Prevalence, incidence, and reported global distribution of noma: a systematic literature review

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Noma (*cancrum oris*) is a severely debilitating orofacial disease. The global annual incidence and prevalence figures of noma are outdated and were not based on epidemiological studies. Therefore, we systematically reviewed the scientific literature about the prevalence, incidence, and reported global distribution of noma. We searched ten databases and Google Scholar from 1950 up to Sept 23, 2020. We used an adapted Newcastle–Ottawa scale for quality assessment of the studies we included. Epidemiological data could be extracted from eight publications. Because of the differences in quality and the limited geographical range of the studies, no new estimate of the global incidence and prevalence of noma could be calculated. Our updated world map indicates that patients with noma were diagnosed in at least 23 countries in the past decade. Additionally, we identified a strong focality, with most cases being reported from only a few countries in west Africa. This systematic review has identified a striking scarcity of research and surveillance programmes considering noma. We argue that a first step to noma elimination should be the inclusion of noma in the WHO list of neglected tropical diseases, followed by broad-based integrated control programmes aiming at noma elimination.

Lancet Infect Dis 2022

Published Online
March 15, 2022
https://doi.org/10.1016/S1473-3099(21)00698-8

See Online/Comment
https://doi.org/10.1016/S1473-3099(22)00136-0

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Introduction

Noma (*cancrum oris*) is a rapidly progressing, invasive, and debilitating orofacial disease that affects the most vulnerable and marginalised populations worldwide. First descriptions of the disease date back to antiquity.[1,2] Throughout history, the disease accompanied conditions of extreme food insecurity, poverty, poor health, and deficient sanitary conditions.[1] Indeed, the people most at risk of acute noma are children between the ages of 2 years and 6 years, living in poverty and exposed to other key risk factors, such as malnutrition and infectious diseases including measles, malaria, and HIV, which weaken the immune system.[3] The absence of safe water, poor sanitation, and living in proximity to live stock have also been associated with the disease.[4–6] Risk factors of noma persist through inequities, many of which are targeted by the UN Sustainable Development Goals (SDGs) in the 2030 agenda.[7] Given the living conditions of those affected and considering that noma causes severe facial disfigurement, the term face of poverty has been used to describe the disease.[8,9]

In endemic countries, noma is described by a variety of local names derived from different beliefs about the disease.[10,11] Moreover, the different disease stages are often viewed as separate entities by traditional healers.[12] The causes of noma are not fully understood. Immune-system impairments, such as those that occur following chronic malnutrition and as a result of certain infectious diseases appear to have a major role in the pathogenesis of noma.[13] Genomic studies suggest that in affected individuals, a disequilibrium in the oral microflora might allow opportunistic pathogens to proliferate and ultimately cause noma.[14,15] The non-communicable disease presents in five stages, the first three stages develop over 1–2 weeks. If left untreated, noma is estimated to result in a mortality rate of 80–90%.[2,8,16] An early warning sign in at-risk individuals is simple gingivitis, which can develop into acute necrotising gingivitis (ANG), the first stage of noma. Stage two is characterised by the formation of a transient facial oedema with halitosis and high fever, which represents the start of acute noma and is a medical emergency because it is the last reversible stage of the disease. If left untreated, the infection can progress into the life-threatening third stage, characterised by a rapidly-spreading necrotising gangrenous infection with irreversible effects on the perioral skin, mucosa, muscles, and bones. If the child survives to the fourth stage, wound healing and scarring occur over several months, leading to facial deformities and potentially trismus and ankyloses of bones and joints.[16] The final stage, noma sequelae, is reached after around 1 year, and is often characterised by major functional, visual, and physical disabilities, which complicate nutritional intake and are highly stigmatising, often resulting in social exclusion and important effects on mental health.[16–18]

Key messages

- This is the first systematic literature review focusing on the global incidence and prevalence of noma
- Most noma cases have been reported in west Africa, where noma programmes are in place, whereas the number of noma cases reported correlates with the amount of literature per country
- New countries with noma incidence or prevalence, especially in southeast Asia and Latin America, where noma occurrence has been missed in previous reports have been identified in this study
- This Systematic Review identified a prominent data gap in noma research, especially with regard to population-based epidemiological studies investigating noma incidence and prevalence
- A first step towards integrated control programmes and efforts towards elimination is the inclusion of noma in the WHO list of neglected tropical diseases

A diagnosis of noma is established clinically and criteria differ across stages. In the differential diagnosis of noma stage four to five, congenital malformations, such as cleft lip, as well as ulcerous and necrotising infections with shared characteristics have to be considered, including agranulocytic angina, malignant oral lesions, midline granuloma of the face, and syphilis.[2,3,5] A related disease with a similar clinical picture is noma neonatorum. This disease mainly affects preterm or low-birthweight infants, in most cases with *Pseudomonas aeruginosa, Escherichia coli, Klebsiella* spp, or *Staphylococcus* spp infections.[3,19] Almost all patients who have noma neonatorum succumb to the disease following sepsis.[5] Noma neonatorum and other common ulcerous and necrotising infections are readily distinguished from well established noma in children.[5,20] Cases of noma-like lesions in adults who are immunocompromised with HIV or leukaemia have also been reported.[4,21] By contrast to classical noma in children, this form of the disease occurs anywhere in the world.[4,22] The treatment of noma is dependent on the disease stage. Up until stage two, noma can be cured relatively easily with antibiotics directed against opportunistic infections, improved oral hygiene including chlorhexidine mouthwash, and nutritional support. In the third and fourth stage, treatment of lesions and debridement of necrotic tissues are additionally required to prevent sepsis. In stages four and five, physiotherapy is essential for muscular contractures (eg, trismus) and ankylosis prevention. Most survivors of noma need reconstructive surgery.[16] Although systemic noma prevention depends on the elimination of key risk factors related to poverty, such as unsafe water, insufficient sanitation, and malnutrition, effective preventive activities should focus on surveillance and early diagnosis on the basis of awareness raising among parents and health personnel.[12,23]

See Online for appendix

Noma was regularly reported in settings in Europe and North America, especially during and in the aftermath of war and famines.[8] Improvements in health care and hygiene standards, alongside general socioeconomic development, led to a gradual decline in the number of cases in the 19th century. After World War 2, cases became rare in developed countries.[5,8] Today, noma cases are mainly reported in low-income countries, with most cases occurring in west Africa.[3,4,24,25] In 1998, the global annual incidence of noma was estimated at 140 000 cases, with a prevalence of 770 000 noma survivors.[26] Noma prevalence is represented by the survivors of noma, mainly adults with facial deformities and disabilities.

Recognising the scarcity of high-quality evidence on the global incidence, prevalence, mortality, and distribution of noma because of limited awareness and insufficient recording and reporting, we systematically reviewed the existing literature on noma to provide a foundation for policy makers to establish national and international monitoring programmes, offer a reference for non-governmental organisations (NGOs) working with noma survivors, and to support the promotion of child health in low-resource settings. Although the focus was on the classical form of the condition, namely noma with onset in children, evidence for noma among other groups was also collected.

Methods

Search strategy and selection criteria

We did a systematic review in alignment with the requirements laid out in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement and registered with PROSPERO, number CRD42021234680.[27] We searched the following ten databases for peer-reviewed and grey literature on 23 Sept, 2020, from 1950 to 2020: PubMed, ISI Web of Science, Scopus, CINAHL, Global Index Medicus, WHO Institutional Repository for Information Sharing, WHO AFROLIB, Embase, African Journals Online, and the System for Information on Grey Literature in Europe (also known as OpenGrey). The different names of noma, such as *cancrum oris* or gangrenous stomatitis, were used as search terms (appendix p 1). The search strategy made use of the database thesauri wherever applicable and combined the controlled vocabularies with standard keyword searches by applying Boolean operators. In addition, we searched Google Scholar for "noma" and "*cancrum oris*". This search engine works with search syntaxes sorting matches by relevance.[28] Therefore, upon consultation with a librarian and taking into account the scarcity of the available literature on noma, only the first 400 search results were considered in the current review to avoid the screening of large numbers of documents that are not related to the study question. Furthermore, bibliographies of included studies and reference papers on noma were hand searched, and experts were consulted to identify any additional literature.

No language or study-type restrictions were set for the searches. Translation of non-English-language publications was done with Google Translate or by native speakers working in the Swiss Tropical and Public Health Institute. The only criteria for exclusion were studies on animals and publications in which no full text could be obtained even with the help of academic library staff, Google, or Google Scholar, after contacting the authors and noma experts, or with swisscovery, a library catalogue combining more than 470 Swiss libraries.

In a first step, all documents were reviewed and indexed for different research interests. To assess current knowledge and data on the epidemiology of noma, only population-based epidemiological studies published since 1998 and done according to a clearly described survey approach as well as WHO reports were considered. The time period was chosen in view of the last comprehensive attempt at estimating the global incidence of noma in 1998.[26] The reported global distribution of noma (1950–2019) was established on the basis of case reports and surgical reports including noma in adults who were immunocompromised, retrospective

hospital studies and WHO reports, and general publications about noma with a section focusing on its geographical distribution.

Review process

All results obtained from the implementation of the search strategies were imported into the bibliographic software EndNote X9 (Clarivate Analytics, Philadelphia, PA, USA; 2013) for further management. A first set of duplicates was removed using an automated feature in EndNote X9. In a next step, the references were uploaded into the systematic-review software Covidence (Veritas Health Innovation, Melbourne, VIC, Australia), in which another automated search for duplicates was done before manually removing remaining duplicates in the frame of the first screening process. The title and abstract of each document were independently screened by two reviewers (AG and CB) to establish wether the document addressed *cancrum oris* and whether it should be considered for full-text screening. If the two reviewers disagreed on the status of a document, the assessment was discussed until agreement was reached. The full text of all retained articles was screened by at least one reviewer (AG or CB) for relevance against the study objectives. In case of uncertainty, the two reviewers consulted each other. If the consultation did not lead to a decision, another team member (MSW or PS) was consulted. For quality control, 50 full texts were double screened by both reviewers in the first phase of the full-text review to avoid having to repeat the screening of more than 1000 full texts in case of insufficient agreement. Four diverging decisions resulted, and decision parameters were more clearly defined to ensure alignment between reviewers. Relevant data were extracted from retained full texts including the 21 records identified through other sources and entered into a Microsoft Excel (Microsoft Cooperation, Redmond, WA, USA; 2016) spreadsheet. Extracted data included incidence, prevalence, mortality, sequelae, disease stage, treatment, remission and cure rates, diagnostic and verification techniques, study type, study area, year of study, study population, and bibliographic details of the reference.

Study quality assessment

The quality of the included case-control studies was assessed with the Newcastle–Ottawa scale (NOS).[29] Because there is no similar tool for cross-sectional studies, we adapted a scale used for podoconiosis studies, derived from NOS, to our needs (appendix pp 2–3).[29,30] As NOS allocates a maximum of nine quality points and the adapted version a maximum of ten, the different study types were evaluated separately. All of the included studies were independently rated by both reviewers (CB and AG) and consensus was established to ensure consistency.

Mapping the reported global distribution of noma

Maps showing the reported global distribution of noma were created on the basis of several variables, comprising year, number of cases, country, and, if available, subnational location. The number of cases and publications were summarised by country and subnational level for the periods 1950–79, 1980–89, 1990–99, 2000–09, and 2010–19. Reports of noma cases before 1950 were excluded to focus on more recent cases. An entire country was colour coded for the respective decade, even if only one case was reported. Acute noma cases provided the basis for displaying the reported global distribution of noma whereas surgical and noma-survivor reports were included if year of disease onset was available. Noma cases were equally distributed by year for multiyear summary reports. Similarly, whenever cases from more than one subnational region were reported without further geographical information, cases were allocated equally between regions.

On the basis of this information, world maps were created to visualise the reported global epidemiological information of noma. Endemic countries were classified according to the time of the most recent reported noma case among children, whereas distinct locations were identified in cases of noma among adults who were immunocompromised. The number of noma reports and cases per country and at subnational level were also displayed. All maps were created using QGIS Geographic Information System (Open Source Geospatial Foundation 2020, version 3.16; Oregon, USA).

Results

A total of 4238 unique documents were identified by applying the search strategy to the different databases. Another 21 documents were identified by hand searching reference lists and through recommendations of experts (figure 1). The full text was inaccessible for 227 of these documents, mostly old records that were not digitally available. The most common reason for exclusion in subsequent steps was a focus on acute necrotising ulcerative gingivitis or acute necrotising gingivitis (mentioned in figure 1 as wrong outcomes). Epidemiological data such as prevalence, incidence, or mortality could be extracted from seven publications summarising data from cross-sectional studies and one case-control study (table). The description of the sampling strategy was superficial in most cases, with only two studies stating explicit details of their procedures.[31,32] Strategies to address confounding factors were only mentioned by three publications.[31,33,34] Three of the cross-sectional studies were of high quality (NOS scores 7–10), whereas one study had a high risk of bias (NOS score 6), and three studies had a very high risk of bias (NOS score 1–2). The case-control study was of high quality (NOS score 8; table).[13]

Epidemiology

The relevant characteristics of the cross-sectional and case-control studies included in this systematic review are

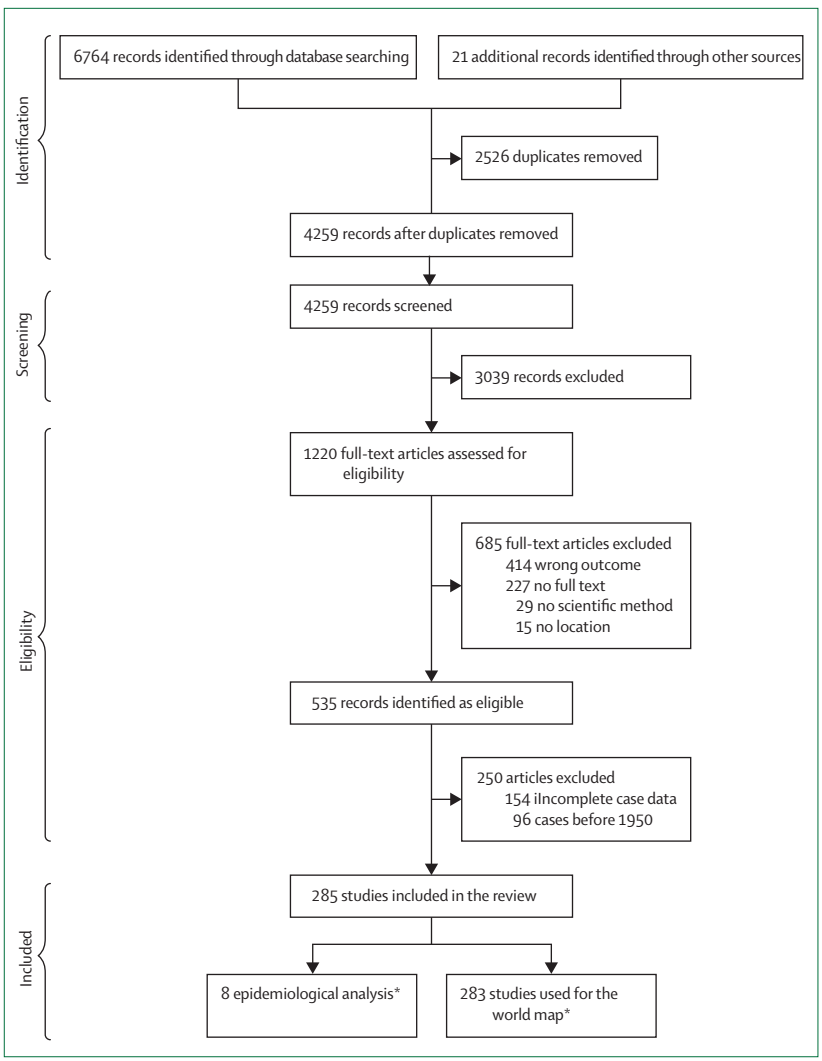

Figure 1: **Prisma flow diagram**
*Overlap between studies used for the epidemiological analysis and the world map.

summarised (table). The studies of high quality were done in Nigeria, Niger, and Ethiopia; the most recent study took place in Nigeria in 2018.[13,31–33] This study was also the only survey that followed a study design that included a clearly randomised sampling method (covering two Nigerian states) using villages as clusters to assess noma prevalence in children younger than 15 years of age.[31] Two other high-quality studies were based on patient data from hospitals and non-governmental organisations (NGOs),[32,33] whereas one study used a prospective matched case-control design.[13] A study done in north-central Nigeria used patient data from surgical outreach locations of the NGO Cleft and Facial Deformity Foundation generated between 2010 and 2018.[33] Similarly, the study done in Ethiopia used patient data from the NGO Project Harar Ethiopia, where patients who were potentially eligible for facial reconstructive surgery were recruited by local social workers.[32] The team also revisited the patients for a follow-up and confirmation of the noma diagnosis. Only one study[31] reported the 95% CIs of calculated prevalence or incidence data. Farley and colleagues[31] were also unique in reporting the survey coverage. All high-quality studies used clinical diagnosis to assess presence of noma with three studies following clearly-stated diagnostic guidelines.[31–33] The same studies reported an age-specific prevalence or incidence that was further refined into subgroups, such as location-specific or sex-specific cohorts. The response rate observed in the surveys was mentioned by two studies.[31,32]

The study with a high risk of bias used patient records from a Nigerian children's hospital but did not elaborate on the origin of the files.[34] Instead, the authors calculated noma incidence by comparing patients with noma to those with cleft lip with a logistic regression model. Noma was diagnosed clinically and the incidence was further divided into subgroups by location.

The studies with a very high risk of bias were done in Nigeria, Senegal, and Mali.[35–37] The Malian study summarised NGO patient data (NGO Au Fil de la Vie) collected from 2004 to 2009.[37] These patients were recruited in the frame of noma detection and sensitisation missions. The Nigerian study[35] used a cross-sectional case-detection design, whereas the project in Senegal[36] did not clearly describe any methodology. All of these studies diagnosed noma clinically.

Prevalence estimates varied widely between these studies, from 0·6 per 100 000 people in Kogi state, Nigeria (NOS score 7),[33] to 3300 per 100 000 people in Sokoto and Kebbi states, Nigeria (NOS score 10).[31] This high estimate is based on the WHO noma classification and includes stages zero to five (ie, simple gingivitis, acute necrotising ulcerative gingivitis, oedema, gangrenous stage, scarring, and sequelae).[31] The next highest prevalence estimate is 23·6 per 100 000 children aged 14 years and younger in the Senegalese St Louis region (NOS score 2).[36]

Noma annual incidence estimates at regional and national level varied from 1·64 to 13·4 per 100 000 children aged 0–9 years in eastern Ethiopia (NOS score 9)[32] to 8·3 per 100 000 people in north-central Nigeria (NOS score 7).[33] Fieger and colleagues[34] calculated an annual incidence of 640 per 100 000 people in northwest Nigeria on the basis of surgical admissions of patients with cleft lip and noma aged 10–30 years (NOS score 6). The incidence at the regional level had been estimated to be 25 600 cases per year in sub-Saharan Africa and 30 000–40 000 globally (NOS score 6).[34] The highest incidence of noma onset was documented in children aged 0–10 years in all of the included studies. Mortality data were scarce in the surveys. Only Baratti-Mayer and colleagues[13] reported a mortality rate of 8·5% in the 85 children included in their case-control study done in the Zinder region of Niger from 2001 to 2006 (NOS score 8). Of note, these children were admitted for health care and received appropriate treatment.

	Country and location	Survey year	Study design	Diagnostic approach	Active cases	Sample size	Prevalence per 100 000 people	Incidence per 100 000 people	Age of onset, years	Mortality	Quality score
Farley et al, 2020[31]	Nigeria: villages in Sokoto and Kebbi states	2018	Two stage cluster-based cross-sectional surveys	Clinical diagnosis following WHO guidelines	194 total cases: ten stage 1, three stage 2, and zero stage 3–5 cases	7122 children aged <15 years	3300 cases of any stage and 150 stage 1 or stage 2 cases	NA	0–5	NA	10
Lafferty, 2012[32]	Ethiopia: three administrative zones (west Hararghe, Harari, and east Hararghe)	2002–12	Retrospective cross-sectional study with interviews of former patients	Clinical diagnosis or retrospective diagnosis with photos, or sequelae scars and interviews	39 cases	Rural population of 4 301 765	0·91 cases in all three zones, 0·82 cases in west Hararghe, 0·92 cases in east Hararghe, 2·38 cases in Harari, and 4·53–18·13 cases in rural Ethiopian populations	1·64–13·14 children aged 0–9 years in Ethiopia	NA	NA	9
Baratti-Mayer et al, 2013[13]	Niger: Zinder region	2001–06	Prospective matched case-control study	Clinical diagnosis	82 active cases and 327 controls	409 people	NA	NA	3·7	8·5%	8
Bello et al, 2019[33]	Nigeria: surgical outreach locations in north-central Nigeria	2010–18	Retrospective cross-sectional study of records	Clinical diagnosis following WHO guidelines	78 total cases: 12 acute cases and 66 with sequelae	45·7% of individuals living beneath the poverty line	1·6 cases in total: 1·7 male cases, 1·5 female cases, 1·3 cases in Nasarawa state, 0·6 cases in Kogi state, 1·4 cases in Niger state, and 3·3 cases in the Federal capital territory	8·3 people in total: 17·9 people in Nasarawa state, 4·1 in Kogi state, 5·1 in Niger state, and 14·2 in the Federal capital territory	2–10	NA	7
Fieger et al, 2003[34]	Nigeria: Sokoto Noma Children Hospital	1996–2001	Statistical analysis of cases (noma incidence based on logistic regression with the expected difference in patients with noma and cleft lip)	Clinical diagnosis	378 cases	80 000 000 people in sub-Saharan Africa	NA	640 children aged 10–30 years in northwest Nigeria, 25 600 in total in sub-Saharan Africa, and 30 000–40 000 in total globally	2–9	NA	6
Idigbe et al, 1999[35]	Nigeria: nine states	1996–98	Cross-sectional case detection	Clinical diagnosis	Four acute cases and six with sequelae in southwest Nigeria, and 42 acute cases and 87 with sequelae in northwest Nigeria	>1000 people per state	NA	NA	3–8	NA	2
Ndiaye et al, 1999[36]	Senegal: 35 health centres in the St Louis region	NA	Not clearly described (cross-sectional methods)	Clinical diagnosis following WHO guidelines	25 total cases: 12 individuals with noma aged 0–14, and 1058 with necrotising ulcerative gingivitis	50 808 children aged 0–14 years	23·6 cases in children aged ≤14 years	NA	NA	NA	2
Kante, 2009[37]	Mali: regions of Mopti, Gao, and Tombouctou	2004–09	Retrospective case review of NGO data (cross-sectional methods)	Clinical diagnosis	163 total cases: 95 cases in Mopti, 33 in Gao, and 35 in Tombouctou	1 765 029 cases in Mopti, 459 298 in Gao, and 554 972 in Tombouctou	5·9 cases in total: 5·4 cases in Mopti, 7·2 cases in Gao, and 6·3 cases in Tombouctou	NA	6–10	NA	1

Quality was assessed with the adapted Newcastle–Ottawa scale for cross-sectional and case-control studies (appendix pp 2–3). NA=not applicable.

Table: **Characteristics of the studies included in this systematic review on noma**

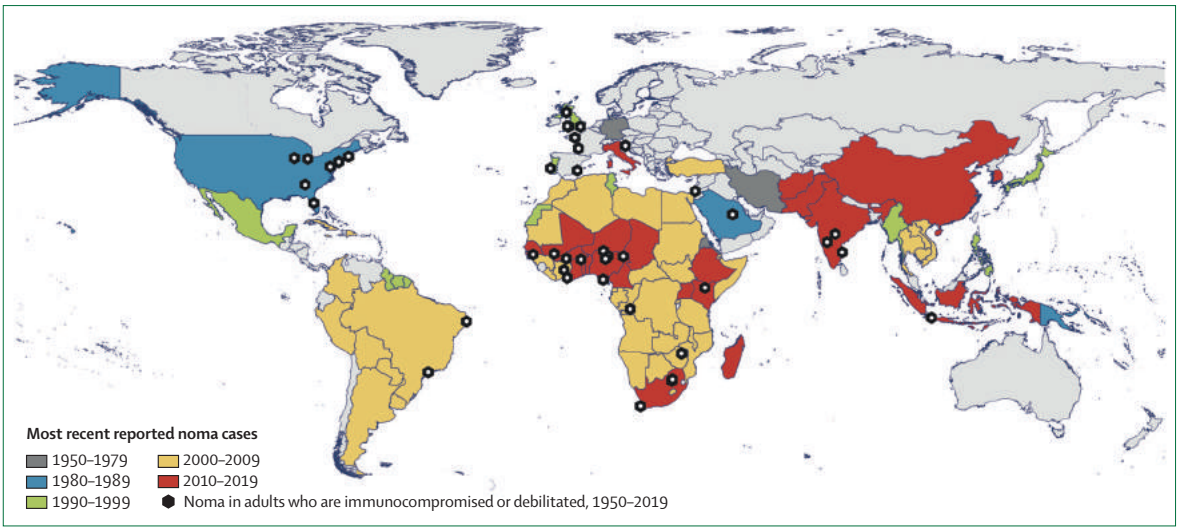

Figure 2: **Reported global occurrence of noma cases from 1950 until 2019 based on the last reported noma case in each country**
Appendix (pp 4–9).

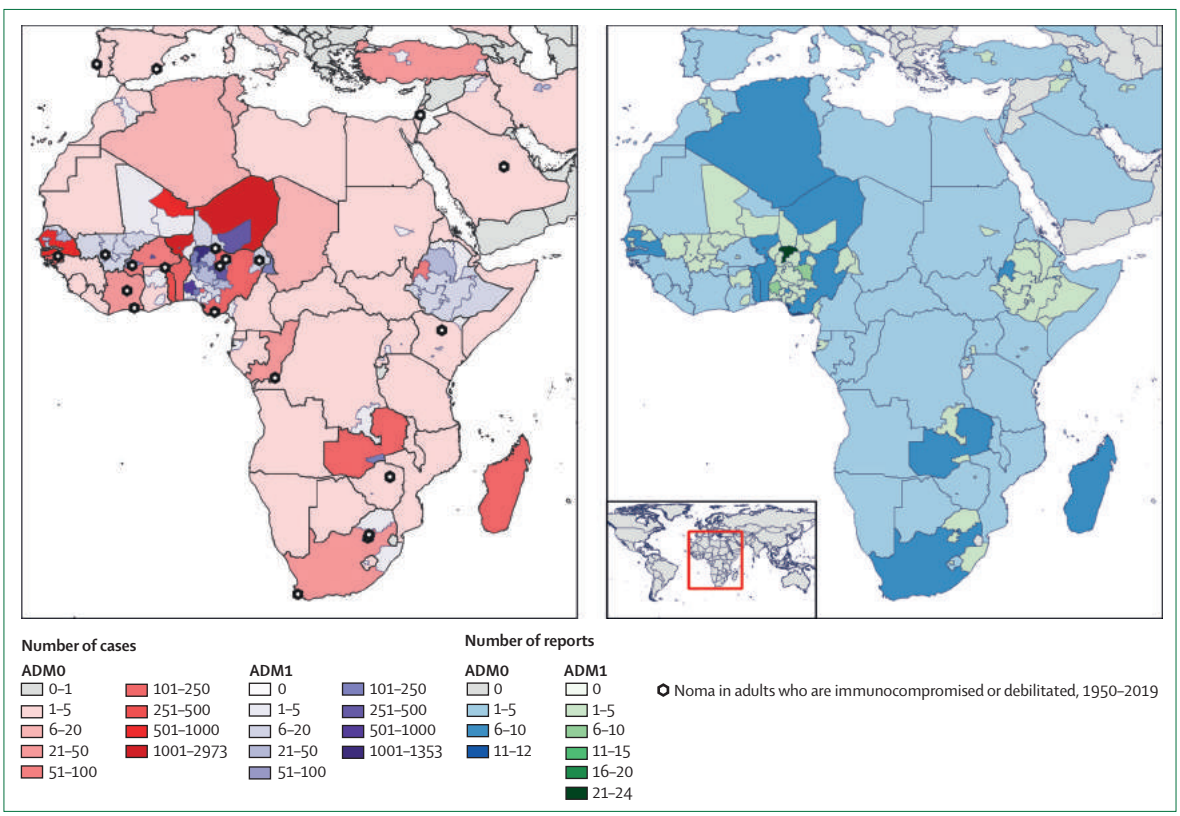

Figure 3: **Number of reported noma cases and number of reports on noma cases at national and subnational levels in Africa**
ADM0=national administrative division. ADM1=upper subnational administrative division.

Reported global distribution

A total of 535 references were initially included for the generation of maps showing the reported global occurrence of noma. However, sufficient data could only be extracted from 283 references (appendix pp 4–9). Most of the 250 excluded publications were not considered because they reported cases that had occurred before 1950 or because of incomplete data on noma cases (eg, no onset date, no location, or no focus on bacterial diversity). In the time period from 1950 to 2019, patients with noma

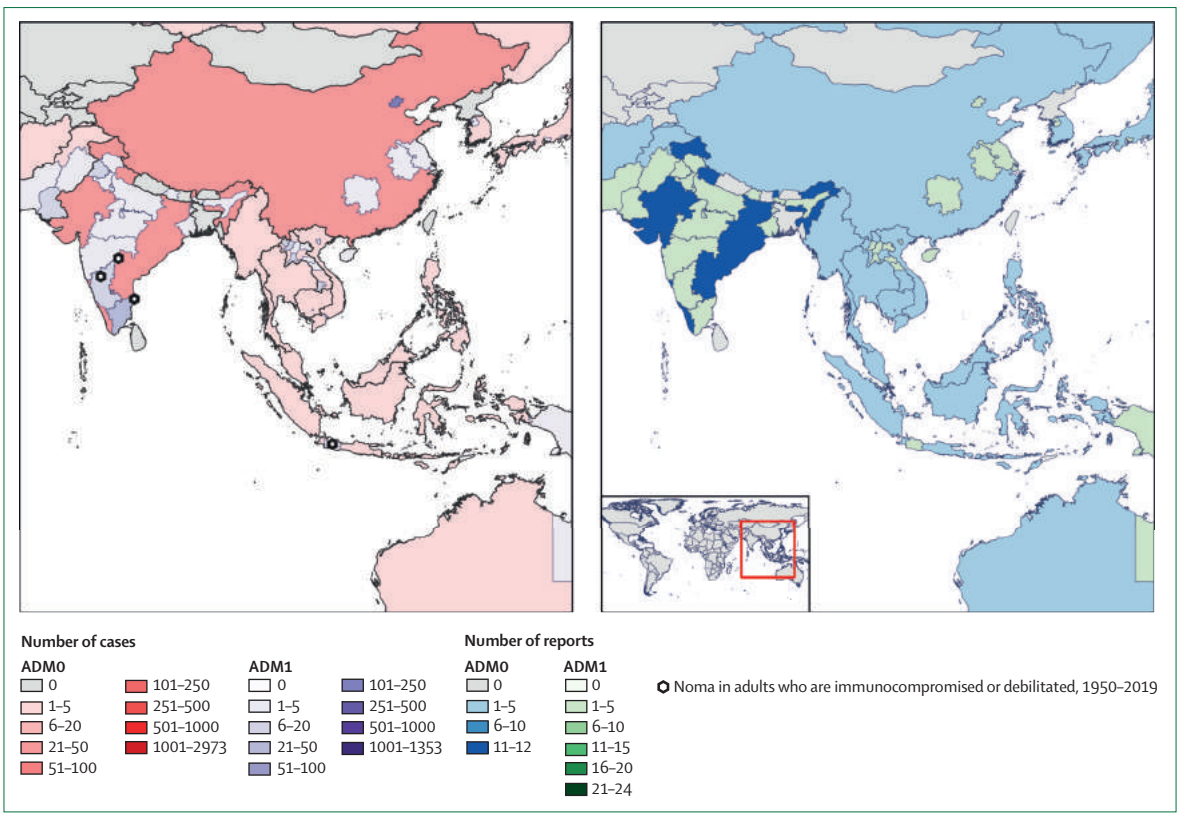

Figure 4: **Number of reported noma cases and number of reports on noma cases at national and subnational levels in southeast Asia**
ADM0=national administrative division. ADM1=upper subnational administrative division.

were reported in 88 countries (figure 2). During the last decade (2010–19), noma cases were reported in 23 countries (Afghanistan, Benin, Burkina Faso, Cameroon, Chad, China, Ethiopia, Ghana, Guinea-Bissau, India, Indonesia, Italy, Kenya, Madagascar, Mali, Niger, Nigeria, Pakistan, Senegal, South Africa, South Korea, Togo, and Uganda).

The countries reporting the highest number of cases at country level, but without more detailed subnational-distribution information, were Niger (n=2973), Senegal (n=530), Mali (n=525), Togo (n=333), and Zambia (n=250; figure 3). The countries with the most reports at country level were India (n=12), Nigeria (n=10), Niger (n=9), and Benin (n=7; figure 3 and figure 4). The three subnational administrative divisions with the highest numbers of reported cases were all in Nigeria, comprising Sokoto (n=1353), Oyo (n=564), and Kaduna (n=462), followed by the Zinder region in Niger (n=371) and the Centre region in Burkina Faso (n=270; figure 3).

Discussion

This systematic review focused on publications on the geographical distribution, prevalence, incidence, and mortality of noma. High-quality epidemiological data on noma are extremely scarce; indeed, only one study used a randomised sampling strategy to assess noma prevalence[31] and no population-representative mortality data could be identified. The scarcity of data is a direct consequence of the rapid progression of the disease, its high fatality, weak health systems, the absence of dedicated or integrated surveillance systems, difficult access to health care for the people most affected by noma, limited or no recognition of noma by health-care workers and traditional healers, active hiding of noma survivors because of social stigmatisation and the disregard of symptoms, and unawareness of the disease's severity by caretakers.[12,23,38] Estimates indicate that only 10–15% of those affected by noma access health care.[23,39]

The identified literature had a geographical focus on western Africa with a hotspot in northern Nigeria, southern Niger, eastern Burkina Faso, Mali, and Togo. Beyond this region, the situation on the rest of the African continent remains largely unknown. Of note, these findings do not indicate that noma is non-existent elsewhere. Rather, through the work of NGOs such as Médecins Sans Frontièrs, Sentinelles, the International NoNoma Federation, and the Winds of Hope Foundation, who have a regional focus on west Africa, a disproportionate amount of publications originate from this region. Without active case detection, the non-existence of noma cannot be concluded, as demonstrated by the identification of noma cases in Laos.[40] The studies

identified in this Review report widely-differing prevalence and incidence estimates within Nigeria, not to mention at regional level. Further, the definition of noma is often unclear and we often do not know which stages of noma were included in the studies. These unknown factors render comparisons difficult. Moreover, the definition of incidence is challenging, such as in the study of Fieger and colleagues[34] in 2003, in which the authors calculated noma incidence on the basis of surgery admission data. Patients admitted to surgery are noma survivors and can therefore not be regarded as representative of the number of children with incident disease.

WHO global incidence (140 000 people globally), prevalence (770 000 people globally), and mortality (90%) figures from 1998 remain the most widely cited.[26] However, these figures have evident limitations. First, some elements of this estimation resulted from a Delphi expert consultation.[41] Second, scientific evidence supporting these estimates resulted, among others, from referral records of hospitals, and therefore did not capture the prevalence or incidence in the population, but rather of the people who could reach a hospital.[41] Therefore, we advise to use these figures cautiously. To conclude, estimating current global noma incidence, prevalence, or mortality is not possible because there is a scarcity of representative data generated through standard methods and across the different affected regions.

Comparing the reported global distribution of noma generated in the frame of this study with older noma maps[3,5] suggests that several countries, especially in southeast Asia, are only now recognised as being home to noma cases. For example, in Laos, 36 noma survivors and one person with active noma were reported in the year 2002.[42] Of note, some of these cases occurred decades ago but have only now been brought to the attention of the international medical and scientific community.[40] It is also noteworthy that the number of studies and the number of reported cases are closely correlated. Indeed, most noma cases have been reported from countries and regions where many studies have been done. It is currently unclear whether this aspect represents an artefact or a sensible allocation of scarce resources—ie, whether current research focuses on the global hotspots of noma or whether regional research foci highlight cases that go unreported in other areas. Although we are confident that the number of noma cases is particularly high in Burkina Faso, Niger, Nigeria, and Mali, it is arguably not correct to assume that noma is completely absent from other countries that do not report noma cases despite similar socioeconomic, nutritional, and health system constraints.

Beyond the inconsistent data on prevalence and incidence, reliable data on mortality and disability caused by noma are unavailable. The burden of noma has been estimated for the first time in northwest Nigeria, resulting in 44 329 disability-adjusted life years per 100 000 children aged between 0 years and 15 years who had received timely treatment, whereas the number of disability-adjusted life years was 198 152 per 100 000 children not receiving treatment.[43] However, these estimates are local estimates, based on the prevalence study included in this Review[31] that focused on a specific age group. Therefore, the global burden of disease cannot be estimated with any degree of accuracy. Noma mortality remains mostly undocumented because the children often succumb to the disease before reaching health-care facilities.[23] Our Review did not identify any data documenting noma mortality of untreated patients, undoubtedly reflecting the near-total absence of proper death certification among poverty-affected populations where noma is endemic. Therefore, the mortality estimate of 90% put forth by WHO remains the common reference in the medical and scientific literature. This absence of epidemiological information complicates any attempt at evidence-based intervention planning and resource mobilisation. The scarcity of robust data on noma was already mentioned by the WHO initiative on noma originating in the oral health programme of 1994.[44] Despite this initiative, the promotion of research on noma was not successful for more than two decades. Therefore, the need for high-quality epidemiological research on noma is as urgent as ever.

Noma shares important characteristics with the neglected tropical diseases (NTDs), most notably skin NTDs such as leprosy and Buruli ulcer.[45,46] Noma affects marginalised and destitute populations with very limited access to often rudimentary health services. The disease burden might be considerable locally, but is not recognised as a global health priority, and the condition is stigmatising and associated with long-term disability and dire socioeconomic consequences.[43] Although theoretically simple, prevention and control interventions are hampered by competing priorities, low capacity of the health system, and challenging access to the affected population.[47] Of note, the condition would probably largely disappear without targeted interventions once broad-based living conditions including nutrition, hygiene, and access to vaccination and other child health services improve. By striving for the UN SDGs or broader social development, noma would be addressed concurrently. Until this development has occurred, targeted and concerted actions are needed.[48] These actions might be provided through integrated programmes, such as those aligned for instance with leprosy services that have managed to establish relatively robust systems in many poverty-affected areas. Leprosy programmes routinely address issues related to stigma, access to specialised medical care, and social rehabilitation.[49] An important research question pertaining to prevention is the effect of population-based single-dose antibiotic treatment, such as treatment with azithromycin in the frame of trachoma and yaws elimination or with

rifampicin for leprosy prevention.[50,51]

To our knowledge, this is the first systematic literature review focusing on the global incidence and prevalence of noma. The inclusive search strategy covering ten databases and only basic exclusion criteria allowed for the minimization of study selection bias. Still, we recognise several limitations that we would like to offer for discussion. Noma has been around for centuries and over time the name of the disease has changed.[8] Therefore, reports using a different nomenclature might have been missed. Additionally, older documents are more difficult to access and hence we could not analyse the full text of more than 200 publications. Considering our more contemporary interest, this difficulty of access probably only had a minor effect on the validity of our results, but might be an important issue in more historically focused studies. In view of the challenges in the diagnosis of noma, absence of timely accessibility to health services, and the stigma related to the disease, some included studies potentially contain cases of misdiagnosed patients, although genuine cases of noma might have been missed because of misdiagnosis or underreporting. Further, noma mainly occurs in patients at the fringes of society for which access to health care and reporting of deaths are erratic and incomplete. Similarly, families might opt to hide patients with noma. On the basis of these issues, we suggest that quantitative epidemiological and clinical research on noma should be complemented by social science-supported investigations to better understand attitudes and perceptions linked to noma.[52–54] Systematic study quality assessment was challenging because no established scale really fit our needs. Despite these challenges and limitations, we are confident that the results presented here provide an accurate picture of the current evidence on the global distribution of noma and illustrate the urgent need to allocate more resources to the research and management of noma.

On the basis of the findings of our systematic review, we suggest the following actions to address key root problems related to noma elimination. First, on a conceptual level, the epistemology and nosology of noma need to be uniformly defined across sectors (eg, WHO, health services, surveillance, and academia), taking into account cultural components. By doing qualitative research, different persisting names of noma can be identified. With this qualitative knowledge, classifications such as the WHO noma stages should be reconsidered, and if appropriate, promoted across studies to guarantee comparability. Second, there is a need for representative population-based epidemiological studies in regions of great poverty and food insecurity to assess noma incidence and prevalence, complemented by social science studies. This research should include randomised cross-sectional studies, surveillance and reporting systems within communities and health systems, active case detection, and qualitative data collection. Although all high-quality epidemiological studies will be valuable to better understand and document noma, they should also include countries beyond west Africa.[40] Third, noma prevention, recognition, surveillance, and treatment should be integrated in existing programmes targeting NTDs, malnutrition, poverty reduction, and health education. For example, oral screenings could be included in vaccination campaigns or pre-existing malnutrition surveys. Fourth, health-care providers and traditional healers need to be trained on screening for oral diseases, especially in connection to predisposing diseases of noma such as measles or malaria.[55] Abnormalities have to be recognised at an early stage and referred to corresponding practitioners. Consequently, noma or other oral diseases could be treated easily before evolving to more debilitating stages. On a communal level, the integration of noma in campaigns aiming at poverty reduction, decreasing malnutrition, and health education for mothers and fathers[56] in high-incidence populations would facilitate early detection of noma. Finally, the extent of the public health problem caused by noma needs to be acknowledged by relevant bodies and resources allocated to reinforce research and noma intervention programmes.

This systematic review has identified several recent studies on noma, but overall documented a scarcity of evidence-driven research and surveillance programmes. A global focus in the west African Sahel region has been confirmed. We argue that noma elimination might be feasible with broad-based integrated control programmes, with a first step being the inclusion of noma in the WHO list of NTDs.

Contributors

TF contributed to the creation of The Noma Project and secured funding, and conceved the study. AG, CB, TF, MSW, and PS designed the search strategy and data-extraction form. AG, CB, MSW, and PS screened studies for selection. AG and CB extracted and analysed the data. CB generated the maps. NM provided expert medical advice. TF, AG, CB, NM, MSW, and PS wrote the first draft of the manuscript. AG, CB, TF, NM, MSW, and PS critically revised and finalised the manuscript. All authors have read and approved the final version of the manuscript.

Declaration of interests

We declare no competing interests.

Acknowledgments

This Review was done by The Noma Project (https://thenomaproject.org), an interdisciplinary consortium of international partners focusing on the epidemiology of noma, the experiences of noma survivors and the human rights dimension of the disease. We thank the consortium members of The Noma Project, namely Prof Emmanuel Kabengele Mpinga, Dr Margaret Leila Srour, Dr Denise Baratti-Mayer, Dr Gabriel Alcoba, and Dr Ioana Cismas for their invaluable inputs during the review and manuscript development. We would also like to thank Giovanni Casagrande for his advice during the development of the search strategies. Swiss Network for International Studies, Hilfsaktion Noma, Noma Hilfe Schweiz, Winds of Hope, and the International Social Service Geneva funded The Noma Project.

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