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REVIEW

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Antimicrobial resistance in Noma control: a costly neglect within existing neglect

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Abstract

Introduction Noma is a severe gangrenous orofacial disease affecting malnourished children aged 2–6 years in extreme poverty, with 85–90% mortality if untreated. Recently classified as a Neglected Tropical Disease, it is managed mainly with empirical broad-spectrum antibiotics. Antimicrobial resistance (AMR) threatens to undermine treatment, yet AMR remains largely absent from Noma research and policy. This review examines AMR prevalence and drivers in Noma, identifies knowledge and policy gaps, and proposes recommendations.

Methods We reviewed literature on Noma microbiology and documented AMR, plus WHO NTD and AMR policy documents. Community and health system factors and surveillance capacity in Noma-endemic regions, primarily Sub-Saharan Africa, were synthesized.

Results Noma lesions show marked dysbiosis with frequent detection of Fusobacterium necrophorum, Prevotella spp., Staphylococcus aureus, Pseudomonas aeruginosa, and a novel "Treponema sp. A". A 25-year retrospective analysis found that >92% of patients presented late, requiring prolonged antibiotics. Direct AMR data are scarce. Case reports documented MDR-*Escherichia coli* in Afghanistan (2012), *Vancomycin-resistant Enterococci* in South Korea (2022), *ESBL E. coli* in Mali (2021), *Serratia marcescens* (Ticarcilline, amoxicillin, and sulfamethoxazole-trimethoprim) and *Pseudomonas aeruginosa* (Rifampicin) in Chad (2014); and *Pseudomonas aeruginosa* (penicillins, carbapenems, aminoglycosides, sulfamethoxazole-trimethoprim, and nitrofurantoin) in Italy (2015). A recent metagenomic study reported high β-lactam and metronidazole resistance determinants, especially in *Prevotella* spp. Drivers include empirical broad-spectrum antibiotic use, self-medication, irrational prescribing, and weak diagnostics, with only a small share of laboratories across 14 SSA countries performing routine bacteriology and susceptibility testing. Policy gaps persist: WHO NTD and AMR strategies are siloed, anaerobes are excluded from GLASS surveillance, and Noma guidelines lack AMR triggers.

Conclusion AMR risks reversing gains in Noma control, and treatment centers may become AMR amplification sites without stewardship. Given limited microbiology data, we recommend adding AMR indicators to WHO and national Noma strategies, integrating anaerobic AMR surveillance at sentinel sites, generating Noma-specific antibiograms, and mandating antimicrobial stewardship in Noma programs. Mainstreaming AMR in Noma research and policy is essential to preserve therapeutic options.

Keywords Noma, Antibiotics, Antimicrobial resistance, Neglect

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Background

Noma, described as *a social marker of extreme poverty and malnutrition, and affecting the most vulnerable populations,* is a severe gangrenous disease of the mouth and face, primarily affecting malnourished children between the ages of 2 and 6 years in regions of extreme poverty, but it can affect any age group [1, 2]. Mostly found in sub-Saharan Africa (91.2%), Noma is caused by infection with oral bacteria and is associated with multiple inequity-linked risk factors, including poor oral hygiene, malnutrition, compromised immunity, infections, and extreme poverty [3, 4]. About 140,000 cases/year have been reported globally, and up to 85% mortality rate if left untreated. Mortality is reduced to about 20% when treated [1]. The global burden of the disease is estimated to be between 1 and 10 million disability-adjusted life years (DALYs), mostly due to premature mortality and disability among survivors [3, 4].

The World Health Organization (WHO) officially recognized Noma as a Neglected Tropical Disease (NTD) in December 2023, to heighten global awareness, advance research, secure funding, and reinforce disease control through collaborative, multi-sectoral interventions, and ultimately enhance the achievement of universal health coverage (UHC) [5]. Patients with Noma are not exempt from the menace of AMR, and the rise of antibiotic resistance could further complicate the care of patients with Noma, potentially increasing an already significantly high morbidity and mortality. AMR burden is greatest in Sub-Saharan Africa, where the burden of Noma, including the risk factors, is also greatest [3, 5].

AMR remains a significant public health crisis, leading to increased morbidity and mortality globally. Significant inequality exists across regions, and the greatest burden of AMR exists in low-resource settings, especially in Sub-Saharan Africa [4]. This is driven by misuse and overuse of antibiotics, insufficient diagnostics, widespread substandard and falsified medications, poorly controlled antibiotic access due to an insufficient regulatory landscape, poor infection prevention and control (IPC), weak antimicrobial stewardship (AMS), limited access to newer antibiotics, inadequate water, sanitation, and hygiene (WASH) facilities, and weak health systems, amongst others [6]. According to the Institute of Health Metrics (IHME), more than one million people died each year as a result of AMR between 1990 and 2021, more than 39 million people globally could die from antibiotic-resistant infections over the next 25 years, and antibiotic-resistant infections could be involved in about 8 million deaths each year, either as the direct cause of death or as a contributing factor by 2050 [7].

Patients with Noma are not excluded from the menace of AMR, and the rise of antibiotic resistance could further complicate the care of patients with Noma. Noma management relies heavily on readily available antibiotics, including metronidazole, amoxicillin, and ceftriaxone, and AMR could hinder progress in global efforts. However, there is no published data on resistance profiles in Noma lesions. In addition, AMR is often overlooked in the consideration of patients with treatment failure, which may be evidenced by surgical wound breakdown, fistula formation, and recurrence. A 1-day symposium was held recently to define a research agenda for Noma, organized by the Swiss Tropical and Public Health Institute [8]. However, research into the intersection of AMR and Noma was not included in the agenda. The critical intersection of Noma risk factors and antibiotic use creates potential AMR hotspots, which need to be understood.

The objective of this review paper is to synthesize evidence gaps in the intersection of Noma and AMR, argue for AMR surveillance in patients with Noma, and propose a research agenda to strengthen the existing research agenda.

Methodology

We conducted a narrative review to summarize existing evidence on the burden and impact of AMR in Noma care and stimulate policy considerations that will lead to the integration of AMR mitigation and control in the broader Noma control. A literature search was conducted in April and July 2026 in PubMed, MEDLINE, Google Scholar, Directory of Open Access Journals (DOAJ), Semantic Scholar, and African Journals Online (AJOL). We combined MeSH and free terms, "Noma" and "antimicrobial resistance", with necessary Boolean Operators including AND, OR, and NOT. The PubMed search strategy is provided as a Supplementary Material. Articles consulted are mostly from SSA, as the burden is highest in this region. Other articles from outside of SSA were also sought, where available. All indicated databases were searched for relevant articles with no time restrictions. The oldest article that reported antimicrobial resistance in Noma patients was published in 1999.

We included peer-reviewed literature that reports on patterns of AMR among Noma patients (either phenotypic or molecular) and broader risk factors for Noma and antimicrobial resistance. We also searched for and included grey literature from the WHO and relevant organizations working in Noma care, including WHO NTD and AMR-related policy documents, reports, and treatment guidelines. Articles not written in English or French were excluded. We synthesized community and health system factors for AMR in Noma-endemic regions. We also included peer-reviewed articles that document the Noma research agenda.

No formal systematic review methodology was applied in this study. Article selection was guided by its relevance to the objectives of this narrative review. All articles were uploaded in CSV (Comma Separated Value) or RIS (Research Information System) format, imported into Rayyan software, duplicates were removed, and further screening was done. A hand search was also conducted through the reference lists of relevant articles.

A total of 58 peer-reviewed articles and grey literature were reviewed (42 peer-reviewed, 16 grey literature). The literature search for peer-reviewed articles yielded a total of 358 peer-reviewed articles; 12 duplicates were removed from it. After screening (title/abstract and full text), 42 peer-reviewed articles were selected: original research articles that reported antibiotic treatment and AMR occurrence in Noma care, and articles that discussed the broader AMR and Noma theme. 16 grey sources on AMR, Noma, and NTD-related policy documents and treatment guidelines were also included from the WHO, Médecins Sans Frontières, and the African Society for Laboratory Medicine.

Extracted information included study title, author, year, country, study design, study population, sample size, incidence/prevalence of AMR in Noma, antibiotic treatment pattern, and Antibiotic Sensitivity Testing (AST).

Result

Noma model of care and standard antibiotic regimens

The WHO described five stages of Noma (Table 1), and treatment is dependent on the stage of diagnosis [1].

Successful treatment of Noma is dependent on the early detection of the disease. Management of Noma encompasses the use of broad-spectrum antibiotics covering implicated anaerobes and gram-negative bacteria. Most common antibiotics reportedly used (after 1950) are WHO "Access" groups, including penicillin, metronidazole, clindamycin, streptomycin, and "Watch" groups, including Ceftriaxone and Streptomycin, across the stages, whether as oral or intravenous [3]. Table 2 describes the standard antibiotic regimen used and its dosages according to WHO, and an adaptation from the Médecins Sans Frontières Noma treatment guideline [1, 9]. Other components of care include nutrition supplements, advice and support on practices to improve oral hygiene, and use of disinfectant mouthwash (salt water or chlorhexidine). Late stages (stages 3–5) of Noma will require surgical intervention and wound dressing. Table 2 presents the comprehensive model of care described by Isah et al. at the Médecins Sans Frontières–supported Noma Children Hospital in Sokoto, Nigeria, which consists of four main components: acute care, care for Noma sequelae, integrated hospital-based services, and community-based services [10].

Challenges of antibiotic use in Noma treatment

Significant challenges arise in the treatment of Noma. According to a study by Braimah et al. analyzing 1386 Noma cases over a 25-year period, more than 92% presented at stage 3 or higher [11]. The overuse of empirical broad-spectrum antibiotics has been identified as a key contributor to the development of AMR. With a greater percentage of patients presenting at stage 3 and above, there is potential for increased empirical use of acute care, including surgical prophylaxis and postoperatively to prevent graft infection. Late presentation may contribute significantly to antimicrobial exposures, either due to community-level antibiotic use or a potential increase in the need for in-hospital antibiotics [11, 12].

Standard antibiotic treatment in Noma

In line with the probable organisms that have been identified in the lesions of patients with Noma, standard antibiotic treatment has been defined for patients with Noma. Below is a summary of antibiotic treatment, adapted from the WHO and Médecins Sans Frontières treatment protocol (Table 3) [1, 9].

Table 1 The five stages of Noma [1]

Stage	Nomenclature	Description
Pre-Noma	Warning signals (Gingivitis)	Characterized by gum inflammation
Stage 1	Acute Necrotizing Ulcerative Gingivitis (ANUG)	Characterized by spontaneous bleeding, gingival papillae ulceration, pain, and/or greyish pseudomembrane
Stage 2	Oedematous stage	Characterized by a sudden onset of facial oedema & characteristic halitosis, often considered pathognomonic
Stage 3	Gangrene & Necrotic stage	Destruction of the soft tissue & bones in the mouth with eventual sloughing off, leaving behind a circular defect known as Noma
Stage 4	Scarring	Facial tissues are destroyed by severe bacterial infection, leading to extensive scarring. Complications include trismus, oral incontinence, chewing difficulties, speaking difficulties, and disfigurement
Stage 5	Sequelae	Facial deformities & challenges in eating, speaking, & social interaction resulting from trismus or mandibular ankylosis

Table 2 Comprehensive model of care in Noma [10]

SN	Components of care	Description
1	Acute care	Antibiotics
		Oral hygiene, e.g., with the use of chlorhexidine
		Treatment underlying morbidities, e.g., malnutrition
		Wound debridement and dressing
2	Care of Noma sequelae	Surgical interventions
		Post-operative care
3	Integrated hospital-based services	Nutrition
		Mental Health and Psychosocial Support
		Physiotherapy
		Laboratory services
		Water and sanitation and Infection Prevention & Control
		Vaccinations—EPI, catch-up vaccination
4	Community-based services	Follow-up
		Active case finding
		Awareness raising, health promotion, and education

Most frequently identified organisms in Noma

There is significant dysbiosis reported in Noma cases. Historical evidence, documented by a systematic review of about 366 publications (from year 1839 to 2022), which included 15,082 patients across 69 countries, reported about 117 microorganisms across 113 studies. The most frequently documented organisms include *Staphylococcus aureus* (19%), *Pseudomonas aeruginosa* (18%), *fusiform* bacilli (16%), spirochaetes (12%), *Fusobacterium necrophorum* (11%), *Prevotella* genus (11%), *Klebsiella pneumoniae* (10%), *Peptostreptococcus g*enus (7%) and *Actinomyces species* (5%). However, none was more consistently linked to Noma development [3].

A 1999 study by Falkler et al. identified *Prevotella intermedia (88%)* and *Fusiform necrophorum (75%) among 8 children 3–15 years with noma lesions 6 months–2 years old. A 2025 study by* Rikhotso et al. documented 29 different organisms among 20 noma patients 3–57 years, with *Escherichia coli (20%)* and *Klebsiella species (20%)* dominating, followed by Proteus mirabilis (15%), Enterococcus spp. (15%) and Candida albicans (15%) [13]. *Prevotella spp was only found in one out of the 20 patients.*

A recent study by Olaleye et al. through deep shotgun metagenomic profiling of oral saliva microbiomes from 19 acute Noma cases, demonstrated significant enrichment of *Treponema, Porphyromonas*, and *Bacteroides*, alongside depletion of *Streptococcus and Rothia*, as "key microbial signatures of Noma disease" [14]. The study also identified a novel species designated *"Treponema* sp. *A"* detected in 15 of the 19 samples, but absent in the healthy control group, made up of an internationally representative healthy saliva metagenome. This was also consistent with findings from re-analysis of previously published 16S rRNA datasets from Nigerien children with Noma, which showed that *Treponema* sp. A was highly prevalent [14]. According to the metagenomic analysis*, Treponema* sp. *A* was the most consistent organism identified in any Noma case or study, with presence in about 80% of cases studied [14].

Prevalence of AMR among the Noma-affected population

There is a significant scarcity of published phenotypic Antimicrobial Sensitivity Testing (AST) data from Noma lesions, with no robust Noma-specific antibiograms currently available. This indicates that much attention has not been given to AMR in Noma research. Most of the available studies on Noma were focused either on Noma epidemiology with emphasis on patterns of presentation, predictors, structural complications, surgical interventions, and stigma; knowledge, attitude, and practice. Most studies on Noma microbiology limited their reporting to the identification of organisms.

Few studies were found to report on AMR in Noma care, summarized in Table S1. Five case reports documented AMR in patients with Noma, with three from low-income countries and two from high-income countries. One is a report from Afghanistan (2012), which reported multidrug-resistant *Escherichia coli* before any use of antibiotics; the second report, from South Korea (2022) reported the identification of *Vancomycin-resistant enterococci* (VRE), the third, from Mali (2021) reported the isolation of *Extended-Spectrum Beta-Lactamase (ESBL)-producing Escherichia coli* [15–17]. The fourth report is from Chad (2014), which reported Serratia marcescens resistant to Ticarcillin, amoxicillin, and sulfamethoxazole-trimethoprim, and *Pseudomonas*

Table 3 Standard antibiotic treatment in Noma [1, 9]

Standard antibiotic treatment for Noma		References
Stage I (community settings)	Amoxicillin PO 100 mg/kg every 12 h for 14 days + metronidazole PO 15 mg/kg every 12 h for 14 days	WHO AFRO Information brochure [1]
Stage II (community settings)	(Amoxicillin-Clavulanic Acid 8:1 PO 50 mg/kg/dose twice daily + Metronidazole 15 mg/kg/dose twice daily) for 14 days	WHO AFRO Information brochure [1]
	OR	
	Option 2	
	Amoxicillin PO: 100 mg/kg/dose twice daily for 14 days + Metronidazole PO: 15 mg/kg/dose twice daily for 14 days	
Stage III (in-hospital settings)	Option 1	WHO AFRO Information brochure [1]
	Amoxicillin/Clavulanic acid IV 50 mg/kg/dose every 6 h for 14 days + Gentamicin slow IV: 5 mg/kg/day for 5–7 days + Metronidazole slow IV: 15 mg/kg/dose every 12 h for 14 days	
	OR	
	Ampicillin IV 100 mg/kg every 6 h for 14 days + Gentamicin slow IV 5 mg/kg every 24 h for 5–7 days + Metronidazole slow IV 15 mg/kg every 12 h for 14 days	
Stage IV (in-hospital setting)	Option 1	WHO AFRO Information brochure [1]
	Amoxicillin/Clavulanic acid IV 50 mg/kg/dose every 6 h for 14 days + Gentamicin slow IV: 5 mg/kg/day for 5–7 days + Metronidazole slow IV: 15 mg/kg/dose every 12 h for 14 days	
	OR	
	Option 2	
	Ampicillin IV 100 mg/kg/dose every 6 h for 14 days + Gentamicin slow IV: 5 mg/kg/day for 5–7 days + Metronidazole slow IV: 15 mg/kg/dose every 12 h for 14 days	
Surgical antibiotic prophylaxis (not more than 24 h)		
Children (< 40 kg body weight)	Cefazolin IV 30 mg/kg + Metronidazole IV 15 mgs/kg over 30–60 min. (to be repeated every 8 h)	MSF Noma protocol (2015)
Adults (> 40 kg body weight)	Cefazolin IV 2 g + Metronidazole IV 500 mg over 30–60 min (to be repeated every 8 h)	
Penicillin allergies (replace cefazolin with clindamycin)		
Children (< 40 kg body weight)	Clindamycin 20 mg/kg/day IV in 3–4 divided doses (not exceeding 40 mg/kg/day)	MSF Noma protocol (2015)
Adults (> 40 kg body weight)	Clindamycin 900 mgs IV, single dose	

aeruginosa resistant to Rifampicin; and the fifth is from Italy, a case of Noma neonatorum with *Pseudomonas aeruginosa cultured, resistant to penicillins, carbapenems, aminoglycosides, sulfamethoxazole-trimethoprim, and nitrofurantoin*. A study by Falker et al. [18, 19] also documented AMR among Noma patients. One of seven *P. intermedia* isolates (14.3%) showed resistance to penicillin, another showed intermediate resistance to tetracycline (14.3%), while one out of six strains of *Fusobacterium necrophorum* (16.7%) showed intermediate resistance to penicillin [18, 19].

A recent metagenomic analysis of saliva samples from 19 Noma patients, compared with internationally representative samples from healthy individuals, identified antimicrobial resistance genes (ARGs) at concerning levels. Resistance determinants for beta-lactams and tetracyclines were the most common, with CfxA3 (beta-lactam) detected in 89.5% (17/19) of participants and Tet(Q) (tetracycline) in 94.7%. The metronidazole resistance gene NimI was found in 42.1% of samples, while the aminoglycoside resistance determinant aph(3″)-Ib was present in 63.2% (12/19). ARGs that confer resistance to antibiotics commonly used in Noma treatment—particularly β-lactams and metronidazole—were especially prevalent among Prevotella spp [14].

Overall, not much has been documented about AMR in Noma from the available literature. This may be an overall reflection of the bacteriological diagnostic limitations and access as reported by the African Society of Laboratory Medicine: only 1.3% of the 50,000 medical laboratories forming the laboratory networks of the 14 participating countries conduct bacteriology testing, and even fewer can conduct sensitivity testing. Limitations also exist in culturing organisms in Noma due to the complex polymicrobial nature of the disease, the strict anaerobic environmental requirements of these bacteria, the necrotic environment, and logistical constraints in endemic, resource-limited areas. Identifying *Fusobacterium necrophorum* among other fusiform bacteria can be complex. *Prevotella intermedia* requires specialized media to isolate and often grows slowly, while *Spirochetes* are difficult to culture or too small to be seen under a standard light microscope, except under dark microscopy, special stains like the Warthin-Starry stain, and immunofluorescence [18]. The combined lack of capacity and accessibility of bacteriology and AMR testing services, including for organisms with complex requirements, in Africa, may significantly contribute to the non-availability of AST data among Noma patients [20–22].

Drivers of antimicrobial resistance in Noma care

Community-level drivers of AMR in Noma

The drivers of AMR among the Noma-affected population are not different from the drivers among the general population, and are generally similar to the determinants of Noma itself (Fig. 1). The combined effect of poverty leading to malnutrition, poor access to WASH facilities, low vaccination coverage, and high infection burdens, including measles, malaria, HIV/AIDS, amongst others, potentially contributes significantly to AMR in the Noma-affected population by causing severe immunosuppression that further increases susceptibility to infections, thereby driving the overuse of antibiotics and disrupting local microbiome balances [23, 24]. In addition, antibiotic self-medication and use of over-the-counter drugs for children with fever or mouth sores, due to lack of health care access or poor health-seeking behaviors, potentially play a significant role [24]. The misuse of antibiotics in veterinary medicine and agriculture is a major driver of AMR, and environmental contamination remains a significant source of antimicrobial exposure to the Noma-affected population, as in the general population [25]. There is a high overall risk of AMR, evidenced by the Drug Resistance Index (DRI) from selected Noma-endemic areas, including Burkina Faso (64%), Nigeria (65.9%), and Senegal (79.8%) [20].

Health system-level drivers

Some health system challenges potentially contribute to AMR among Noma-affected populations. Limited access to diagnostic services, especially microbiology, leading to limited availability of local microbiology data, including AST, remains a critical health system driver of AMR in Noma-endemic areas [20]. Weak AMS in hospitals performing Noma surgery may also be a key driver. Studies from surgical settings in Low- and Middle-Income Countries (LMICs) indicate poor adherence to recommended surgical antibiotic prophylaxis timing, with antibiotics often continued for extended postoperative periods or prescribed in the absence of a clear indication [26].

Furthermore, according to a WHO study evaluating the status of national core elements for AMS in the WHO African region, 42% of countries have not commenced the implementation of AMS core elements [6]. Studies from surgical settings in LMICs indicate poor adherence to recommended surgical antibiotic prophylaxis timing, with antibiotics often continued for extended postoperative periods or prescribed in the absence of a clear indication [26]. This leads to an increase in antibiotic exposure among surgical patients, thereby leading to strong selection pressure and potentiating the growth and multiplication of resistant organisms.

Critically, dedicated funding is lacking for both the National Action Plan on AMR (NAP-AMR) and AMS activities, with no national AMS implementation strategy with defined goals, targets, and operational plans. Moreover, AMS principles and the WHO AWaRe (Access, Watch, Reserve) classification have been integrated into national clinical guidelines for infection management in only 12 (38.7%) and 11 (34.5%) of the countries, respectively.

Poor IPC structure and practices, including the lack of IPC-trained health workers, are other key contributors. The risk of hospital-acquired infections (HAIs) is 2–20 times higher in developing countries, particularly in sub-Saharan Africa. WHO estimates the pooled incidence of surgical site infections (SSIs) in LMICs, including SSA countries, at 11.8 per 100 surgical procedures (range: 1.2–23.6). The endemic burden of HAIs in LMICs is also 2–3 times higher than in high-income nations, increasing the risk of multidrug-resistant organism transmission [27, 28]. Surgical site infections (SSIs), such as surgical sepsis, account for 30% of all septic patients in LMICs like Africa, and there has been an increase in cases of AMR in health care facilities [27]. A 2020 systematic review and meta-analysis reported a pooled surgical site infection (SSI) global prevalence of 14.8%, with the highest incidence (12.6%) observed in sub-Saharan Africa, particularly in the WHO Africa Region countries. Antimicrobial-resistant

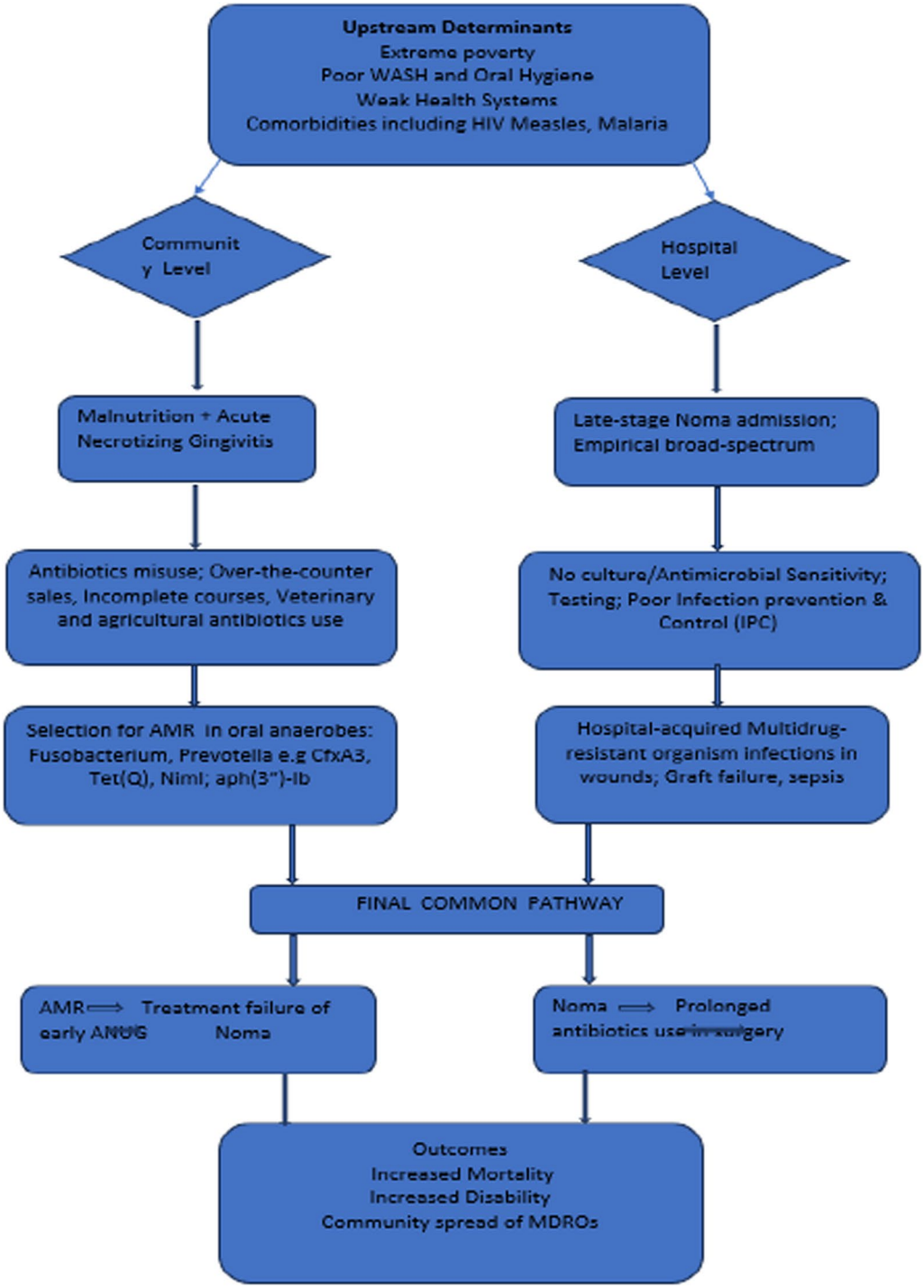

Fig. 1 Conceptual framework for AMR in Noma [2, 9, 11, 23, 24, 30–35]

organisms account for over 50% of the reported SSIs and are resistant to the most widely used antibiotics [29].

Other contributing factors include mistrust of health-care professionals and a lack of clear differentiation

between qualified and unqualified practitioners, which together promote antibiotic self-medication [24].

Conceptual framework: Noma-AMR feedback loop

Figure 1 describes the determinants of AMR in Noma patients and how both Noma and AMR influence each other in a vicious cycle, with AMR worsening Noma outcomes and Noma care. The determinants of Noma arise from both factors from the community and hospital based, some of which include; extreme poverty, poor health system and poor oral hygiene, which causes patient to seek for drugs over the counter and present only, most likely when complications have set in, requiring surgical interventions with consequent prolonged use of antibiotics (from prophylactic use pre-surgery, post-surgery wound care and possible multiple oral procedures), prolonged hospital stay and increase the potential for multidrug resistance, ultimately increasing mortality, spread of multidrug resistance to the community and increased disability.

Discussion

This review highlights the currently known occurrence of AMR in Noma care and associated drivers. Even though there is a widespread increase in reports of AMR in healthcare globally, especially in low- and middle-income countries, the true burden of AMR among Noma patients is unknown. More than 70% [5] of the articles on direct AMR occurrence in Noma patients were case reports, and the rest were cross-sectional studies with small sample sizes (Table S1).

Evidence gaps: what we don't know

There is currently very limited evidence on the prevalence of AMR among Noma patients and the AMR profile of organisms implicated in Noma lesions, as there are currently no antibiograms specific for Noma, even though there is increasing evidence of rising AMR among patients with other forms of necrotizing fasciitis [36–38]. The absence of this evidence makes the optimal antibiotic treatment protocol for Noma practically difficult. The optimal treatment protocol is meant to be informed by evidence of bacterial species and local resistance patterns, which are unavailable [26, 39]. At the moment, even though the standard treatment guideline has been defined by the WHO, the current pattern of antibiotic use in Noma care is unknown.

The impact of AMR on Noma-related morbidity and mortality remains largely unknown; however, there are possibilities for consideration. Theoretically, AMR could lead to treatment failure in the early stages of Noma. According to the WHO target, 95% of clinically confirmed Noma cases should be diagnosed in an early stage of the disease (stages 1–2) and treated to reduce sequelae from the late stages of Noma [37]. However, according to Braimah et al. about 92% of cases were seen at stages 3–5 between 1999 and 2024 at the Noma Hospital in Sokoto, Nigeria [11]. We hypothesize that AMR has the potential to make the WHO target ineffective due to the possibility of leading to treatment failure, thereby potentially leading to progression to severe stages. Hypothetically, post-surgery, AMR can lead to persistent wound infections, graft necrosis and loss, and increased mortality among Noma patients, although direct evidence remains scarce. Recurrence has also been reported among some patients treated for Noma, ranging from 4 months to 2 years post-treatment, and response to antibiotics was documented in the cases. However, it was not reported whether the responses were to standard treatment or if antibiotic treatment was escalated [40, 41]. Whether AMR is a potential contributor to recurrence is a question to be answered through further original research [24].

There is also a significant gap in our understanding of the baseline antimicrobial resistance gene (ARG) burden, such as carriage of ESBL or Carbapenemase genes, in communities where Noma is endemic, due to limited data [42–44]. This is not surprising, as areas endemic for Noma are also faced with reduced access to diagnostics. This makes it difficult to distinguish between community-acquired AMR in Noma lesions and treatment-induced selection, thereby complicating both empirical therapy and stewardship.

Significant policy gaps also exist. While the basic principles and strategies outlined in the Global Action Plan for AMR apply also to the antibiotic management of Noma, the current Noma-related policy documents and action plans, with core components including epidemiology and surveillance, prevention, early detection and treatment, and rehabilitation, and partnership and integration, do not take into consideration the potential impact of AMR on Noma treatment, and its potential to reverse current gains in Noma control in the near future. Antibiotic treatment regimen for Noma relies essentially on empirical broad-spectrum antibiotics. Furthermore, the current WHO Global Action Plan for AMR does not have as part of its surveillance priorities any of the organisms implicated in Noma disease [37, 45, 46].

In addition, AMR surveillance, AMS, and drug-resistant Noma are not part of the considerations or priorities of the current Noma global and national policy documents and treatment guidelines. Understandably, the NTD roadmap document was written and operationalized in 2021, 2 years before the official recognition and inclusion of Noma as part of the list of NTDs, to run through 2030 [37]. However, it has been integrated since 2024 [47]. AMR is currently not captured in the NTD

roadmap document. While there is significant dysbiosis in noma microbiology, with our understanding of implicated organisms still evolving from current evidence, organisms that have shown relative consistency in Noma, including *Prevotella* spp. *and Fusobacterium spp*, are also not considered as part of the priority organisms for AMR surveillance. Non-endemic countries are not prioritized for anaerobic organism culture and surveillance [45].

Implications of AMR for Noma control

AMR could have significant implications for the clinical outcome of Noma patients and the overall Noma control. Hypothetically, AMR in early-stage Noma may lead to potential treatment non-response, thereby leading to the possibility of progressing to severe stages. It may also be a potential contributor to surgical failure, including graft necrosis and loss, documented recurrence, and mortality among Noma patients. It may also lead to an increase in the average length of hospital stay and the cost of health care [48]. Overall, AMR could lead to an arrest of progress already made in Noma control. With the rise of multi-drug resistance in SSA, AMR may become one of the greatest challenges for Noma control in the coming years, despite progress in access to surgical interventions for many Noma patients, with mortality from Noma increasing AMR-associated and attributable deaths [25, 49].

Noma treatment centers in endemic regions may also become sites that amplify and drive AMR among vulnerable populations through increased empirical antibiotic use and transmission of resistant organisms [49, 50]. This may, in turn, potentially lead to an extended period of antibiotic exposure, leading to potential treatment failures and poor surgical outcomes. In addition, AMR amongst the Noma-affected population may potentially result in a double burden on populations already facing the highest disease burden and the least resources.

Recommendations

Research recommendation

Evidence from this study demonstrated a significant paucity of microbiological studies, including culture and AST. The study by Olaleye et al. has opened up a path to be explored. We recommend a significant investment in the original research examining the microbiology of Noma, especially the resistance pattern for commonly implicated organisms, including the most recently discovered Treponema spp A. Culture and AST of Noma lesions across different stages of Noma must be understood through research implemented in endemic regions. This will enable the availability of local antibiograms for targeted antibiotic therapy in Noma management, thereby reducing the use of broad-spectrum antibiotics in Noma treatment. Both community and hospital-setting treatments can be tailored, influenced by the knowledge of local Noma AST data [25]. While the metagenomic analysis remains the most effective, allowing for high-resolution detection and tracking of AMR genes, it is not widely available for operational use, though there is a gradual transition [51]. Building on the recent study that documented *"Treponema spp A"*, more investment should be made into this to establish a definite causative agent for Noma, as the role of *Treponema spp A is yet unclear.* Further research will help establish its actual contribution to Noma pathology [14].

In addition, clinical epidemiology research may be able to establish the incidence of AMR, associated risk factors or predictors, including pre-hospital antibiotic exposure, whether pre-hospital or at the hospital level. This will help to distinguish between community-acquired and hospital-acquired resistance. A prospective cohort study, utilizing normal flora control from local communities, to establish the association between AMR carriage and Noma progression and/or outcomes, will inform necessary interventions to reduce Noma-related morbidity and mortality. While the WHO guidance document recommends certain antibiotics for the management of Noma, cross-sectional studies (whether prospective or retrospective) that describe the actual pattern of antibiotic use in Noma care on the field remain necessary [1]. Interventional research exploring the impact of the implementation of antibiotic stewardship programs in Noma treatment centers will also prove invaluable in generating evidence to strengthen advocacy for AMS implementation.

The latest priority organisms for surveillance were published in 2024, based on various criteria, including mortality attributable, incidence of resistant organisms, non-fatal health burden such as DALYs, trend of resistance, transmissibility, and preventability in community and hospital settings [45]. We suggest that the key pathogens implicated in Noma should be included to monitor the resistance pattern.

A research agenda was defined for Noma in 2025 at a 1-day symposium organized by the Swiss Tropical and Public Health Institute, which gathered about 100 individuals from different organizations, including clinicians, experts in NTDs, persons with lived experiences of Noma, public health experts, including researchers, and health advocates [8]. However, this research agenda did not consider AMR as a major research theme to be included. We recommend that AMR in Noma care should be considered for inclusion in the defined research priorities. These various research efforts will enable more evidence generation for the development of Noma-related antibiograms, which will serve to improve

rational and more targeted antibiotic use, expand overall AMR surveillance, inform AMR mitigation strategies, and strengthen Noma control, thereby improving treatment outcomes.

Policy recommendations

Regions endemic for Noma also bear a significantly high AMR burden, especially in SSA. The WHO NTD Roadmap was drafted and published in 2021, more than two-and-a-half years before the official recognition of Noma as an NTD. While current limited evidence about AMR in Noma may not yet allow for major policy changes, AMR surveillance remains a key consideration for inclusion in the NTD roadmap for Noma. Sentinel-site surveillance in Noma treatment centers, especially in Sub-Saharan Africa, may support the generation of high-quality AMR data among Noma patients. In addition to data on drug resistance, key risk factor data should be collected at such sentinel sites, including the documentation of previous exposure to antibiotics. We further recommend the development of Joint NTD-AMR research proposals, with a focus on addressing key drivers of AMR in NTDs, especially Noma [3, 8, 25, 52]. This will support the extension of current evidence over time, with the potential to shape Noma and NTD-related policies in the near future.

AMS in the Noma treatment facilities remains a key strategy to limit antimicrobial exposures among Noma patients, most effective within the context of good infection prevention and control practices. We suggest that AMS be integrated into existing activities of the Noma treatment centers, or strengthened it where it is already integrated. This should an implementation of standard AMS protocols for acute care, surgical prophylaxis, and post-surgical antibiotics use. This will potentially encourage a more rational antibiotic prescription for Noma patients, thereby reducing the risk of AMR in Noma care [53, 54].

A study across 14 countries by the African Society of Laboratory Medicine found that only 1.3% of the 50,000 medical laboratories in the 14 participating SSA countries perform routine bacteriological testing to identify infections in symptomatic patients, and of these, only 1.3% have the capacity to conduct antimicrobial susceptibility testing to determine drug resistance, with only a few able to perform culture of anaerobes. In addition, only five of the fifteen priority pathogens are tested consistently in most countries [20]. There is a need to expand the current microbiological capacity in the region. In light of increasing surveillance, the WHO should continue to support the expansion of laboratory capacities in countries endemic for Noma, particularly laboratories serving Noma treatment centers, to strengthen microbiology laboratory capacity for testing, including aerobic and anaerobic culture. It may also be helpful to have minimum AST panels for clinically relevant organisms like the Prevotella spp. We also recommend that organizations supporting Noma care, especially in the African region, including donor organizations such as Hilfsaktion Noma e.V. and medical humanitarian organizations such as Médecins Sans Frontières, should continue to expand their support to include microbiological testing.

Health promotion is identified as one of the key activities in the model of care for Noma patients at the MSF-supported Noma treatment center in Nigeria. While it is useful in the treatment facilities, community-based health promotion and engagement activities, especially in Noma-affected communities, may increase awareness about Noma, improve oral hygiene practices, health-care-seeking behaviour, and early case identification and presentation at treatment centers. The health promotion efforts should also incorporate AMR-related messaging into their communications. This may potentially reduce pre-hospital antibiotic self-medication and over-the-counter medication use, and overall help the community to take ownership of their health [10, 55].

Conclusion

Despite the paucity of data on AMR in Noma-affected populations, there are increasing reports of AMR in Noma patients. Noma and AMR share determinants, with the potential to amplify each other. Ignoring AMR in Noma control may pose a risk of future potential treatment failure and may endanger the progress already made in the control of Noma, for a disease that is already about 90% fatal without treatment. While the WHO has recognized Noma as an NTD to increase awareness, stimulate funding, encourage research, and boost control efforts, AMR remains a potential threat to progress in Noma control. There is an urgent need to strengthen Noma prevention practices in endemic communities, including oral hygiene; reinforce IPC and AMS programs in Noma treatment centers; and mainstream AMR in Noma control, especially in Noma-endemic regions. to avoid losing the limited therapeutic agents we currently have.

Abbreviations

WHO	World Health Organization
NTD	Neglected Tropical Disease
AMR	Antimicrobial resistance
SSA	Sub-Saharan Africa
AMS	Antimicrobial stewardship
GLASS	Global Antimicrobial Resistance and Use Surveillance System
DALYs	Disability-adjusted life years
UHC	Universal Health Coverage
IPC	Infection prevention and control
IHME	Institute of Health Metrics
WASH	Water, sanitation, and hygiene

DRI	Drug resistance index
LMICs	Low- and Middle-Income Countries
SSIs	Surgical site infections
NAP-AMR	National Action Plan on Antimicrobial Resistance
HAIs	Hospital-acquired infections
ESBL	Extended-Spectrum-Beta-Lactamases
ARGs	Antimicrobial resistance gene
AST	Antimicrobial sensitivity testing
OTC	Over-the-counter (refers to over-the-counter medications)
AWaRe	Access, watch, reserve

Supplementary Information

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Supplementary material 1.

Supplementary material 2.

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