)

Stage 3: Necrosis and tissue loss (late acute)

Stage 4: Tissue and bone loss and wound healing process

Stage 5: Sequelae lesion

END OF SURVEY

Thank you very much for your time and for agreeing to participate in our study. Do you have any questions for me?

Appendix 7 Informed consent and assent forms

7.1 Language and beliefs informed consent forms

7.1.1 Focus group discussion informed consent form

Project Title: Risk factors for diagnosed noma in North Western Nigeria, a sequential mixed methods study - 2017.

Organization: Médecins sans Frontières (MSF) and the Ministry of Health.

This informed consent has two parts:

- The information sheet – which gives you information about the study;
- Certificate of consent study participation – which you will sign to demonstrate that you agree to participate with the interview for this study.

Introduction: We are conducting this study for Médecins Sans Frontières (MSF) and the Ministry of Health in Sokoto to find out more about the risk factors of a disease called noma, which affects mostly children in this part of Nigeria. MSF has been running a program to assist noma patients in Sokoto Nigeria, and in order to better understand the disease and improve these services, we would like to ask patients and community members some questions.

What is the study about? Very little is understood about the disease noma, what causes it and why some children develop the disease and others do not. We are wanting to run focus group discussions with caretakers to discuss the names used to describe disease, and their beliefs about the disease.

Who will participate in the study? Caretakers of noma patients at the Noma Children's Hospital.

What does the participation in the study request from me? We will ask a group of noma patient caretakers to spend between 45 - 60 minutes answering the questions we have. This will be a group discussion led by the researcher.

We would like to ask you some questions about the names used to describe the disease, and their beliefs about the disease. We would like to record your answers on a tape recorder, so that we can have an accurate record of what is said during the discussions.

If you do not understand a question, please ask me to explain it to you. If you do not want to answer a question or if you would like to stop at any time, please tell me.

Do we have to participate? Whether you choose to be in the study or not is up to you. There will be no effect on your family if you decide you do not want to be in the study.

What will happen with the information that you collect? We will collect the information from everyone in the group, and we will then collate all information to see if there are patterns in the names noma is called, and the beliefs about the disease. This information could assist us in gaining and understanding about the disease. We may use some of the stories and experiences you share with us to write reports or press releases to draw attention to noma, if we do so, we will always ensure to anonymize your name and any places you mention.

Where will the study take place? We can conduct the interview anywhere where the group feels comfortable.

Will I or my family receive anything to participate? You will not get anything, such as money or extra food, for taking part in this survey.

Is it dangerous to participate? You may find some questions upsetting. If a question makes you uncomfortable, we can skip this question and go on to the next question.

What might we get from this study? You are free to stop at any time during the interview. Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are. We hope that the results will help us better understand noma and contribute to finding better ways to prevent and treat this disease in your community.

Confidentiality: The recordings from this study are private. Only the people who are doing the study can see the answers you give to the questions. We do not ask for your name so there will be no record that you participated in the study. I will not repeat what you have told me to anyone else. We cannot assure confidentiality as others in the group will know what you have said, but we will ask all group members to respect confidentiality.

Approvals: The ethical aspects of this research have been approved by Médecins sans Frontières Ethics
Review Committee and by the Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee.

Queries and Concerns: You can call and speak to us at any time if you want to find out more about this project.

Study coordinator name and phone number [to be inserted]

Local Ethics Committee Details for questions regarding rights as research participants:

Dr. Nma Jiya, Address: UDUTH; Phone: +234 805 038 1688.

Thank you very much for your time and participation.

Consent Certificate Adult Study Participant – Copy Study Team

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the discussion about the child in my care. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the survey team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him/her about the child under his/her care.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Interviewer's name: _____

Interviewer's signature: _____

Consent Certificate Adult Study Participant – Copy Study Participant

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the discussion about the child in my care. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): |__||__| / |__||__| / |__||__|

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the survey team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him about the child under his/her care.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date (insert day/month/year of study): |__||__| / |__||__| / |__||__|

Interviewer's name: _____

Interviewer's signature: _____

7.1.2 In-depth interview informed consent forms

Project Title: Risk factors for diagnosed noma in North Western Nigeria, a sequential mixed methods study - 2017.

Organization: Médecins sans Frontières (MSF) and the Ministry of Health.

This informed consent has two parts:

- The information sheet – which gives you information about the study;
- Certificate of consent study participation – which you will sign to demonstrate that you agree to participate with the interview for this study.

Introduction: We are conducting this study for Médecins Sans Frontières (MSF) and the Ministry of Health in Sokoto to find out more about the risk factors of a disease called noma, which affects mostly children in this part of Nigeria.

What is the study about? Very little is understood about the disease noma, what causes it and why some children develop the disease and others do not. We are wanting to hold key informant interviews with staff at the Noma Children's Hospital to discuss the names used to describe disease, and their beliefs about the disease.

Who will participate in the study? Staff at the Noma Children's Hospital.

What does the participation in the study request from me? The interview should take approximately 30 minutes during your working hours. We would like to ask you some

questions about noma and your role in the project. We would like to record your answers, so that we can have an accurate record of what is said during the interview.

If you do not understand a question, please ask me to explain it to you. If you do not want to answer a question or if you would like to stop at any time, please tell me.

Do we have to participate? Whether you choose to be in the study or not is up to you. There will be no effect on you if you decide you do not want to be in the study. Participation in the study and whatever you say during the interview, will not affect your employment in any way.

What will happen with the information that you collect? We will collect the information from the interviews, and we will then collate all information to see if there are patterns in the information. This information could assist us in gaining an understanding about the disease. We may use some of the stories and experiences you share with us to write reports or press releases to draw attention to noma, if we do so, we will always ensure to anonymize your name and any places you mention.

Where will the study take place? We can conduct the interview anywhere which is convenient for you.

Will I or my family receive anything to participate? You will not get anything, such as money or extra food, for taking part in this survey.

Is it dangerous to participate? You may find some questions upsetting. If a question makes you uncomfortable, we can skip this question and go on to the next question.

What might we get from this study? You are free to stop at any time during the interview. Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are. We hope that the results will help us better understand noma and contribute to finding better ways to prevent and treat this disease in your community.

Confidentiality: The recordings from this study are private. Only the people who are doing the study can see the answers you give to the questions. We do not ask for your name so there will be no record that you participated in the study. I will not repeat what you have told me to anyone else.

Approvals: The ethical aspects of this research have been approved by Médecins sans Frontières Ethics Review Committee and by the Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee.

Queries and Concerns: You can call and speak to us at any time if you want to find out more about this research project.

Study coordinator name and phone number [to be inserted]

Project coordinator name and phone number [to be inserted]

Local Ethics Committee Details for questions regarding rights as research participants:

Dr. Nma Jiya, Address: UDUTH; Phone: +234 805 038 1688.

Thank you very much for your time and participation.

Consent Certificate Adult Study Participant – Copy Study Team

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the interview. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): |__||__| / |__||__| / |__||__|

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the survey team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him/her.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date (insert day/month/year of study): |__||__| / |__||__| / |__||__|

Interviewer's name: _____

Interviewer's signature: _____

Consent Certificate Adult Study Participant – Copy Study Participant

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the interview. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the survey team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him/her.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Interviewer's name: _____

Interviewer's signature: _____

7.2 Risk factors informed consent forms

7.2.1 Cases informed consent form

Project Title: Risk factors for diagnosed noma in North Western Nigeria, a sequential mixed methodology study - 2017.

Organization: Médecins sans Frontières (MSF) and the Ministry of Health.

This informed consent has two parts:

- The information sheet – which gives you information about the study;
- Certificate of consent study participation – which you will sign to demonstrate that you agree to participate with the interview for this study.

Introduction: We are conducting this study for Médecins Sans Frontières (MSF) and the Ministry of Health in Sokoto to find out more about the risk factors of a disease called noma, which affects mostly children in this part of Nigeria. MSF has been running a program to assist noma patients in Sokoto Nigeria, and in order to better understand the disease and improve these services, we would like to ask patients and community members some questions.

What is the study about? Very little is understood about the disease noma, what causes it and why some children develop the disease and others do not. We are trying to understand what factors put some children more at risk of developing noma compared to other children. This information might help MSF and the Ministry of Health to implement programmes to prevent children from developing noma in the future.

First, we will ask the parents or caretakers of parents of noma patients in the MSF project in the Noma Children's Hospital some questions. We will ask the same questions to caretakers or parents of children from the same village without noma who are the same ages and sex as the patients. This will allow us to identify specific risk factors in patients of noma to help us design ways to avoid more children getting this disease in the future.

Who will participate in the study? We will be asking the parents/caretakers of all the patients that are 16 years and younger at the noma project at Noma Children's Hospital in Sokoto to participate in the study, as well as the parents/caretakers of children that are similar to the patients in their home village.

What does the participation in the study request from me? As you are a parent/caretaker of a child who is a noma patient in the Sokoto hospital, we will ask you to spend between 45 minutes to one hour answering the questions we have.

We would like to ask you some questions about things in your life such as the food you eat, where you live, your lifestyle, your health and the health care facilities in your village.

We will ask you questions about the following things:

- People that live in the same house as the participant.
- Living conditions of your household.
- Vaccination status of the child in question at the time of the interview.
- Breastfeeding practices of the mother for the child in question.
- Child's health and access to care for disease in the child in question in the 12 months prior to the interview (apart from noma).

- Access to health care in a general way for your family.
- Child's oral health.

We would also like to measure the circumference of your child's upper arm using this measurement tool (show the MUAC).

If you do not understand a question, please ask me to explain it to you. If you do not want to answer a question or if you would like to stop the survey at any time, please tell me. Also, if you do not want us to measure your child's arm, please tell us and we will not.

Do we have to participate? Whether you choose to be in the study or not is up to you. There will be no effect on your family or your treatment at the hospital if you decide you do not want to be in the study.

What will happen with the information that you collect? We will collect the information from everyone in the study through the interviews like the interview we are conducting with you. We will then compare the answers that parents/caretakers of noma patients gave to the questions to those given by the parents/caretakers of the other children. This will give us some information on understanding what might be contributing to making specific children sick of noma.

The records from this study are private. Only the people who are doing the study can see the answers you give to the questions. We do not ask for your name so there will be no record that you participated in the study. I will not repeat what you have told me to anyone else.

Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are.

Where will the study take place? We can conduct the interview anywhere where you feel comfortable: in your house, at the clinic, anywhere else in the village.

Will I or my family receive anything to participate? You will not get anything, such as money or extra food, for taking part in this survey.

What are the risks of participating in the study? You may find some questions upsetting. If a question makes you uncomfortable, we can skip this question and go on to the next question. Stopping the questionnaire does not impact on the medical care that MSF was providing for you.

What might we get from this study? You are free to stop at any time during the interview. Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are. We hope that the results will help us better understand noma and contribute to finding better ways to prevent and treat this disease in your community.

Confidentiality: The records from this study are private. Only the people who are doing the study can see the answers you give to the questions. We do not ask for your name so there will be no record that you participated in the study. I will not repeat what you have told me to anyone else. Answers from everyone who participates in the study will be grouped together and looked at and it is these findings that will be published, not your specific answers.

Approvals: The ethical aspects of this research have been approved by Médecins sans Frontières Ethics Review Committee and by the Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee.

Queries and Concerns: You can call and speak to us at any time if you want to find out more about this research project.

Study coordinator name and phone number [to be inserted]

Project coordinator name and phone number [to be inserted]

Local Ethics Committee Details for questions regarding rights as research participants:

Dr. Nma Jiya, Address: Usman Danfodiyo University Teaching Hospital.

Phone: +234 805 038 1688.

Thank you very much for your time and participation.

Consent Certificate Adult Study Participant – Copy Study Team

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the questionnaire about the child in my care. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the survey team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him about the child under his/her care.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Interviewer's name: _____

Interviewer's signature: _____

Consent Certificate Adult Study Participant – Copy Study Participant

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the questionnaire about the child in my care. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the survey team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him about the child under his/her care.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Interviewer's name: _____

Interviewer's signature: _____

7.2.2 Controls informed consent form

Project Title: Risk factors for diagnosed noma in North Western Nigeria, a sequential mixed methodology study - 2017.

Organization: Médecins sans Frontières (MSF) and the Ministry of Health.

This informed consent has two parts:

- The information sheet – which gives you information about the study;
- Certificate of consent study participation – which you will sign to demonstrate that you agree to participate with the interview for this study.

Introduction: We are conducting this study for Médecins Sans Frontières (MSF) and the Ministry of Health in Sokoto to find out more about the risk factors of a disease called noma, which affects mostly children in this part of Nigeria. MSF has been running a program to assist noma patients in Sokoto Nigeria, and in order to better understand the disease and improve these services, we would like to ask patients and community members some questions.

What is the study about? Very little is understood about the disease noma, what causes it and why some children develop the disease and others do not. We are trying to understand what factors put some children more at risk of developing noma compared to other children. This information might help MSF and the Ministry of Health to implement programmes to prevent children from developing noma in the future.

First, we will ask the parents and caretakers or parents of noma patients in the MSF project in the Noma Children's Hospital some questions. We will ask the same questions to caretakers

or parents of children from the same village without noma who are the same ages and sex as the patients. This will allow us to identify specific risk factors in patients of noma to help us design ways to avoid more children getting this disease in the future.

Who will participate in the study? We will be asking the parents/caretakers of all the patients that are 16 years and younger at the noma project at Noma Children's Hospital in Sokoto to participate in the study, as well as the parents/caretakers of children that are similar to the patients in their home village.

What does the participation in the study request from me? As you are a parent/caretaker of a child close to the age of a noma patient, we will ask you to spend between 45 - 60 minutes answering the questions we have.

We would like to ask you some questions about things in your life such as the food you eat, where you live, your lifestyle, your health and the health care facilities in your village.

We will ask you questions about the following things:

- People that live in the same house as the participant.
- Living conditions of your household.
- Vaccination status of the child in question at the time of the interview.
- Breastfeeding practices of the mother for the child in question.
- Child's health and access to care for disease in the child in question in the 12 months prior to the interview.
- Access to health care in a general way for your family.
- Child's oral health.

We would also like to measure the circumference of your child's upper arm using this measurement tool (show the MUAC).

If you do not understand a question, please ask me to explain it to you. If you do not want to answer a question or if you would like to stop the survey at any time, please tell me. Also, if you do not want us to measure your child's arm, please tell us and we will not.

Do we have to participate? Whether you choose to be in the study or not is up to you. There will be no effect on your family if you decide you do not want to be in the study.

What will happen with the information that you collect? We will collect the information from everyone in the study through the interviews like the interview we are conducting with you. We will then compare the answers that parents/caretakers of noma patients gave to the questions to those given by the parents/caretakers of the other children. This will give us some information on understanding what might be contributing to making specific children sick of noma.

The records from this study are private. Only the people who are doing the study can see the answers you give to the questions. We do not ask for your name so there will be no record that you participated in the study. I will not repeat what you have told me to anyone else.

Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are.

Where will the study take place? We can conduct the interview anywhere where you feel comfortable: in your house, at the clinic, anywhere else in the village.

Will I or my family receive anything to participate? You will not get anything, such as money or extra food, for taking part in this survey.

What are the risks of participating in the study? You may find some questions upsetting. If a question makes you uncomfortable, we can skip this question and go on to the next question.

What might we get from this study? You are free to stop at any time during the interview. Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are. We hope that the results will help us better understand noma and contribute to finding better ways to prevent and treat this disease in your community.

Confidentiality: The records from this study are private. Only the people who are doing the study can see the answers you give to the questions. We do not ask for your name so there will be no record that you participated in the study. I will not repeat what you have told me to anyone else. Answers from everyone who participates in the study will be grouped together and looked at and it is these findings that will be published, not your specific answers.

Approvals: The ethical aspects of this research have been approved by Médecins sans Frontières Ethics Review Committee and by the Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee.

Queries and Concerns: You can call and speak to us at any time if you want to find out more about this research project.

Study coordinator name and phone number [to be inserted]

Project coordinator name and phone number [to be inserted]

Local Ethics Committee Details for questions regarding rights as research participants:

Dr. Nma Jiya, Address: Usman Danfodiyo University Teaching Hospital.

Phone: +234 805 038 1688.

Thank you very much for your time and participation.

Consent Certificate Adult Study Participant – Copy Study Team

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the questionnaire about the child in my care. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the survey team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him/her about the child under his/her care.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Interviewer's name: _____

Interviewer's signature: _____

Consent Certificate Adult Study Participant – Copy Study Participant

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the questionnaire about the child in my care. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the survey team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him/her about the child under his/her care.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Interviewer's name: _____

Interviewer's signature: _____

7.3 Outcomes informed consent and assent forms

7.3.1 Information sheet and informed consent for retrospective outcome measurement

Project Title: Long-term followup of noma patients after surgical, nutritional and mental health interventions at the Noma Children's Hospital in northwest Nigeria, 2018 - 2020.

Organization: Médecins sans Frontières (MSF) and the Ministry of Health.

This informed consent has two parts:

- The information sheet – which gives you information about the study;
- Certificate of consent study participation – which you will sign to demonstrate that you agree to participate in the assessment for this study.

Introduction: We are conducting this study for Médecins Sans Frontières (MSF) and the Ministry of Health in Sokoto to find out more about the complications after medical treatment for noma at the Noma Children's Hospital. MSF has been running a program to assist noma patients in Sokoto Nigeria, and in order to better understand the disease and improve these services, we would like to ask patients and community members some questions.

What is the study about? Very little is understood about the disease noma. We are trying to understand what complications arise after treatment for noma, and what the factors are that favour survival. This information might help MSF and the Ministry of Health to implement programmes to more efficiently and effectively treat noma patients in the future. During this study, assessments will be conducted on patients who have been treated at the Noma Children's Hospital.

Who will participate in the study? We will be asking noma patients who were cared for at the Noma Children's Hospital since 2015 and are not scheduled for follow up surgery to participate in the study.

What does the participation in the study request from me? As you are a parent/caretaker of a noma patient or a noma patient in the Sokoto hospital, we will ask to examine you/your child. This should take between 10 – 15 minutes.

We will conduct a physical exam to see how you/your child is/are healing.

We would like to take some photographs of you/your child to show to some doctors who will then be able to assess how you are healing. If you do not want us to take any photographs, please tell us and we will not take any. We may use these photographs in presentation, reports or in published articles. If you are not wanting your photograph to be taken, this will not in any way impact the care you receive.

If you do not want to answer a question or if you would like to stop the exam at any time, please tell me as we can stop at any time.

We would also like permission to access your medical files which are stored at the Noma Children's Hospital. This is voluntary and if you would not like us to access your files, this will not in any way impact the care you receive.

I consent to participate in this study (circle)	Yes	No
I consent to grant the research team access to my medical files (circle)	Yes	No

Do we have to participate? Whether you choose to be in the study or not is up to you. There will be no effect on your family or your future treatment at the hospital if you decide you do not want to be in the study.

What will happen with the information that you collect? The records from this study are private. Only the people who are doing the study can see the answers you give to the questions. I will not repeat what you have told me to anyone else. Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are. The pictures we are taking will be stored in a secure folder and only the surgeons assessing the pictures and selected research staff will have access to these. It may be necessary to use your picture in a publication, if you consent to this use. You are free to say no.

Where will the study take place? We can conduct the assessment anywhere where you feel comfortable: in your house, at the clinic, anywhere else in the village.

What are the risks of participating in the study? You may find the physical exam uncomfortable. Stopping the assessment does not impact on the future medical care that MSF may provide for you.

Will I or my family receive anything to participate? There are no direct benefits to the individual. You will not get anything, such as money or extra food, for taking part in this survey.

Will I be told about the results of the study? Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are. We hope that the results will help us better understand noma and contribute to finding better ways to prevent and treat this disease in your community.

Confidentiality: The records from this study are private. Only the people who are doing the study can see the assessment results. I will not repeat what you have told me to anyone else. Answers from everyone who participates in the study will be grouped together and looked at and it is these findings that will be published, not your specific answers.

Approvals: The ethical aspects of this research have been approved by Médecins Sans Frontières Ethics Review Committee and by the Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee.

Thank you very much for your time and participation.

Consent Certificate Adult Study Participant - Copy for Study Team

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to be a part of the assessment. I understand that I can stop the assessment at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): |__||__| / |__||__| / |__||__|

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

If necessary, name and signature of witness: _____

Assessor's name: _____

Assessor's signature: _____

Consent Certificate Adult Study Participant - Copy Study Participant

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to be a part of the assessment. I understand that I can stop the assessment at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

If necessary, name and signature of witness: _____

Assessor's name: _____

Assessor's signature: _____

Queries and Concerns: You can call and speak to us at any time if you want to find out more about this research project.

Principal Investigator: Elise Farley, email: noma-research@oca.msf.org;

Phone: 08025737703

Local Ethics Committee Details for questions regarding rights as research participants:

Dr. Nma Jiya, Address: Usman Danfodiyo University Teaching Hospital.

Phone: +234 805 038 1688.

7.3.2 Assent Form for any Under 18's

Project Title: Outcomes of noma patients following surgical, nutritional and mental health interventions at the Noma Children's Hospital in northwest Nigeria, 2018 - 2020.

Organization: Médecins sans Frontières (MSF) and the Ministry of Health.

This informed assent has two parts:

- The information sheet – which gives you information about the study;
- Certificate of assent study participation – which you will sign to demonstrate that you agree for you to participate in this study.

Introduction: My name is _____ and I work for the organization Médecins sans Frontières (MSF) here in Nigeria. We are working hard to reduce the number of cases of noma in your community and are now doing a study to help us better understand how we can best treat those people who do have noma.

We have already spoken to the head of your household and have also asked your parents for their approval to speak to you and ask you to help us in this study. We will now give you some information about the study and what it would mean for you to participate. You do not have to agree to participate if you do not want to, even if your parents agreed.

You may discuss anything in this form with your parents or friends or anyone else you feel comfortable talking to. You can decide whether to participate or not after you have talked it over. You do not have to decide immediately.

There may be some words you don't understand or things that you want me to explain more about because you are interested or concerned. Please ask me to stop at any time and I will take time to explain).

What is the study about? Very little is understood about the disease noma. We are trying to understand what problems arise after treatment for noma, and what the things help keep people alive. This information might help MSF and the Ministry of Health to implement programmes to more efficiently and effectively treat noma patients in the future. During this study, exams will be conducted on patients who have been treated at the Noma Children's Hospital.

Who will participate in the study? We will be asking noma patients who were cared for at the Noma Children's Hospital to participate in the study.

Do I have to do this? Whether you choose to be in the study or not is up to you. There will be no effect on your treatment at the hospital if you decide you do not want to be in the study.

Check that the child understands what you are telling them by asking: "Do you have any questions at this point? Do you understand that you do not have to participate in the study if you do not want to?

I have checked with the child and they understand that participation is voluntary:

_____ (initial of study interviewer)

What is going to happen to me? As you are a patient who was cared for at the Noma Children's Hospital we would like to conduct some examinations and also ask you/your caretaker some questions. We would also like to take some photographs of you.

We will conduct the following examinations:

- Physical exam to see how you are healing.
- We would also like to measure how much you weight and how tall you are (show the scale and measuring tape).
- We would like to take some photographs of you to show to some doctors who will then be able to assess how you are healing. If you do not want us to take any photographs, please tell us and we will not take any. We may use these photographs in presentation, reports or in published articles. If you are not wanting your photograph to be taken, this will not in any way impact the care you receive.

We will ask you questions about the following things:

- Eating and drinking.
- Social interaction and inclusion.

If you do not understand a question, please ask me to explain it to you. If you do not want to answer a question or if you do want us to conduct a physical exam or if you would like to stop the exam at any time, please tell me.

Check that the child understands what you are telling them by asking: "Can you repeat to me what you remember from me telling you about what will happen to you as part of this study?

I have checked with the child and they understand that procedures of the study:

_____ (initial of study interviewer)

Is it bad or dangerous for me or will it hurt? You may find some questions upsetting and the physical exam uncomfortable. If a question makes you uncomfortable, we can skip this question and go on to the next question, of if you want to stop the physical exam, we can at any time. Stopping the questionnaire does not impact on the medical care that MSF will provide for you.

Check that the child understands what you are telling them by asking: "Do you understand what could be uncomfortable today when we examine you? Can you repeat it back to me?

I have checked with the child and they understand that risks and discomforts of the study:

_____ (initial of study interviewer)

Is there anything good that I might happen to me from this study? You will not get anything extra like food or money for participating in this study. You are free to stop at any time during the interview.

I have checked with the child and they understand the benefits of the study:

_____ (initial of study interviewer)

Is everyone going to know about this and will you tell me the results? The records from this study are private. Only the people who are doing the study can see the answers you give to the questions. I will not repeat what you have told me to anyone else. Answers from everyone

who participates in the study will be grouped together and looked at and it is these findings that will be published, not your specific answers.

Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are. We hope that the results will help us better understand noma and contribute to finding better ways to prevent and treat this disease in your community.

I have checked with the child and they understand that that there is no remuneration for participating in the study and that their information will be kept confidential:

_____ (initial of study interviewer)

What happens if I get hurt? We do not think that you will get hurt today, but in case you don't feel well today or later, you can always ask to be referred and we will try and take care of you as best as possible.

Can I withdraw or refuse to participate? Whether you choose to be in the study or not is up to you. There will be no effect on your family if you decide you do not want to be in the study.

Who can I talk to if I have a question? I will give you copy of the information we have talked about today and this has my information on it, so you can always come and find me or contact me in case you have other questions.

I have checked with the child and they understand what to do if they are hurt, that they can withdraw/refuse to participate at any time and how to contact us if they have more questions:

_____ (initial of study interviewer)

Queries and Concerns: You can call and speak to us at any time if you want to find out more about this research project.

Local Ethics Committee Details for questions regarding rights as research participants:

Dr. Nma Jiya, Address: Usman Danfodiyo University Teaching Hospital (UDUTH).

Phone: +234 805 038 1688.

The ethical aspects of this research have been approved by Médecins Sans Frontières Ethics Review Committee and by the Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee.

Thank you very much for your time and participation.

Assent Certificate Child Study Participant – Copy Study Team

I have read this information (or had the information read to me) and I have had my questions answered and know that I can ask questions later if I have them.

☐	I agree to take part in the research
☐	I do not wish to take part in the research and have not signed the assent below – Initials of the child _____

Only if child assents:

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Print name of child: _____

Signature of child: _____

If the child is illiterate:

A literate witness must sign (if possible, this person should be selected by the participant, not be a parent, and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

I have witnessed the accurate reading of the assent form to the child, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Print name of witness (not a parent): _____

Signature of witness: _____

AND Thumb print of participant

I have accurately read or witnessed the accurate reading of the assent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given assent freely.

Print name of researcher: _____

Assent Certificate Child Study Participant – Copy Study Participant

I have read this information (or had the information read to me) and I have had my questions answered and know that I can ask questions later if I have them.

☐	I agree to take part in the research
☐	I do not wish to take part in the research and have not signed the assent below – Initials of the child _____

Only if child assents:

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Print name of child: _____

Signature of child: _____

If the child is illiterate:

A literate witness must sign (if possible, this person should be selected by the participant, not be a parent, and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

I have witnessed the accurate reading of the assent form to the child, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Print name of witness (not a parent): _____

Signature of witness: _____

AND Thumb print of participant

I have accurately read or witnessed the accurate reading of the assent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given assent freely.

Print name of researcher: _____

7.4 Traditional healer study informed consent forms

7.4.1 Information sheet and informed consent – caretakers

Project Title: Noma and traditional healing in northwest Nigeria, 2018.

Organization: Médecins Sans Frontières (MSF) and the Ministry of Health

This informed consent has two parts:

- The information sheet – which gives you information about the study;
- Certificate of consent study participation – which you will sign/give your thumbprint to demonstrate that you agree to participate in an interview for this study.

Introduction: We are working with Médecins Sans Frontières (MSF) and the Ministry of Health in Sokoto to find out more about a disease called noma, which you may know as *ciwon daji* or *ciwon iska*, this disease mostly affects children in this part of Nigeria.

What is the study about? We want to talk with mothers and other caretakers of noma patients admitted at the Noma Children's Hospital to help us understand more about traditional healing and noma. With your agreement, we would like to ask you some questions on how you feel about traditional healing, your relationships with traditional healers, and if you have visited traditional healers for help with your child's current noma condition.

Who will participate in the study? Caretakers of noma patients admitted at the Noma Children's Hospital and traditional healers will be invited to take part. You were chosen as you are the caretaker of a noma patient who is admitted at the Noma Children's Hospital at the time we are conducting the study. We are hoping to include 40 people in the study.

What does the participation in the study mean for me? The interview should take approximately 30 - 60 minutes. We would like to ask you some questions about traditional healing and the health care you tried for noma. With your permission we would like to audio-record your answers, so that we can have an accurate record of what is said during the interview.

If you do not understand a question, please ask me to explain it to you. If you do not want to answer a question or if you would like to stop at any time, please tell me.

Do we have to participate? Whether you choose to be in the study or not is up to you. There will be no effect on you if you decide you do not want to be in the study. Participation in the study and whatever you say during the interview, will not affect the health care you or your family receive in any way. You are free to stop the interview at any time.

What will happen with the information that you collect? We will collect the information from the interviews to learn as much as we can about traditional healing and noma in this area. This information could assist us in gaining an understanding about the disease. We may use some of the stories and experiences you share with us to write reports or news stories to draw attention to noma, or give presentations. If we do this, we will make sure not to include your name and any places you mention so that no-one will know it is you.

Where will the study take place? We can conduct the interview anywhere which is convenient for you.

Will I or my family receive anything to participate? You will not get anything, such as money or extra food, for taking part in this study.

Is it dangerous to participate? There will be no danger to you in this study. You may find some questions upsetting. If a question makes you uncomfortable, we can skip this question and go on to the next question. If you would like to see one of the mental health officers we can arrange an appointment.

What might we get from this study? Once we have the results of this study, we will send an announcement to the health clinics and with the outreach team and you will be able to find out more about what we have learned. We hope that the results will help us better understand noma so we can find better ways to prevent and treat this disease in your community.

Confidentiality: The recordings from this study are private. Only the people who are doing the study can see the answers you give to the questions. We do not ask for your name while conducting the interview, only on the consent form. I might repeat what you tell me to other people in the research team, but I will never link it to you directly or use your name.

Approvals: This study has been approved by Médecins Sans Frontières Ethics Review Board and by the Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee. [reference numbers to be added once approved]. If you have questions about the study you can contact [details of ERB] and [details of PI].

Consent Certificate Adult Study Participant – Copy Study Team

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the interview and for my answers to be recorded. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Study participant agrees to the audio recording

of interview signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the research team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him/her.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Interviewer's name: _____

Interviewer's signature: _____

Consent Certificate Adult Study Participant – Copy Study Participant

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the interview and for my answer to be recorded. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Study participant agrees to the audio recording

of interview signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the research team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him/her.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Interviewer's name: _____

Interviewer's signature: _____

Queries and Concerns: You can call and speak to us at any time if you want to find out more about this research project. For questions around the ongoing research you should contact the study investigator. For any concerns around ethical implications of the research, you should contact the ERB.

Study coordinator name and phone number [to be inserted]

Local Ethics Committee Details for questions regarding rights as research participants:

Dr. Nma Jiya, Address: Usman Danfodiyo University Teaching Hospital.

Phone: +234 805 038 1688.

7.4.2 Information sheet and informed consent – traditional healers

Project Title: Noma and traditional healing in northwest Nigeria, 2018.

Organization: Médecins sans Frontières (MSF) and the Ministry of Health

This informed consent has two parts:

- The information sheet – which gives you information about the study;
- Certificate of consent study participation – which you will sign to demonstrate that you agree to participate with the interview for this study.

Introduction: We are conducting this study for Médecins Sans Frontières (MSF) and the Ministry of Health in Sokoto to find out more about a disease called noma, which you may know as *ciwon daji* or *ciwon iska*, this disease mostly affects children in this part of Nigeria.

What is the study about? We want to ask some questions to traditional healers in Sokoto State to understand what they think of noma, their relationship with community members and to understand more about the treatments offered for noma patients.

Who will participate in the study?

Caretakers of noma patients admitted at the Noma Children's Hospital and traditional healers will be invited to take part. You were invited to participate in the study as you are known in the community as someone who provides health care to the population. We are hoping to include 40 people in the study.

What does the participation in the study mean for me? The interview should take approximately 30 - 60 minutes. We would like to ask you some questions about your work and noma disease. We would like to audio-record your answers, so that we can have an accurate record of what is said during the interview.

If you do not understand a question, please ask me to explain it to you. If you do not want to answer a question or if you would like to stop at any time, please tell me.

Do we have to participate? Whether you choose to be in the study or not is up to you. There will be no effect on you if you decide you do not want to be in the study. You are free to stop the interview at any time.

What will happen with the information that you collect? We will collect the information from the interviews to learn as much as we can about traditional healing and noma in this area. This information could assist us in gaining an understanding about the disease. We may use some of the stories and experiences you share with us to write reports or news stories to draw attention to noma, or give presentations. If we do this, we will make sure not to include your name and any places you mention so that no-one will know it is you.

Where will the study take place? We can conduct the interview anywhere which is convenient for you.

Will I or my family receive anything to participate? You will not get anything, such as money for taking part in this study. A refreshment of water and a snack will be given.

Is it dangerous to participate? There will be no danger to you in this study. You may find some questions upsetting. If a question makes you uncomfortable, we can skip this question and go on to the next question or we can stop the interview at any time.

We are not trying to test your knowledge on any subject, and we do not want to learn your healing techniques so that we can use them ourselves. We are trying to understand what you think about the disease, and how we can work together to help the people who suffer from this disease.

What might we get from this study? Once we have the results of this study, we will send an announcement to the health clinics and with the outreach team and you will be able to find out more about what we have learned. We hope that the results will help us better understand noma so we can find better ways to prevent and treat this disease in your community and we may find better ways to work together.

Confidentiality: The recordings from this study are private. Only the people who are doing the study can see the answers you give to the questions. We do not ask for your name while conducting the interview, only on the consent form. I might repeat what you tell me, but I will never link it to you directly.

Approvals: This study has been approved by Médecins Sans Frontières Ethics Review Board and by the Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee. [reference numbers to be added once approved]. If you have questions about the study you can contact [details of ERB] and [details of PI].

Consent Certificate Adult Study Participant – Copy Study Team

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer the questions in the interview and for my answers to be recorded. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): |__||__| / |__||__| / |__||__|

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Study participant agrees to the audio recording

of interview signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the research team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him/her.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Interviewer's name: _____

Interviewer's signature: _____

Consent Certificate Adult Study Participant – Copy Study Participant

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the interview and for my answer to be recorded. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Study participant agrees to the audio recording

of interview signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the research team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him/her.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Interviewer's name: _____

Interviewer's signature: _____

Queries and Concerns: You can call and speak to us at any time if you want to find out more about this research project. For questions around the ongoing research you should contact the study investigator. For any concerns around the ethical implications of the research, you should contact the ethics review board.

Study coordinator name and phone number [to be inserted]

Local Ethics Committee Details for questions regarding rights as research participants:

Dr. Nma Jiya, Address: Usman Danfodiyo University Teaching Hospital.

Phone: +234 805 038 1688.

7.5 Prevalence informed consent and assent forms

7.5.1 Information sheet and informed consent

Project Title: Determining the prevalence of all stages of noma and n0ma in northwest Nigeria.

Organization: Médecins sans Frontières (MSF) and the Ministry of Health.

This informed consent has two parts:

- The information sheet – which gives you information about the study;
- Certificate of consent study participation – which you will sign to demonstrate that you agree to participate with the interview for this study.

Introduction: We are conducting this study for Médecins Sans Frontières (MSF) and the Ministry of Health in Sokoto to find out how many people have noma in northwest Nigeria. MSF has been running a program to assist noma patients in Sokoto Nigeria, and in order to better understand the disease and improve these services, we would like to ask community members some questions.

What is the study about? Very little is understood about the disease noma. We are trying to find out how many people have noma in northwest Nigeria. This information might help MSF and the Ministry of Health to implement programmes to more efficiently and effectively treat noma patients in the future.

Who will participate in the study? During this study, questions will be asked to community members who live in either Sokoto or Kebbi states. Your village and household was chosen at random by the research team.

What does the participation in the study request from me? As you are a parent/caretaker of a child who lives in either Sokoto or Kebbi States, we will ask you to spend between 15 - 30 minutes answering some questions and being examined.

We will conduct the following examinations:

- Physical oral health exam.
- We would also like to measure the circumference of you/ your child's upper arm using this measurement tool (show the MUAC).
- Weight.
- Height.

We will ask you questions about the following things:

- Vaccinations.
- Previous illness.
- Health seeking practices.
- Feeding practices.
- Water source.

We will also ask if any children under the age of 15 years who live in your household have died in the year preceding data collection, and if so, we would like to assess the cause of death and so will request to ask you some questions about the signs and symptoms that occurred before death. You do not have to answer any of these questions if you do not wish to.

If you do not understand a question, please ask me to explain it to you. If you do not want to answer a question or if you would like to stop the survey at any time, please tell me. Also, if you do not want us to conduct any of the measurements, please tell us and we will stop.

What will happen if the exam shows that my child may have noma? If the research team think your child may have noma, then if it is at a very early stage, the team will give you advice on the best things you can do to look after your child. If the team think your child is at a later stage of the sickness, then they will either refer you to your closest health centre or to the Noma Children's Hospital (NCH) in Sokoto, where you will be taken care of by the Ministry of Health and MSF. If the team advises you to go to the NCH, transportation will be provided for you.

Do we have to participate? Whether you choose to be in the study or not is up to you. There will be no effect on your family if you decide you do not want to be in the study.

What will happen with the information that you collect? The records from this study are private. Only the people who are doing the study can see the answers you give to the questions. I will not repeat what you have told me to anyone else. Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are.

Where will the study take place? We can conduct the interview anywhere where you feel comfortable: in your house, at the clinic, anywhere else in the village.

Will I or my family receive anything to participate? You will not get anything, such as money or extra food, for taking part in this survey.

What are the risks of participating in the study? You may find some questions upsetting or the physical measurements and exams uncomfortable. If you are uncomfortable at any time, tell us and we can stop and skip this question and go on to the next question.

What might we get from this study? You are free to stop at any time during the interview. Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are. We hope that the results will help us better understand noma and contribute to finding better ways to prevent and treat this disease in your community.

Confidentiality: The records from this study are private. Only the people who are doing the study can see the answers you give to the questions. I will not repeat what you have told me to anyone else. Answers from everyone who participates in the study will be grouped together and looked at and it is these findings that will be published, not your specific answers.

Approvals: The ethical aspects of this research have been approved by Médecins Sans Frontières Ethics Review Committee and by the Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee.

Thank you very much for your time and participation.

Consent Certificate Adult Study Participant – Copy Study Team

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the questionnaire about the child in my care. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the survey team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him/her about the child under his/her care.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Interviewer's name: _____

Interviewer's signature: _____

Consent Certificate Adult Study Participant – Copy Study Participant

Please administer the information sheet before seeking consent!

I have understood the information sheet and my questions have been answered to my satisfaction. I give voluntary consent to answer all the questions in the questionnaire about the child in my care. I understand that I can stop the interview at any time.

I hereby declare that I consent to the above.

Date (insert day/month/year of study): ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦

Name of study participant (≥18 years): _____

Study participant signature/thumb print: _____

Interviewer's name: _____

Interviewer's signature: _____

If the person is illiterate (to be completed by the survey team):

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that we will conduct an interview with him/her about the child under his/her care.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Consent Certificate has been provided to the participant.

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Interviewer's name: _____

Interviewer's signature: _____

Queries and Concerns: You can call and speak to us at any time if you want to find out more about this research project.

Local Ethics Committee Details for questions regarding rights as research participants:

Dr. Nma Jiya, Address: Usman Danfodiyo University Teaching Hospital.

Phone: +234 805 038 1688.

7.5.2 Information sheet and verbal assent for study participation by child from 8 to 15 years of age (following informed consent of parent/caretaker).

Project Title: Determining the prevalence of all stages of noma and noma in northwest Nigeria.

Organization: Médecins sans Frontières (MSF) and the Ministry of Health.

This informed consent has two parts:

- The information sheet – which gives you information about the study;
- Certificate of consent study participation – which you will sign to demonstrate that you agree to participate with the interview for this study.

Information Sheet Child Assent

Introduction: My name is _____ and I work for the organization Médecins sans Frontières (MSF) here in Nigeria. We are working hard to reduce the number of cases of noma in your community and are now doing a study to help us better understand how many people are getting sick in Nigeria from this disease and what else we can do to help stop new cases from occurring.

We have already spoken to the head of your household and have also asked your parents for their approval to speak to you and ask you to help us in this study. We will now give you some information about the study and what it would mean for you to participate. You do not have to agree to participate if you do not want to, even if your parents agreed.

You may discuss anything in this form with your parents or friends or anyone else you feel comfortable talking to. You can decide whether to participate or not after you have talked it over. You do not have to decide immediately.

There may be some words you don't understand or things that you want me to explain more about because you are interested or concerned. Please ask me to stop at any time and I will take time to explain).

What is the study about? Very little is understood about the disease noma. We are trying to find out how many people have noma in northwest Nigeria. This information might help MSF and the Ministry of Health to implement programmes to more efficiently and effectively treat noma patients in the future.

Who will participate in the study? During this study, questions will be asked to community members who live in either Sokoto or Kebbi States. Your village and household was chosen at random by the research team.

Do I have to do this? You can choose if you want to participate in the study or not. It is completely up to you. If you decide not to participate in this study, that is ok and nothing changes. You and your family can still come to our hospital when you are sick. If you say yes now, but change your mind later to not participate, that is also ok!

Check that the child understands what you are telling them by asking: "Do you have any questions at this point? Do you understand that you do not have to participate in the study if you do not want to?

I have checked with the child and they understand that participation is voluntary:

_____ (initial of study interviewer)

What is going to happen to me? As you are a child who lives in either Sokoto or Kebbi States, we will ask you to spend between 15 - 30 minutes answering some questions and being examined.

We will conduct the following examinations:

- Physical oral health exam.
- We would also like to measure the circumference of you/ your child's upper arm using this measurement tool (show the MUAC).
- Weight.
- Height.

We will ask you questions about the following things:

- Vaccinations.
- Previous illness.
- Health seeking practices.
- Feeding practices.
- Water source.

If you do not understand a question, please ask me to explain it to you. If you do not want to answer a question or if you would like to stop the survey at any time, please tell me. Also, if you do not want us to conduct any of the measurements, please tell us and we will stop.

Check that the child understands what you are telling them by asking: "Can you repeat to me what you remember from me telling you about what will happen to you as part of this study?

I have checked with the child and they understand that procedures of the study:

_____ (initial of study interviewer)

Is it bad or dangerous for me or will it hurt? You may find some questions upsetting or the physical measurements and exams uncomfortable. If you are uncomfortable at any time, tell us and we can stop and skip this question and go on to the next question.

Check that the child understands what you are telling them by asking: "Do you understand what could be uncomfortable today when we examine you? Can you repeat it back to me?

I have checked with the child and they understand that risks and discomforts of the study:

_____ (initial of study interviewer)

Is there anything good that I might happen to me from this study?

You will not get anything extra like food or money for participating in this study. You are free to stop at any time during the interview.

I have checked with the child and they understand that benefits the study:

_____ (initial of study interviewer)

Is everyone going to know about this and will you tell me the results? The records from this study are private. Only the people who are doing the study can see the answers you give to the questions. I will not repeat what you have told me to anyone else. Answers from everyone who participates in the study will be grouped together and looked at and it is these findings that will be published, not your specific answers.

Once we have the results of this study, we will send an announcement to the health clinics and you will be able to find out what our conclusions are. We hope that the results will help us better understand noma and contribute to finding better ways to prevent and treat this disease in your community.

I have checked with the child and they understand that that there is no remuneration for participating in the study and that their information will be kept confidential:

_____ (initial of study interviewer)

What happens if I get hurt? We do not think that you will get hurt today, but in case you don't feel well today or later, you can always ask to be referred and we will try and take care of you as best as possible.

Can I withdraw or refuse to participate? Whether you choose to be in the study or not is up to you. There will be no effect on your family if you decide you do not want to be in the study.

Who can I talk to if I have a question? I will give you copy of the information we have talked about today and this has my information on it, so you can always come and find me or contact me in case you have other questions.

I have checked with the child and they understand what to do if they are hurt, that they can withdraw/refuse to participate at any time and how to contact us if they have more questions:

_____ (initial of study interviewer)

Queries and Concerns: You can call and speak to us at any time if you want to find out more about this research project.

Local Ethics Committee Details for questions regarding rights as research participants:

Dr. Nma Jiya, Address: Usman Danfodiyo University Teaching Hospital.

Phone: +234 805 038 1688.

The ethical aspects of this research have been approved by Médecins Sans Frontières Ethics Review Committee and by the Usman Danfodiyo University Teaching Hospital (UDUTH) Health Research and Ethics Committee.

Thank you very much for your time and participation.

Assent Certificate Child Study Participant – Copy Study Team

I have read this information (or had the information read to me) and I have had my questions answered and know that I can ask questions later if I have them.

☐	I agree to take part in the research
☐	I do not wish to take part in the research and have not signed the assent below – Initials of the child _____

Only if child assents:

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Print name of child: _____

Researcher confirms that child offers verbal assent_____

Print name of researcher: _____

Assent Certificate Child Study Participant – Copy Study Participant

I have read this information (or had the information read to me) and I have had my questions answered and know that I can ask questions later if I have them.

☐	I agree to take part in the research
☐	I do not wish to take part in the research and have not signed the assent below – Initials of the child _____

Only if child assents:

Date: ¦__¦¦__¦ / ¦__¦¦__¦ / ¦__¦¦__¦ *[insert day/month/year of the study]*

Print name of child: _____

Researcher confirms that child offers verbal assent_____

Print name of researcher: _____