Interventions to Eliminate Tetanus in Nigeria: A Systematic Review

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ABSTRACT

Tetanus, though vaccine preventable, is a commonly occurring life-threatening affliction of new-borns and pregnant women in low- and middle-income countries, including Nigeria. This is mostly due to the infection of wounds with Clostridium tetani from unhygienic delivery and cord care practices. While tetanus cannot be eradicated, elimination is possible through a combination of strategies. A literature review from 2015 to 2024 was conducted in PubMed/MEDLINE, African Journals Online, Google Scholar, and the Grey literature, following PRISMA guidelines to identify relevant publications. Eight studies met the inclusion criteria and were assessed for evidence quality using an expanded PRISMA checklist. The studies identified the several interventions operationalized for the elimination of tetanus in Nigeria and the outcomes of these interventions, inclusive of: conditional cash transfer (single conditionality – N5 vs N300 vs N800) for maternal vaccination with tetanus toxoid vaccine, single dose (versus none) maternal tetanus toxoid vaccination during pregnancy (AOR=3.2; 95% CI =1.1, 10; p=0.04), improved maternal antenatal care follow-up (AOR=3.3; 95% CI= 1.2, 8.3; p=0.03), and improved access to tetanus toxoid immunization information in pregnancy (last 12 months: AOR = 2.5; 95% CI = 1.1, 2.5; p=0.02). The key demand-side and supply-side factors influencing these outcomes include: lack of knowledge of the current immunization schedule, dependence on physician referral for immunization, inefficient immunization records keeping systems, poor health staff attitude as well as lack of community participation. Targeted health education and promotion, maximisation of opportunities for vaccination of high-risk groups, adequate financing of immunization and improved disease surveillance at all levels are essential for achieving elimination targets.

INTRODUCTION

Tetanus, though vaccine preventable, is an endemic life-threatening affliction of new-borns and pregnant women in Low-and-middle-income-countries, including Nigeria. This is due to the impregnation of wounds with Clostridium tetani from unhygienic delivery and umbilical cord care practices [15]. Common risk factors associated with the disease include: inadequate number of antenatal care visits, inadequate number of Tetanus Toxoid Containing Vaccine (TTCV) injections received during pregnancy, place of confinement at birth and poor or substandard unorthodox cord care practices [2], [15], [20]. Whereas diagnosis is essentially clinical and mortality rates for infected neonates and adults hover around one hundred percent, this statistic can be significantly reduced by appropriate treatment and professional supportive care [20], [26]. While tetanus cannot be eradicated due to the endemic nature of the causative organism, it can be eliminated [29].

To this end, the World Health Organization defines neonatal tetanus elimination as the occurrence of less than one neonatal tetanus case per 1000 live births per district per year; and launched Neonatal Tetanus (NT) and Maternal and Neonatal Tetanus Elimination (MNTE) in the years 1989 and 1999 respectively, with a focus on fifty-nine priority countries [29]. Following this launch by the World Health Organization and partners, however,

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the target dates for global elimination of tetanus as set for the years 1995, 2005 and 2015, have been missed [29]. In this context, thirteen countries, including Nigeria, have yet to achieve validation for maternal and neonatal tetanus elimination (MNTE) [29]. The key contributing factors to this are: numerous hard-to-reach areas and communities, significant health inequalities, cultural practices and societal norms that affect vaccination uptake, and the widespread distribution of large populations across vast region [1].

Additionally, widely recommended strategies for achieving maternal and neonatal tetanus elimination (MNTE) in all settings primarily include the 'five cleans,' vaccination with tetanus toxoid-containing vaccines (TTCV) for neonates, women of childbearing age, and pregnant women, as well as comprehensive surveillance in all its forms [15]. Concerning the ‘five cleans’, its role in reducing tetanus mortality in neonates is recognized, though when considered principally in the context of Skilled Birth Attendants [19], [20]. While vaccination with TTCV is credited with significantly reducing tetanus mortality over two decades starting from 1990, particularly in sub-Saharan Africa, surveillance—an essential pillar for the elimination of the disease—remains highly inadequate [12], [13], [19]. This has influenced the christening of Maternal and Neonatal Tetanus as a “silent killer” as the timelines, completeness and quality of reporting still remains a significant challenge [19].

Though tetanus has been eliminated in the global north, with near eradication, due to the success of routine and or primary immunisation programs, there has however been a sputtering of cases particularly in frail elderly people in recent times. This could be due to waning immunity which brings to the fore the need for booster vaccination and continued surveillance [9]. The converse is, however, the case in sub-Saharan African countries such as Nigeria, where routine immunisation programs, especially of high risk and/or target groups are not as effective. This among other inequities in health care service delivery does not beg the question regarding the abysmal ranking of the health system of Nigeria as 163 of 193 [29].

More concisely, tetanus accounts for two percent (2%) of all neonatal deaths globally but the burden of neonatal tetanus in Nigeria is significantly higher than this [1]. Additionally, Nigeria is one of 27 countries that account for 90% of the global burden of the disease [1]. However, it is critical to note that these figures are a scant representation of the true burden of the disease, in country, as only about five percent (5%) of cases present at hospital [21]. Add to this the miniscule coverage of TT2+ immunisation in Nigeria, estimated to be a mere forty percent (40%) as of the year 2019 and the magnitude of the problem becomes more glaring [31].

In Nigeria, disease mitigation interventions are often fragmented with limited collaboration and coordination between programs. This results in parallel programs being implemented for any singular project. For tetanus, most studies have revolved around the interrogation of demand and supply side factors affecting vaccination with TTCV in target groups [20], [21], [26]. However, available literature on interventions targeting Tetanus elimination in Nigeria is remarkably sparse.

In response to the issues highlighted above, this review evaluates Nigeria’s tetanus elimination interventions, seeking to provide comprehensive evidence-based, context-specific recommendations for addressing constraints and enhancing outcomes over the short, medium and long term. This is more so as the focus of maternal and neonatal tetanus elimination initiatives in the country has predominantly been on vaccinating infants, women of childbearing age and pregnant women.

MATERIALS AND METHODS

Search Strategy

A systematic approach was used to conduct the literature review in PubMed/MEDLINE and African Journals Online data bases, following PRISMA guidelines, to identify publications on interventions for the elimination of tetanus in Nigeria spanning the period 2015 to 2024. Manual bibliographic searches for relevant papers, as well as search on Google, Google Scholar and other journal hosting sites, were also carried out. These revealed studies in the grey literature.

The key words and/or MeSH terms for literature search did include the following: “Interventions” OR “factors” OR “outcomes” AND “for” OR “of” OR ‘associated with” OR “influencing” OR “affecting” OR “contributing to” AND “elimination” AND “tetanus” AND “Nigeria”.

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The search was conducted for the aforementioned time period with a view to elucidating the interventions instituted by the World Health Organization (WHO), governments, and partners for the elimination of maternal and neonatal tetanus in Nigeria. See PRISMA diagram (Figure 1) below.

Quality of Evidence

Using the expanded PRISMA checklist (2020), overall assessment of the quality of evidence, of selected studies, as well as compliance with same was carried out through indicating 'Yes' and "No' answers to the interrogations and/or requirements, in the designated areas of inquiry derived therefrom, for quality of evidence as follows: Usefulness and relevance of study (Title, abstract, introduction), appropriateness of and assessment of summary outcomes (methodology), incisiveness and specificity of findings (results, analysis and reporting), results use and decision modelling (discussion and findings). For a complete presentation, see Table 1 below.

Inclusion Criteria

Key articles reporting interventions to eliminate tetanus in Nigeria were included based on the following criteria:

1. Original studies published in English.
2. Studies published between 2015 and 2024 (as the period matched the pre-MNTE campaign proposed date (2015), by the World Health Assembly, for the elimination of tetanus in Nigeria).
3. Studies on interventions geared towards the elimination of tetanus in Nigeria.
4. Studies espousing the outcome of interventions geared towards the elimination of tetanus in Nigeria.
5. Studies that considered factors affecting the elimination of Tetanus in Nigeria, in the following categories:
   i. Demand-side factors (Target group related/Economic/Sociocultural/Education)
   ii. Supply-side factors (Health system related/Logistics/Access/Utilization).
   iii. Miscellaneous factors (Information/ Media/Peer groups).
6. Studies that satisfied the criteria for quality of evidence (as delineated in the assessment for quality of evidence –Table 1).

Exclusion Criteria

1. All studies not meeting the above inclusion criteria were excluded.
2. Editorials, editorial reviews, and comments, emanating therefrom, were excluded.

Data Extraction

Following the search, duplicate citations were excluded and/or removed. Thereafter, screening of article titles and abstracts, followed by examination of full text articles based on the inclusion criteria. Selected papers were then retrieved, and full-length versions read thoroughly. The following information was extracted from the selected papers:

a. Study population and area where the study was carried out.
b. Methodological approach and follow-up period.
c. Key findings of study, as regards the following, by year.
   i. Interventions geared towards the elimination of tetanus in Nigeria.
   ii. Strategies for and progress towards elimination of maternal and neonatal tetanus in Nigeria.
   iii. Outcomes and related factors for elimination of tetanus in Nigeria.
d. Health system nuances that contribute to the outcomes of vaccination of the target group.

Articles that used multiple methodologies were included in more than one category. Any disagreements in extracted data between the authors were resolved by consensus or by arbitration of a third review author (CTW).

Data Management and Analysis

Retrieved data are presented as tables and charts; Egger's regression test was carried out to assess for publication bias.

The magnitude of the intervention, measured by the effect sizes of the studies, was reported within the context of the independent variables against which the outcome was obtained.

Following this, discussion of the findings is entertained, highlighting key findings and proffering possible reasons for these and solutions to the same.

RESULTS

A total of eight studies were included in the systematic review. All study designs were considered. Seven of the studies were primary studies, and one was a systematic review. The eight studies were published between the years 2016 and 2020. Six of the studies focused completely on interventions for the elimination of tetanus in Nigeria, while one study interrogated the cost of prosecuting focused tetanus elimination interventions in thirteen countries, including Nigeria. The systematic review examined interventions for the elimination of tetanus in countries across sub-Saharan Africa, specifically Ivory Coast, Kenya, Ethiopia, and Nigeria. The primary studies were carried out in rural and urban areas, as was the case for the studies that made up the systematic review.

The studies revealed the following common demand-side themes as responsible for the propagation of maternal and neonatal tetanus in Nigeria:

Adedire et al, 2016: investigated the key factors responsible for the propagation of maternal and neonatal tetanus (MNT) in Nigeria [2]. In this study, the principal factors associated with the continued propagation of MNT were: Antenatal care follow-up {Yes vs No - AOR=3.3; 95% CI = 1.2, 8.3; p = 0.03}, maternal tetanus toxoid vaccination {1 dose vs None – AOR = 3.2; 955 CI = 1.1, 10; p = 0.04}, maternal knowledge of routine immunization {Good vs Poor – AOR = 2.4; 95% CI = 1.6, 3.8; p = 0.01} and access to immunization information in the last twelve months { Yes vs No – AOR = 2.5; 955 CI = 1.1, 2.5; p = 0.02}. Consistent with the foregoing, therefore, the following interventions, specifically, health education and promotion of tetanus immunization, antenatal care and skilled birth attendance as well as TTCV immunization of target groups, are considered tacit for attainment of MNTE in this clime.

Bashir et al, 2016: considered the subject of tetanus immunization in HIV positive women, with the following summary findings being noted: Lower cord and maternal serum tetanus antibody levels in HIV infected women due to the wholesome effect of maternal HIV, as well as its effect on trans placental transfer of protective antibodies [4]. To this end, therefore, prevention and/or limitation of the transmission of HIV/AIDS, routine TTCV immunisation of HIV positive women as well as the administration of booster doses of TTCV to HIV infected women, as required, over time, were considered to be veritable strategies for the elimination of tetanus in Nigeria.

Vouking et al, 2017: summarily looked at the subject of missed opportunities for vaccination with respect to MNTE. The principal findings in this study included poor knowledge of the TTCV immunisation schedule, poor maternal socioeconomic and educational status, dependence on referral by physician for immunisation, poor immunization record keeping and peculiarities of the geographical terrain, which collectively contribute to or amplify missed opportunities for vaccination [28]. Other factors such as poor social and community mobilisation and enlightenment, vaccine hesitancy and/or rejection due to local norms, culture and beliefs, distance to health facility and difficulty of access due to cost of transportation to and from the health facility were also veritable culprits [28]. Furthermore, vaccination of target groups is considered status-barred by barriers emanating from competing obligations, domestic, civil or secular, which place heavy premiums or constraints on time available to access health services for immunisation and/or other procedures, particularly for women and their children [28]. The proffered interventions for tetanus elimination in this regard were, improved availability, affordability, and accessibility to maternal tetanus toxoid vaccination as well as health education and community mobilization.

Nass et al, 2017: interrogated the associations between selected neonatal tetanus risk factors and neonatal tetanus mortality. The key findings in this study were the association between the number of maternal tetanus toxoid injections, the frequency of antenatal care visits, the place of confinement during delivery as well as the prevalent cord care practices, and tetanus related neonatal mortality [20]. In this regard, neonates whose mothers had one dose of TTCV were 4% less prone to NNT mortality compared to neonates whose mothers did not have any dose of TTCV during pregnancy (OR = 4.12; 955 CI = 1.04, 16.29; p <0.05) [20]. Consequently, the strengthening of NNT surveillance systems, TTCV vaccination or immunization of pregnant mothers, and health promotion are considered effective strategies for the attainment of MNTE.

Nass et al, 2017: compared NNT prevalence and mortality rates from existing local hospital records to those from the contemporary surveillance system and the key finding was a local prevalence of NNT and associated mortality of 336 cases and 3.4 deaths per 100,000 population, respectively, compared to the reported surveillance system NNT prevalence of 111 cases and 1 death per 100,000 population, respectively [19]. This signified gross underreporting of NNT in the existing IDSR system. Consequently, active surveillance and strengthening of the same are considered necessary for the elimination of MNTE in Nigeria.

Majiyagbe et al, in 2018: examined common factors that facilitate and propagate maternal and neonatal tetanus. The outcomes from the study revealed that low socioeconomic class and low level of education are common twin vicissitudes that facilitate and propagate MNT, in this clime. More specific demand side factors, in this regard, were: poverty, low immunization with TTCV, unhygienic home deliveries with attendant poor cord care practices, as well as strong sociocultural belief in Traditional Birth Attendants. Other factors, more commonly referred to, include the high cost of hospital deliveries as well as lack of financial protection due to the use of out-of-pocket mode of health care financing and lack of health insurance [17]. In consonance, thereof, the following were considered as veritable strategies for the elimination of tetanus in this clime: strengthening of routine immunisation of target groups, increased availability and provision of Skilled Birth Attendance, health education of target groups, and community mobilisation for vaccination action.

Laing et al 2019: The study by Laing et al in 2019 interrogated the investment case for MNTE in Nigeria (and other countries) by looking at the projected costs for clean delivery and cord care, increasing TTCV immunization at antenatal care (pregnant women), as well as the cost of standard TTCV immunization campaigns such as Supplementary Immunization Activities (SIA's) for Women of Child Bearing Age (WCBA) and pregnant women [16]. The cost of clean delivery and chlorhexidine for cord care (for 20,500,000 pregnant women) was estimated to be $4, 303,002 and $1, 592, 111 respectively, while the additional cost of increasing routine TTCV immunization at antenatal care over three years was put at $2, 687, 185. Furthermore, the cost of three standard TTCV immunization campaigns to cover 16,400,000 WCBA/pregnant women was put at $39, 478,907 [16]. These cost computations give impetus for appropriate investments in the assessed interventions, especially as financing of clean delivery and clean cord care practices are estimated to reduce neonatal tetanus rates by as much as twenty-five percent (25%) and are deemed to be comparatively cost-effective [16]. Consequently, targeted financial investments in increasing routine vaccination of WCBA & pregnant women, promotion of clean deliveries and clean cord care, Neonatal Tetanus (NNT) surveillance strengthening and in MNTE validation exercises are proffered strategies for elimination of tetanus in Nigeria.

Sato et al, 2020: Similarly, the findings from the study by Sato et al, in 2020 showed that distance from the clinic or vaccination site, lack of a convenient mode of transport to and from the clinic or vaccination site, high cost of transportation to and from the vaccination site (including high cost of the preferred alternative) as well as the remote location of settlements and communities as cogent contributors to suboptimal TTCV immunisation [26]. To this end, the researchers considered conditional cash transfer (single conditionality) for the decision to be vaccinated with TTCV as a strategy for tetanus elimination.

In consonance with the findings above, a myriad cross cutting supply side factors such as dearth of appropriately qualified and trained health care personnel, healthcare workforce attrition, poor cold chain infrastructure and vaccine management protocols, poor monitoring, evaluation and supportive supervision of vaccination and elimination interventions, poor funding of processes and programs for tetanus elimination, as well as poor enlightenment, social and community mobilisation for immunisation (particularly, supplementary immunisation

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campaigns) are noted to contribute significantly to the low level of TTCV immunisation in children, women of child bearing age and pregnant women, particularly, in this clime.

To this end, immediate and hybrid, strategies and interventions volunteered as plausible for the elimination of tetanus among high risk groups in Nigeria include: financial investments in tetanus elimination activities such as routine and supplementary immunisation activities in women of child bearing age and pregnant women, communication as an added tool for community engagement, mobilisation and participation in immunisation programs, community co-management of immunisation programs through involvement at each stage of the program from planning to implementation to monitoring and evaluation. Others are immunisation of target groups through incorporation of TTCV vaccination in the routine immunisation of children and pregnant women as well as through supplementary immunisation activities and/or campaigns (for women of childbearing age) and, improvements in service delivery and/or supply through appropriate scheduling of sessions (fixed, outreach and supplementary), staffing, logistics and supervision as well as continuous active surveillance for maternal and neonatal tetanus, and strengthening of surveillance as a whole as shown in tables 2a, 2b and 2c below.

DISCUSSION

The importance of maternal and neonatal tetanus as a notifiable public health disease in the global south and Nigeria, in particular, as well as in a number of developing countries, more generally, cannot be overemphasized. This research investigates tetanus elimination strategies and interventions in Nigeria, proposing solutions to address challenges impeding effective program delivery.

Routine immunisation of pregnant women and children using TTCV is volunteered to be a critical tool for the elimination of tetanus in Nigeria. However, myriad socioeconomic factors serve as barriers to the attainment of adequate coverage of tetanus immunization. Studies reveal that socioeconomic constraints, such as unemployment, poor education, and illiteracy, frequently hinder attainment of high TT2+ coverage during pregnancy, which brings to the fore the poor decision-making power of women within the lower socioeconomic bracket. The WHO recommendation of at least four antenatal clinic visits per pregnancy as a means of facilitating appropriate TTCV immunization of pregnant women becomes glaringly unattainable when considered in this context. In this regard, a common recommended addendum to routine vaccination, in defaulting areas, and especially for elimination of tetanus in high-risk countries, such as Nigeria, is supplementary immunisation activities (SIAs) that target women of childbearing age with three doses of TTCV. This summary reveals that the foregoing remedial themes were the common position of a number of studies in this treatise, which are in keeping with the study conducted across sixty low-and middle-income countries, by Zegeye et al [32] and that by Conde et al, in Guinea [7]. However, implementation of the recommended TTCV immunization SIA's have been few in Nigeria, which prompts the suggestion and proposal that attainment of target TTCV immunization, inclusive of SIA's, would best be achieved by executing TTCV vaccination, using an integrated context, through convergence of related maternal health programs.

In consonance with the foregoing, it is noted that improving availability, affordability, accountability, and access to and for vaccination of target groups with TTCV is further considered a veritable panacea for attaining maternal and neonatal tetanus elimination. The volunteered premise for this submission is that there would be cost reduction (direct, indirect, and marginal costs) and/or savings for vaccination of target groups, especially those residing in far-flung and hard-to-reach settlements. This is envisaged to result in improved service delivery, enhanced confidence in the health care system and improved vaccination outcomes in the short, medium, and long terms, especially within the context of optimizing maternal and child health, and universal health coverage. This position corroborates research outcomes by Chopra et al [6], Olayinka et al [22], and other studies in South Africa [14]. However, it is worthy to note that, in this clime, the lack of financial protection, as provided by health insurance, and the almost exclusive use of the out of pocket model of health care financing makes for catastrophic expenditure on the part of patients whilst the ever dwindling official healthcare expenditure puts a strain on affordability and access for relevant TTCV immunization services. To this end, therefore, the promotion of financial protection through health insurance, and the implementation of the community-based aspect of the health insurance scheme, is considered a veritable solution to this problem.

Also, the promotion of skilled birth attendance was noted to be critical for the reduction of maternal and neonatal tetanus in Nigeria through the facilitation of clean delivery practices such as clean surfaces, clean hands, clean cutting of umbilical cord and clean cord care practices. This was the position in several of the studies and is corroborated by other studies by Rahman et al [25], which was conducted across fifty-four low- and middle-income countries in Asia, Africa, the Pacific, the Caribbean, Latin America, and Europe. However, local sociocultural beliefs and practices have continued to see pregnant women attended to, at confinement, by traditional birth attendants with associated increased risk of unhygienic delivery and cord care further propagating maternal and neonatal tetanus. This situation notwithstanding, health education and promotion of Skilled Birth Attendance is considered a lasting solution to this teething problem in the short, medium, and long terms.

As an addendum to the above, health education and health promotion have been identified as key thrusts for the achievement of immunization targets to routine TTCV immunization and maternal and neonatal tetanus elimination. In Nigeria, knowledge and attitude towards TTCV immunization is noted to be poor with suboptimal buy-in, participation, and ownership on the part of women of childbearing age and pregnant women. This could be due to myriad sociocultural factors that impinge on women including of low level of education of women compared to their male counterparts in the country. The foregoing position is further compounded by the inconsistency of poor labelling and the vertical nature of health education and health promotion messages, programs, or activities generally and within the context of MNTE. This position is in keeping with the study by Visalli and colleagues [27], in Italy, and conducted across seventy-six countries, by Garcia-Toledano et al [11]. To this end, appropriate education and enlightenment of women about TTCV immunization will go a long way in ensuring improved uptake of the vaccine and attainment of MNTE.

However, health education and promotion cannot be complete without social mobilization of peoples and communities for immunization action. This could be because the involvement of gatekeepers such as community leaders and influencers, has been shown to, quite often, lead to acceptance and sustainability of immunization programs and activities over time. The need for robust community mobilization to create awareness and foster utilization of health care facilities and health interventions for the elimination of maternal and neonatal tetanus is noted and a reverberating theme of several of the studies in this review. This position is in keeping with the results of studies in Bangladesh [30]. Consequently, for lasting effectiveness, social mobilization should be carried out on a continuous basis and not just during the implementation of targeted programs.

At this juncture, it is worth noting that Nigeria is a large country and the size of the population puts it in a precarious position as regards disease prevalence, vaccine-preventable diseases inclusive. This view is corroborated by statistics, which place the country as one of those responsible for ninety percent (90%) of the prevalence of tetanus worldwide. Thus, the issue of chronic disease conditions, such as HIV/AIDS, and other comorbidities that affect tetanus immunity is one that requires consideration. Whereas the prevalence of HIV/AIDS in Nigeria is but 1.9%, the large population of the country makes this figure a cause for concern, especially as the disease has been noted to decrease serum levels of tetanus protective antibodies in women of childbearing age, as well as in pregnant women and their neonates. This could pose a threat to maternal and neonatal tetanus elimination efforts. There is thus a need to address the transmission of chronic debilitating diseases such as HIV/AIDS in women of childbearing age, pregnant women and neonates as a matter of course. This is also the position of similar studies in the United States of America [3] and Kenya [10]. Thus, shoring up HIV/AIDS prevention, diagnostic and treatment services, as well as PMTCT services at all levels of the health care system would go a long way to ensure attainment of MNTE [3], [10], in this regard.

Furthermore, robust surveillance is recognized as an essential intervention for maternal and neonatal tetanus elimination globally and in this clime. The studies in this review reveal under-reporting of neonatal tetanus in Nigeria as corroborated by other studies by Oyeyemi et al [23], and Peterside et al [24] in Bayelsa State, Nigeria. This could be due to the poor state of active and other surveillance across all geopolitical zones of the country. The reviewed studies consistently highlighted the necessity for enhanced neonatal tetanus surveillance, in consonance with the findings and recommendations from previous research, including the study of Lambo et al in Pakistan [16]. It can therefore be concluded that heightened surveillance along with further strengthening of the disease notification systems is a necessary requirement for achieving maternal and neonatal tetanus

elimination targets [16], [23], [24]. To do this, there will be the need to improve reporting, inclusive of zero reporting, at all levels of the health care system.

Finally, the need for financial investments for the implementation of plans, programs and time-honoured interventions, for the elimination of tetanus is crucial. It is noted that the costs computed, per individual, for the worldwide recommended compendium of interventions for the elimination of tetanus in Nigeria are trifling and mirror costs computed for similar interventions in similar studies by Bhutta et al [5], and Darmstardt et al [8], in other climes. In this regard, there is need for improved funding of immunization of target groups, promotion of clean delivery and cord care practices and strengthening of neonatal tetanus surveillance. However, though investments in health care should be a continuum, and are often referred to as being quite heavy when economic parameters are considered, the significance of the computed costs and the associated savings, become evident when viewed in the light of strengthened health care systems and improved access to care for vulnerable populations [5], [8]. Nonetheless, the call for improved funding must be viewed within the context of a contracted economy and ever dwindling financial resources.

The foregoing exposé teases out the strategic interventions for maternal and neonatal tetanus elimination in Nigeria and the critical issues bedevilling the intervention among women of childbearing age, pregnant women and neonates in this clime. It further proposes and supports the need for concerted effort to tackle the situation, given the circumstances, peculiarities and facilities in-country.

CONCLUSION

The aforementioned limitations, notwithstanding, we submit that the findings of this study can support the enactment and implementation of actionable policies and programs for the vaccination of target groups with tetanus toxoid-containing vaccines, improving maternal and neonatal tetanus surveillance, increasing skilled birth attendance, and increasing financial investments for the elimination of tetanus in Nigeria.

Limitation of the Study

One major limitation of this study is its focus solely on primary studies published in English. Other limitations revolve around the extent, magnitude and level of heterogeneity of the included primary studies.

Declaration of Competing Interests

The authors declare that there are no competing interests, of any nature, that have influenced or appeared to influence the findings in this work. Lastly, it is pertinent to note that the declared views are entirely those of the authors.

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APPENDIX

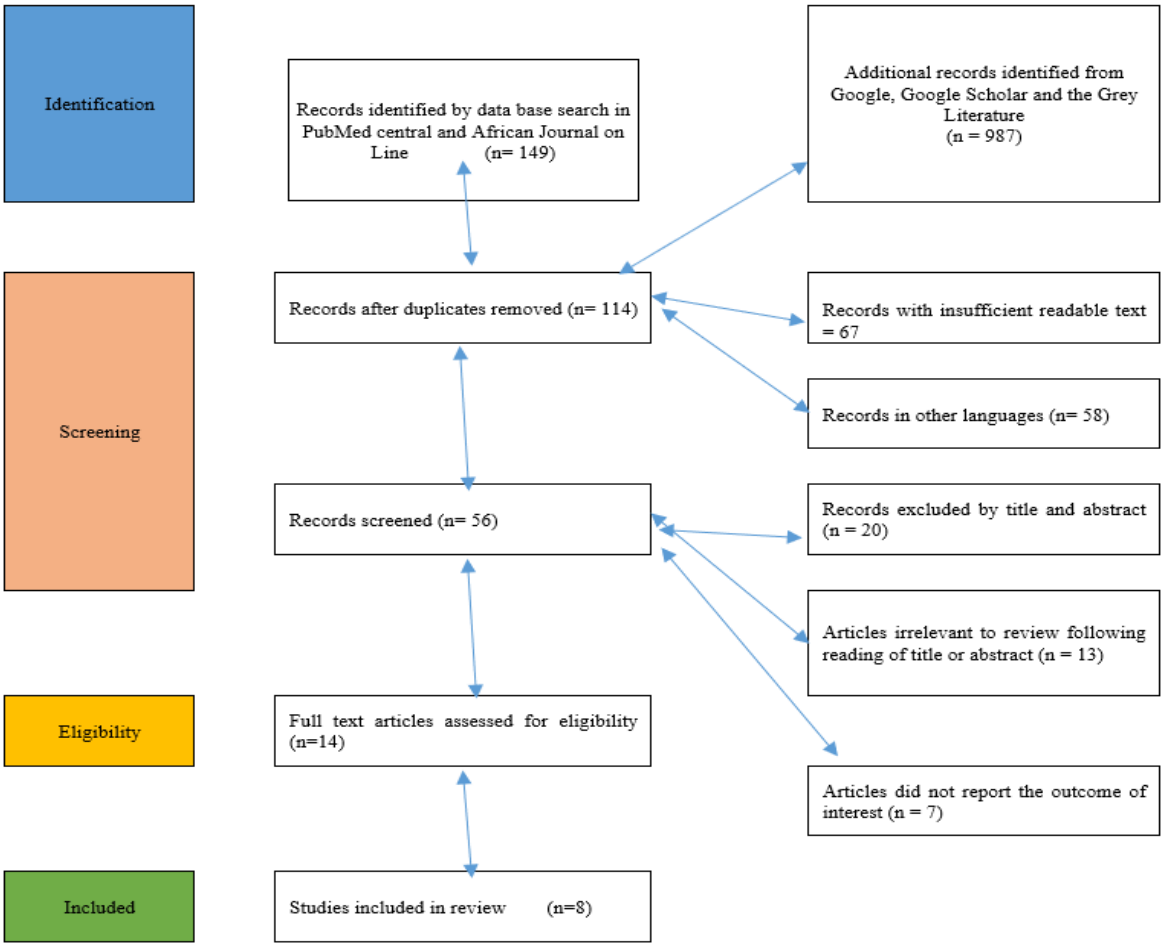

Table 1 Quality of Evidence of Selected Studies

S/N	Study	Title, Abstract and Introduction (Is the study likely to be useful and relevant)	Methodology and Data (Is the applied method appropriate and does it assess the outcome measured)	Analysis and reporting (Are the findings concise and context specific)	Usefulness of Results (Are the results useful for decision modelling)	Quality Assessment (Overall quality Assessment score of study)
1	Adedire et al, 2016	Yes	Yes	Yes	Yes	High
2	Bashir et al, 2016	Yes	Yes	Yes	Yes	High
3	Nass et al, 2017	Yes	Yes	Yes	Yes	High
4	Nass et al, 2017	Yes	Yes	Yes	Yes	High
5	Vouking et al, 2017	Yes	Yes	Yes	Yes	High
6	Majiyagbe et al, 2018	Yes	Yes	Yes	Yes	High
7	Laing et al, 2019	Yes	Yes	Yes	Yes	High
8	Sato et al, 2020	Yes	Yes	Yes	Yes	High
	Key (Questions under each section)					
	Section A		Section B			

	1. Is the title relevant to the topic?		1. Does the methodology address key study constructs?		
	2. Do the rationale and objectives address key study questions?		2. Is the collected data based on PICOS framework?		
	3. Is the study summary thorough and explicit?		3. Is Egger's test for Publication Bias unequivocal?		
	Section C		Section D		
	1. Are the study findings concise and context specific?		1. Do the study results serve as template for decision modelling?		
	2. Are there are no ambiguities left to address?		**Section E**		
			1. Score > 75% (**sections A** to **D)** = **High Quality**		
			2. Score < 75% (**sections A** to **D)** = **Low Quality**		

TABLE 2A Significant Findings from Selected Studies

S/N	STUDY	COUNTRY	AREA WHERE STUDY WAS CARRIED OUT	POPULATION	METHODOLOGY	INTERVENTIONS FOR THE ELIMINATION OF TETANUS IN NIGERIA
1	Adedire et al, 2016	Nigeria	Rural	Women	Cross sectional study	1. Health Education and promotion. 2. Antenatal Care 3. Skilled Birth Attendance 4. Tetanus Toxoid Containing Vaccine immunisation of target groups.
2	Bashir et al, 2016.	Nigeria	Urban	women and neonates	Cross sectional study	1. Limit transmission of HIV/AIDS. 2. Routine Tetanus Toxoid Containing Vaccine immunisation of HIV +ve women. 3. Booster doses of TTCV.
3	Nass et al, 2017	Nigeria	Urban	Neonates	Cross sectional study	Strengthen Neonatal Tetanus surveillance systems
4	Nass et al, 2017	Nigeria	Urban and rural	Neonates	Cross sectional study	1. Strengthen Neonatal surveillance systems. 2. Tetanus Toxoid Containing Vaccine immunization of pregnant mothers. 3. Health promotion.

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5	Vouking et al, 2017	Ethiopia, Ivory Coast, Kenya, Nigeria.	Urban and rural	Women of child bearing age, pregnant women, children.	Systematic review	1. Improve access, affordability & availability of Tetanus Toxoid Containing Vaccine immunization programs. 2. Community mobilisation
6	Majiyagbe et al, 2018	Nigeria	Urban	Neonates	Cross sectional study	1. Strengthen routine immunisation of target groups. 2. Skilled Birth Attendance 3. Health education of Target groups. 4. community mobilisation
7	Laing et al, 2019	Afghanistan, Angola, Central African Republic, Democratic Republic of the Congo, Guinea, Mali, Nigeria, Pakistan, Papua New Guinea, Somalia, South Sudan, Sudan, and Yemen.	Urban and Rural	Women of child bearing age, pregnant women	Cost analysis/Cost effectiveness analysis	Financial investments in: 1. Tetanus Toxoid vaccination of Women of Child Bearing Age & pregnant women. 2. Promotion of clean deliveries and clean cord care. 3. Neonatal Tetanus surveillance strengthening & Maternal and Neonatal Tetanus Elimination validation exercise.
8	Sato et al, 2020	Nigeria	Rural	Women of child bearing age, Pregnant women	Randomized Control Trial	Cash incentive for tetanus toxoid vaccination

TABLE 2B Investment Case for Maternal and Neonatal Tetanus Elimination (Cost of Interventions)

Investment case for Maternal and Neonatal Tetanus Elimination in Nigeria by Study						
			Cost of clean delivery and cord care			
			Target (n)	Clean delivery kits	Chlorhexidine	Delivery
1	Laing et al, 2019	Nigeria	Pregnant women (20,500,000)	$4,303,002	$1,592,111	$4,303,002
2	Laing et al, 2019	Nigeria	Cost of increasing routine immunization with Tetanus Toxoid Containing Vaccine at Antenatal Care			

			Target (n)	% coverage by Year	Additional Cost to routine Vaccination	Total cost
			Pregnant women (20,500,000)	2018 (50%); 2019 (54%); 2020(60%)	$481,894	$2,637,185
3		Nigeria	Cost of standard Tetanus Toxoid Containing Vaccine immunization campaign			
	Laing et al, 2019		Target (n)	Number of campaigns	Cost Per patient	Total cost
			Women of Child Bearing Age /Pregnant women (16,400,000)	3	$2.41	$39,478,907

Outcome/Study	Adedire et al, 2016 [1]	Bashir et al, 2016 [2]	Nass et al, 2017 [3]		Nass et al, 2017 [4]	Sato et al, 2020 [8]	
	aOR[1]	OR[4]	n (%)	Chi Square	aOR[1]	Cash Incentive	OR[4]
Socioeconomic status	NISS[3]	Wald test = 3.052 (p = 0.217)	NIIS[3]	NIIS[3]	NIIS[3]	NIIS[3]	
Access to Immunisation	1.8	NIIS[3]	NIIS[3]	NIIS[3]	NIIS[3]	NIIS[3]	
Antenatal Care (ANC)							
< 1 ANC visit	3.2	NIIS[3]	177 (53)	NIIS[3]	NIIS[3]	NIIS[3]	
1 - 3 ANC Visits		NIIS[3]	54 (16.3)	NIIS[3]	NIIS[3]	NIIS[3]	
4 ANC visits		NIIS[3]	16 (5)	3.93(p = 0.14)	Wald test = 0.25 (p = 0.62)	NIIS[3]	
TTCV immunisation							
1 Dose	3.3	NIIS[3]	Survived 13 (4); Dead 31(9)	7.8 (p = 0.02)	NIIS[3]	C 5(N5)	Reference
						C300(N300)	3.36 (95% CI = 2.60 - 4.35; p = 0.001
						C500(N500)	7.58 (955 CI = 4.51-10.97; p = 0.001
2 or more		Wald test = 0.141 (p = 0.932)	Survived 15 (5); Dead 19(6)		4.12 (95% CI = 1.04 - 16.29; p < 0.05)	NIIS[3]	
Place of Delivery							
Home	NIIS[3]	NIIS[3]	Survived (19.6); Dead (67.8)	12.24 (p = 0.001)	NIIS[3]	NIIS[3]	

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI | Volume XII Issue XV October 2025 | Special Issue on Public Health

Health facility	NIIS[3]	NIIS[3]	Survived (6.3); Dead (6.6)	Reference	NIIS[3]	NIIS[3]
Seronegativity for antitetanus antibody						
HIV[2] +ve Mother	NIIS[3]	16.27 (95% CI = 3.28 - 80.61; p <0.001)	NIIS[3]		NISS[3]	NIIS[3]
HIV[2]+ve Child	NIIS[3]	33.75 (95% CI = 4.12 - 276.40; p <0.001)	NIIS[3]		NISS[3]	NIIS[3]
Likelihood of poor trans placental transfer of Tetanus antibodies						
HIV[2] +ve Mother	NIIS[3]	4.916 (CI = 1.22 - 19.79; p = 0.033)	NIIS[3]	NIIS[3]	NISS[3]	NIIS[3]
HIV[2] -ve Mother	NIIS[3]	Reference	NIIS[3]	NIIS[3]	NISS[3]	NIIS[3]
Surveillance						
Neonatal Tetanus	NIIS[3]	NIIS[3]	336 (100)		NIIS[3]	NIIS[3]
Mortality			247 (73.5)			
Reported						
Neonatal Tetanus	NIIS[3]	NIIS[3]	111(33)		NIIS[3]	NIIS[3]
Mortality			72 (64)			
Underreported						
Neonatal Tetanus	NIIS[3]	NIIS[3]	225 (68)		NIIS[3]	NIIS[3]

1 - Adjusted Odds Ratio 2 - Human Immunodeficiency Virus 3 - Not Indicated In Study 4 - Odds Ratio