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## Field investigation of high reported non-neonatal tetanus burden in Uganda, 2016–2017

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### Abstract

**Background:** Despite providing tetanus-toxoid-containing vaccine (TTCV) to infants and reproductive-age women, Uganda reports one of the highest incidences of non-neonatal tetanus (non-NT). Prompted by unusual epidemiologic trends among reported non-NT cases, we conducted a retrospective record review to see whether these data reflected true disease burden.

**Methods:** We analysed nationally reported non-NT cases during 2012–2017. We visited 26 facilities (14 hospitals, 12 health centres) reporting high numbers of non-NT cases ( $n = 20$ ) or

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#### Author contributions

Conceptualized the evaluation: H.M.S., R.A.T., A.D.R., R.M.C. Collected and/or analysed data: R.M.C., J.N., J.L., H.M.S. Drafted the manuscript: R.M.C., H.S. Reviewed and provided critical feedback on the manuscript: J.N., B.O., I.A., J.L., P.T., B.P.Z., A.K., E.K., R.A.T., B.D., A.D.R., H.M.S. Approved the final version of the manuscript: R.M.C., J.N., B.O., I.A., J.L., P.T., B.P.Z., A.K., E.K., R.A.T., B.D., A.D.R., H.M.S.

#### Ethics approval

The protocol was approved by the medical ethics committee at the Uganda Virus Research Institute (GC/127/17/10/603). In accordance with the human-patients review procedures of the CDC, the evaluation was determined to be non-research. The Uganda Ministry of Health granted permissions for local site visits. All key informants provided informed written consent.

#### Supplementary data

Supplementary data are available at *IJE* online.

#### Conflict of interest

None declared.

zero cases ( $n = 6$ ). We identified non-NT cases in facility registers during 1 January 2016–30 June 2017; the identified case records were abstracted.

**Results:** During 2012–2017, a total of 24 518 non-NT cases were reported and 74% were 5 years old. The average annual incidence was 3.43 per 100 000 population based on inpatient admissions. Among 482 non-NT inpatient cases reported during 1 January 2016–30 June 2017 from hospitals visited, 342 (71%) were identified in facility registers, despite missing register data (21%). Males comprised 283 (83%) of identified cases and 60% were 15 years old. Of 145 cases with detailed records, 134 (92%) were clinically confirmed tetanus; among these, the case-fatality ratio (CFR) was 54%. Fourteen cases were identified at two hospitals reporting zero cases. Among >4000 outpatient cases reported from health centres visited, only 3 cases were identified; the remainder were data errors.

**Conclusions:** A substantial number of non-NT cases and deaths occur in Uganda. The high CFR and high non-NT burden among men and older children indicate the need for TTCV booster doses across the life course to all individuals as well as improved coverage with the TTCV primary series. The observed data errors indicate the need for data quality improvement activities.

### Keywords

Tetanus; Uganda; public health surveillance; vaccination; booster immunization; tetanus toxoid; data quality

## Introduction

Tetanus is a non-communicable disease that occurs when wounds are contaminated with the spores of *Clostridium tetani*, an anaerobic bacterium that produces a potent neurotoxin. Because of the widespread existence of *C. tetani* spores in the environment, the disease cannot be eradicated. Historically, global efforts have focused on maternal and neonatal tetanus elimination (MNTE). However, of the >14 000 tetanus cases worldwide reported to the World Health Organization (WHO) in 2019, 85% were non-neonatal tetanus (non-NT) among persons aged >28 days.<sup>1</sup> The globally reported number of non-NT cases likely underestimates the true burden given that a quarter of countries, mostly in Africa, reported not having non-NT surveillance in 2017.<sup>2,3</sup> A WHO standard for non-NT surveillance was first created in September 2018 and incorporation of this standard into Integrated Disease Surveillance and Response for the WHO African Region (AFR) occurred in 2019.<sup>4,5</sup>

Classical presentation of non-NT includes trismus (lockjaw), risus sardonicus (grimace), opisthotonus (characteristic arching of the back) and generalized seizure-like spasms that occur usually in response to stimuli. In severe cases, autonomic dysfunction, initially manifesting as tachycardia and hypertension, can lead to bradycardia, hypotension and cardiac arrest. The most common causes of death are complications arising from dysautonomia and respiratory arrest secondary to laryngospasm.<sup>6</sup> The diagnosis of non-NT is based entirely on clinical features as definitive laboratory diagnosis is not possible.<sup>4</sup> The three objectives of treatment are wound debridement, neutralization of circulating toxin through administration of human tetanus immunoglobulin (TIG) or equine anti-tetanus serum (ATS) and supportive care. Supportive care for tetanus includes isolation to avoid

noise or light stimuli, treatment with antibiotics and anti-spasmodics, nasogastric tube feeding and respiratory support (e.g. mechanical ventilation), as required. In addition, age-appropriate tetanus-toxoid-containing vaccine (TTCV) should be administered to prevent future disease. Treatment is often limited by scarce resources in low-income countries (e.g. lack of intensive care or antitoxin). Without appropriate inpatient care and medical intervention, the case-fatality ratio (CFR) for tetanus patients is nearly 100%. With intensive care, the CFR can be reduced to 10–20%.<sup>6,7</sup>

The WHO recommends that six doses of TTCV are provided to all persons to ensure lifelong protection against tetanus.<sup>7</sup> The recommended TTCV schedule includes three primary infant doses, with the first dose administered from 6 weeks of age and subsequent doses at a minimum interval of 4 weeks between doses, which induces protective immunity in almost 100% of those vaccinated. Since immunity from infant doses wanes with age, three booster doses at 12–23 months, 4–7 years and 9–15 years should also be included in the national immunization schedule to provide lasting immunity.<sup>7</sup> In countries where maternal and neonatal tetanus remains a public health problem, up to five doses are offered to women during pregnancy.<sup>7</sup> Whereas many countries in AFR have achieved or made progress towards MNTE,<sup>8–10</sup> few have introduced TTCV booster doses for both sexes.<sup>7,8</sup> As a result, the age and sex distributions of reported tetanus cases has shifted<sup>2,7</sup> and tetanus immunity gaps among children aged 5–14 years and adult men have been noted in settings not providing TTCV booster doses for both sexes in childhood and adolescence.<sup>11,12</sup> A TTCV booster programme also represents an opportunity to catch those persons missed with the primary series.

During the pre-vaccine era in Uganda, tetanus was the third leading cause of death, after malnutrition and pneumonia, among children aged <10 years.<sup>13</sup> Uganda achieved MNTE in 2011 through routine vaccination of pregnant women and vaccination of women of reproductive age (WRA) living in high-risk areas.<sup>14</sup> Coverage with the three-dose primary TTCV series among surviving infants gradually increased from 9% in 1981 to >90% in 2016–2017, but was <60% as recently as the year 2000.<sup>15</sup> Uganda does not yet provide the three WHO-recommended booster doses and reports one of the highest numbers of non-NT cases globally.<sup>1,2</sup> The occurrence of six tetanus cases after voluntary medical male circumcision (VMMC) in Uganda during 2013–2015 further raised awareness of this issue.<sup>2,16,17</sup> An analysis of reported data in Uganda found the highest number of tetanus cases reported among females vs males aged 5 years and from outpatient vs inpatient departments.<sup>16</sup> These findings were unexpected given that (i) TTCV vaccination is provided for WRA in Uganda and (ii) tetanus patients usually require inpatient admission. We conducted a review of reported data and field investigation, including key informant interviews and a retrospective medical record review, to evaluate whether the reported number of non-NT cases in Uganda reflects the true disease burden.

## Methods

### Study context

In Uganda, health facilities are designated as Level I to IV health centre, general hospital, regional referral hospital and national referral hospital, according to the level of service

delivery provided. Inpatient services are provided at Level III health centres, Level IV health centres and hospitals. Intensive care is only available at regional and national referral hospitals and some general hospitals, usually private not-for-profit hospitals.

A tetanus patient typically first presents to the facility's outpatient department and the suspected diagnosis is recorded in the outpatient register. Following inpatient admission, the suspected and clinically confirmed diagnosis of tetanus should then also be recorded in the inpatient register. Separate aggregate reporting for cases of neonatal tetanus (NT) (< 28 days of age) and non-NT (>28 days of age) is done monthly using data from both inpatient and outpatient registers through a web-based health management information system in District Health Information System 2 (DHIS2). Reported case data are aggregated by sex and age group (inpatient: 0–4 and 5 years; outpatient: 0–4, 5–59 and 60 years). The number of deaths is also reported from inpatient departments.

### **Review of reported tetanus data**

We conducted a descriptive analysis of national tetanus case data reported to DHIS2 during 2012–2017. We divided cases by the annual population projections from the Uganda Bureau of Statistics (based on the 2014 census) times 100 000 population to calculate incidence of non-NT and total tetanus (sum of NT and non-NT) separately.

### **Field investigation**

Across all four regions of Uganda, we selected 26 health facilities across 10 districts including 20 health facilities (HF) with high numbers of reported non-NT cases and six with zero reported cases during January 2016–June 2017. After a 2-day training, data were collected by four field teams composed of three or four data extractors from Uganda Ministry of Health, Uganda Public Health Fellowship Program and CDC during November 2017.

### **Key informant interviews**

For each selected facility, we undertook structured interviews with key informants in the tetanus reporting system, including District Surveillance Officers (DSOs), Health Information Officers and healthcare workers. We used a standardized questionnaire tool to elicit details on the flow and management of non-NT patients at facilities, as well as the reporting process.

### **Medical records review**

At each selected health facility, we identified clinical settings where tetanus patients would most likely be treated (outpatient clinics, emergency rooms, tetanus wards, general adult and paediatric wards, surgical wards, intensive care units) and conducted a retrospective review of the respective registers to identify tetanus cases during 1 January 2016–30 June 2017. For each of the visited facilities, we compared the number of cases identified in the facility register with the number recorded on inpatient and outpatient paper reporting forms available at the facility and the number entered in the electronic DHIS2 system. To avoid double counting non-NT cases admitted from outpatient departments and because of observed reporting anomalies among outpatients, we calculated incidence among inpatient

cases only. Percentage missingness of inpatient registers was calculated as number of missing months divided by the total number of months for data collection multiplied by 100; a month was defined as missing if lacking 14 days of register entries.

For cases identified in the registers, clinical notes were requested and those available were abstracted using a standardized form including suspected diagnosis, history of the presenting complaint, immunization history, occupation, cause and location of the wound/injury, treatment, final diagnosis and outcome. Incubation period was defined as the time from probable exposure (e.g. date of motor vehicle collision) to onset of symptoms. Length of hospital and intensive care unit stay were also calculated. The case definition for confirmed non-NT was any person >28 days of age with acute onset of at least one of the following: trismus (lockjaw), risus sardonicus (sustained spasm of the facial muscles) or generalized muscle spasms (contractions) and confirmed by a trained clinician/physician.<sup>4</sup> The severity of tetanus was classified into mild (I), moderate (II), severe (III) and very severe (IV) according to the presence and grade of symptoms (trismus, rigidity, muscle spasms, respiratory compromise, dysphagia, autonomic dysfunction) as described by Ablett.<sup>18</sup>

## Statistical analysis

Data collected using paper forms were entered into Microsoft Access. Descriptive analysis was conducted using SAS version 9.4 for Windows (SAS, Cary, NC, USA). For continuous variables, we determined medians and interquartile ranges (IQRs).

## Results

### Review of reported tetanus data

In Uganda during 2012–2017, 7394 (34%) non-NT cases were reported from inpatient departments and 17 124 (66%) were reported from outpatient departments. In five of six reporting years, more outpatient cases were reported among females, whereas more inpatient cases were reported among males in all years (Figure 1). During 2015–2017, 5229 cases were reported from health centre outpatient departments; hospital inpatient departments reported 2079 cases for the same period (Table 1). In 2016, 3933 outpatient tetanus cases were reported from a single urban health centre (Level II health centre). A second health facility (Level III health centre) reported 174 cases in the same year (Supplementary Table S1, available as Supplementary data at *IJE* online).

The average annual total tetanus incidence as reported through inpatient wards during 2012–2017 was 3.43 per 100 000 population with some variation by year (2.65–4.35 per 100 000 annually). Among reported cases, 12% were aged 28 days, 15% aged 29 days–4 years and 74% aged >5 years (Figure 2a). Focusing on non-NT, the highest reported average annual incidence (5.12 per 100 000) was in the Eastern Region (Figure 2b). Reported CFR for inpatient non-NT cases was 17% overall and was higher among cases aged 29 days–4 years (18%) compared with those aged 5 years (13%).

## Field investigation

Field teams visited 26 facilities nationally, including three or four hospitals in each of the four regions. Facilities included the national referral hospital in Kampala, 5 of 14 regional referral hospitals, 8 of 110 general hospitals (including 3 government and 5 private not-for-profit hospitals) and 12 of 5077 health centres.<sup>1</sup> Aside from one Level II health centre, all facilities visited had capacity to take inpatients (median number of beds: 110, range 2–1463) and completed both inpatient and outpatient monthly aggregate reporting. Nine of the 14 hospitals had intensive care units of varying capacities.

## Key informant interviews

Among the 14 DSOs interviewed, commonly reported challenges with tetanus case reporting and case management included: lack of clarity regarding the non-NT case definition, limited logistical capacity to follow up on reported cases and patients not having access to or being able to afford tetanus inpatient treatments, such as antitoxin. At health facilities, 22 (85%) of 26 Health Information Officers said that their facility routinely reported cases of non-NT, including zero reporting, but knowledge of the reporting process and non-NT case definition varied. Of the 38 healthcare workers interviewed (28 nurses, 10 doctors or clinical officers), 22 (58%) reported that they had treated tetanus patients before and 4 (11%) reported a current admission of a tetanus patient at their facility; 20 (53%) reported that tetanus cases were all or mostly male. Only 11 (29%) reported antitoxin (TIG or ATS) being available for tetanus treatment (Supplementary Figure S1, available as Supplementary data at *IJE* online), whereas 33 (87%) reported providing tetanus vaccination for persons presenting with injuries. In terms of reporting, 32 (84%) healthcare workers reported that all tetanus patients are recorded in the facility register.

## Medical records review

During the review of medical records for 1 January 2016–30 June 2017, 342 (71%) non-NT cases were identified in inpatient registers in hospitals compared with the 482 inpatient cases reported to DHIS2 (Figure 3a and Supplementary Table S2, available as Supplementary data at *IJE* online); this was despite missing inpatient register data (21%). Among the 4286 outpatient non-NT cases reported from health centres visited, only 3 (0.07%) cases could be identified in registers at two health centres (Figure 3b); the remaining cases were data errors where TTCV doses or other morbidities were recorded as tetanus cases. Several reporting gaps and data inconsistencies were identified (Box 1). Of the total 345 unique non-NT patients in inpatient and outpatient registers, 285 (83%) non-NT patients were male and the median age was 17 years (range 1–91 years; IQR: 10–40 years).

Among the 342 inpatient non-NT cases, 145 (42%) had records available for further review; of these, 134 (92%) had documented clinically confirmed tetanus. Overall, 81% of non-NT cases with documented final diagnosis of non-NT were male; 5% were aged 29 days–4 years, 14% 5–9 years, 21% 10–14 years and 60% 15 years (Figure 4a). The highest number of cases was observed in the Eastern Region (Figure 4b). In the Eastern Region,

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<sup>1</sup>Total number of each type of facility at the time the evaluation was implemented (noting that the total number of a specific type of health facility may change over time).



48% of reported cases were among children aged <15 years, compared with 46%, 40% and 12% in the Central, Western and Northern Regions, respectively (Figure 4b).

Of the 134 clinically confirmed non-NT cases, 129 (96%) met the case definition for non-NT (Table 2). Documented symptoms included muscle spasm (80%), trismus (67%), opisthotonos (41%) and risus sardonicus (23%). According to the Ablett classification, 106 (79%) confirmed non-NT patients had severe (III) or very severe (IV) disease. The incubation period was known for 45 (34%) patients and ranged from 1 to 46 days, with a mean of 8 days (IQR: 4–9 days). Almost half (45%) of inpatients were documented as having previously visited a different health centre related to the current medical presentation (e.g. for wound care, tetanus vaccination); most represented themselves with tetanus symptoms several days later. Only seven (5%) were referred during the current visit for admission at a larger facility.

In terms of risk factors among tetanus patients, 121 (90%) had no documentation of tetanus vaccination prior to the wound or tetanus symptoms. Among children aged 29 days–4 years, there was one vaccinated case (aged 3 years) compared with six cases among unvaccinated children aged 29 days–4 years. Among 77 persons aged 16 years, documented occupation was farmer or labourer in 20 (15%) case patients. A history of wound was recorded among 114 (85%) cases, most commonly a traumatic puncture wound (23%) or laceration (21%), and the most common site was the lower limbs (57%). Wound infection was reported in 61 (54%). Five (4%) patients had a history of circumcision (two traditional, one VMMC, two unknown type); five (4%) had a history of jigger bites; and four (3%) had a recent ear or dental infection. No portal of entry could be identified in 17 (13%) cases. One of these patients had a recorded history of recurrent dental infections, but no reported recent infection. None of the patients was documented as having a history of diabetes, recent pregnancy or military service (Table 2).

In terms of tetanus management, 98% of patients received antibiotics, 93% received sedative medications (e.g. diazepam) and 72% were treated in isolation facilities. Mean length of hospital stay was 8 days (range 0–41 days;  $n = 130$ ). Just over a third of patients ( $n = 48$ ; 36%) received TIG or ATS; 25% received antitoxin within 24 h of admission. Of the 48 patients receiving ATS or TIG, 36 (75%) had severe or very severe disease; of the 34 patients receiving ATS/TIG within 24 h of admission, 25 (74%) had severe or very severe disease. Less than a quarter of patients were admitted to the intensive care unit (24%) or underwent intubation (22%). TTCV was documented to be administered during admission for 26% of patients (Table 2).

For the final outcome, 72 (54%) of non-NT patients died. The median time from presentation to death was 6 days (IQR 3–10 days). Another 33 (25%) patients were discharged and presumed to have recovered. A further 29 (22%) had unknown outcome (e.g. due to self-discharge), which could have included death (Table 2). Among 48 patients who received ATS or TIG at any time, 50% died compared with 57% among those patients that had no record of receipt of ATS or TIG. Of the 34 tetanus patients who received ATS or TIG 24 h after admission, 56% died compared with 40% among the 10 patients who received ATS or TIG >24 h after admission.

## Discussion

A substantial number of tetanus cases and deaths occurred in Uganda, and the tetanus burden was highest in older children and adult males. Higher tetanus burden in older children and adults is expected due to historic sub-optimal coverage with the TTCV primary series and waning immunity in countries that lack provision of TTCV booster doses.<sup>11,15</sup> Persons born before 1981 were not eligible for TTCV vaccination and <60% of infants up to the year 2000 received the primary TTCV series; infant TTCV coverage still varies by region.<sup>19</sup> In our study, 90% of identified non-NT cases had no documentation of tetanus vaccination prior to the wound or tetanus symptoms. Furthermore, adult men are more likely to have high-risk occupations such as farming or labouring, which was a documented risk factor in 26% of tetanus cases in our study. We also found that the burden of non-NT varies by region.

Non-NT incidence was highest in Eastern Uganda, which also had the highest proportion (48%) of non-NT cases among children aged <15 years, indicating recent gaps in the vaccination programme. Of the total 10 subregions, the East Central (Busoga) sub-region has had the lowest or second-lowest estimated TTCV3 coverage among children aged 12–23 months in Demographic Health Surveys for the 20-year period during 1995–2016.<sup>19</sup> This specific sub-region has also been documented in studies conducted in 2002–2003 and 2005–2008 to have high historic NT and non-NT burden, respectively, concentrated in older children (12% NT, 15% 1 month–4 years, 54% 5–13 years and 12% 14–45 years).<sup>20,21</sup> This is likely due to the combination of lower TTCV coverage, lack of provision of childhood booster doses and contributing tetanus risk factors, including those associated with environment, hygiene, socio-economic status (e.g. not wearing shoes) and healthcare practices (e.g. application of unhygienic substances to wounds), some of which can be targeted with remedial interventions.<sup>19–24</sup> The recent wide-age-range campaign with the TT-conjugate vaccine MenAfriVac targeting ages <30 years in Northern Uganda during January 2017 may have contributed to increased tetanus immunity and the relatively lower non-NT incidence we found in Northern Uganda in 2017, as has been documented in other settings.<sup>12,25,26</sup>

Although much of the focus on tetanus in Africa has been on circumcision as a risk factor, in this review we found a relatively small percentage of patients (4%) with a history of any type of circumcision. Other medical records reviews have similarly concluded that incidence of tetanus within medical male circumcision programmes is generally low but that traditional circumcision providers need to receive the same level of teaching on safe wound care<sup>27</sup> given the lack of protective antibodies in adult men in such settings.<sup>11,28</sup>

We observed a higher CFR among confirmed non-NT cases (54%) in our review compared with that in the reported surveillance data (17%), which included erroneously reported non-NT cases. Similarly, the CFR in this evaluation was higher than that observed in a meta-analysis of non-NT in sub-Saharan Africa where the median CFR was 44%.<sup>2</sup> Treatment of tetanus patients requires a well-established intensive care unit with clinical staff experienced in treating artificially ventilated and haemodynamically unstable patients, and these facilities were not available in most visited facilities in Uganda. Interestingly, tetanus patients were



self-presenting at large referral and private not-for-profit general hospitals with better capacity for treating non-NT, rather than being referred from health centres; nonetheless, more than three-quarters of them were not subsequently admitted to an intensive care unit for further management. ATS or TIG were only available to about a third of patients.

Our findings highlight the need for tetanus vaccine booster doses to protect all individuals across the life course. These findings also serve as a reminder of the critical importance of strengthening delivery of routine vaccinations in infancy, childhood and adolescence, and increasing efforts to identify and close immunity gaps. Equitable immunization and removal of gender-related barriers to vaccination have been highlighted as key steps in achieving and sustaining progress in global immunization goals.<sup>29</sup> This is reflected in Gavi, the Vaccine Alliance's decision to provide support for TTCV booster doses from 2021.<sup>30,31</sup> Worldwide, only 136 (70%) of 194 countries provide one or more TTCV booster doses to both sexes during childhood,<sup>32</sup> which is a hindrance to global progress on broader tetanus control. Following the completion of this review, Uganda decided to prioritize future inclusion of TTCV booster doses in the national immunization schedule. Recently added platforms for vaccine delivery in Uganda (human papillomavirus vaccine, second dose of measles-containing vaccine) can be leveraged to facilitate the introduction of TTCV booster doses. Other measures such as education on tetanus and the importance of TTCV, injury prevention (e.g. adequate footwear, workplace and road safety) and the provision of other mitigation measures for high-risk exposures, such as proper wound management and the receipt of prophylactic TTCV, should be encompassed as part of a comprehensive tetanus control strategy.

Similar efforts to review and validate tetanus burden have tended to focus on medical record abstraction.<sup>16,20,33–39</sup> Our review was unique in that it additionally included documentation of the tetanus reporting process through DHIS2, which is in use in many low- and middle-income countries. We found that unlikely trends in the reported data were due to data recording and entry errors. Notably, data reported from outpatient units were unreliable, especially from health centres where non-NT cases could not be verified, and large errors in reporting administered TTCV doses as non-NT cases were observed. This observation led to the recommendation in the new standards for non-NT surveillance that only hospital inpatient tetanus cases should be included in the reported data (H. Scobie, personal communication, 31 January 2020). Data entry errors of female-predominant conditions, which were proximal on the form to tetanus, were also common. As the DHIS2 system continues to proliferate globally, increased efforts must be made to ensure quality of the reported data, including regular data review, automated data validation checks with suggested corrective actions, verification of reporting anomalies and data triangulation activities to review discrepancies across different data sources. Though there have been historic gaps in non-NT reporting to the WHO, improvements are expected with the new WHO Vaccine-Preventable Disease (VPD) Surveillance Standards<sup>4</sup> and ensuring high-quality reported data will be of paramount importance.

Our evaluation has several potential limitations: purposive sampling limiting generalizability, possible social desirability bias from key informant interviews, missing facility register data and patient records, and sub-optimal quality of documented information

in patient records, including TTCV history, and receipt of TTCV and ATS/TIG during the current visit. This makes it difficult to assess the contribution of waning immunity or to make treatment recommendations for improved outcomes. In addition, historic subnational vaccination coverage data going back to TTCV introduction in Uganda were unavailable for detailed cohort analysis.

## Conclusions

The non-NT burden in Uganda is substantial. The high CFR and high non-NT burden among men and older children indicate the need for TTCV booster doses across the life course to all individuals as well as improved coverage with the TTCV primary series. Globally, this evaluation informed development of the new WHO VPD Surveillance Standard for non-NT. Increased efforts are required to strengthen data quality and data systems, including implementing the new non-NT surveillance standards and DHIS2 data validation and triangulation activities, together with the use of home-based vaccination records.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Data availability

The data underlying this article cannot be shared publicly to protect patient data and the privacy of individuals that participated in the study. Aggregate data can be shared on reasonable request to the corresponding author.

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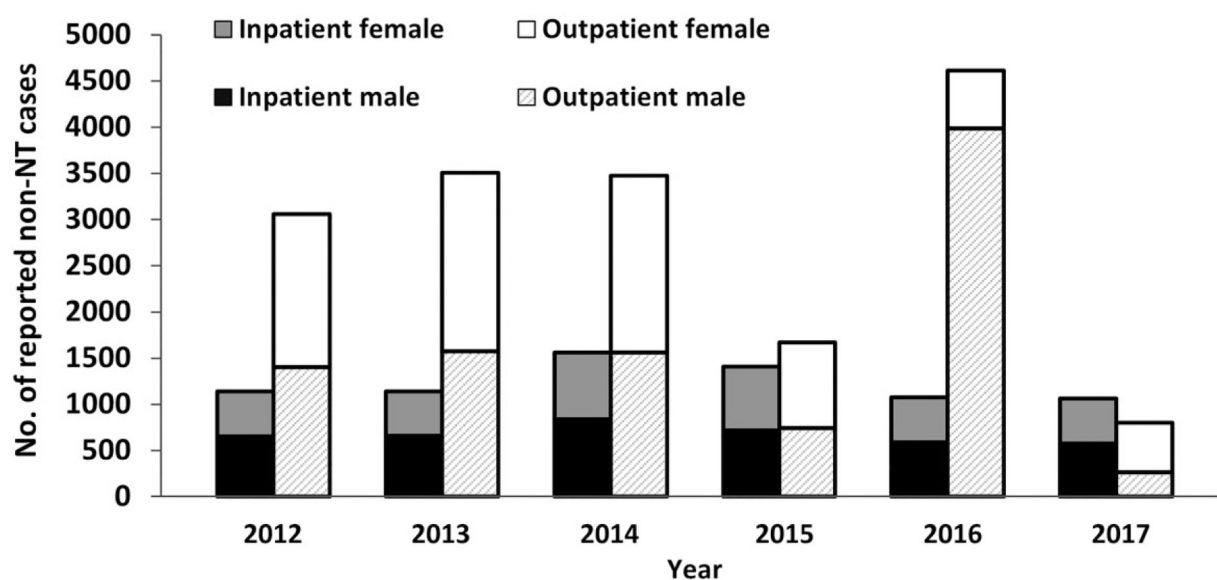
**Key Messages**

- A substantial number of non-neonatal tetanus cases and deaths occur in Uganda.
- Tetanus burden is high among older children and adult males in Uganda.
- Higher tetanus vaccination coverage and booster doses are needed to protect all individuals across the life course.
- Unlikely trends in reported data should be validated and corrected.

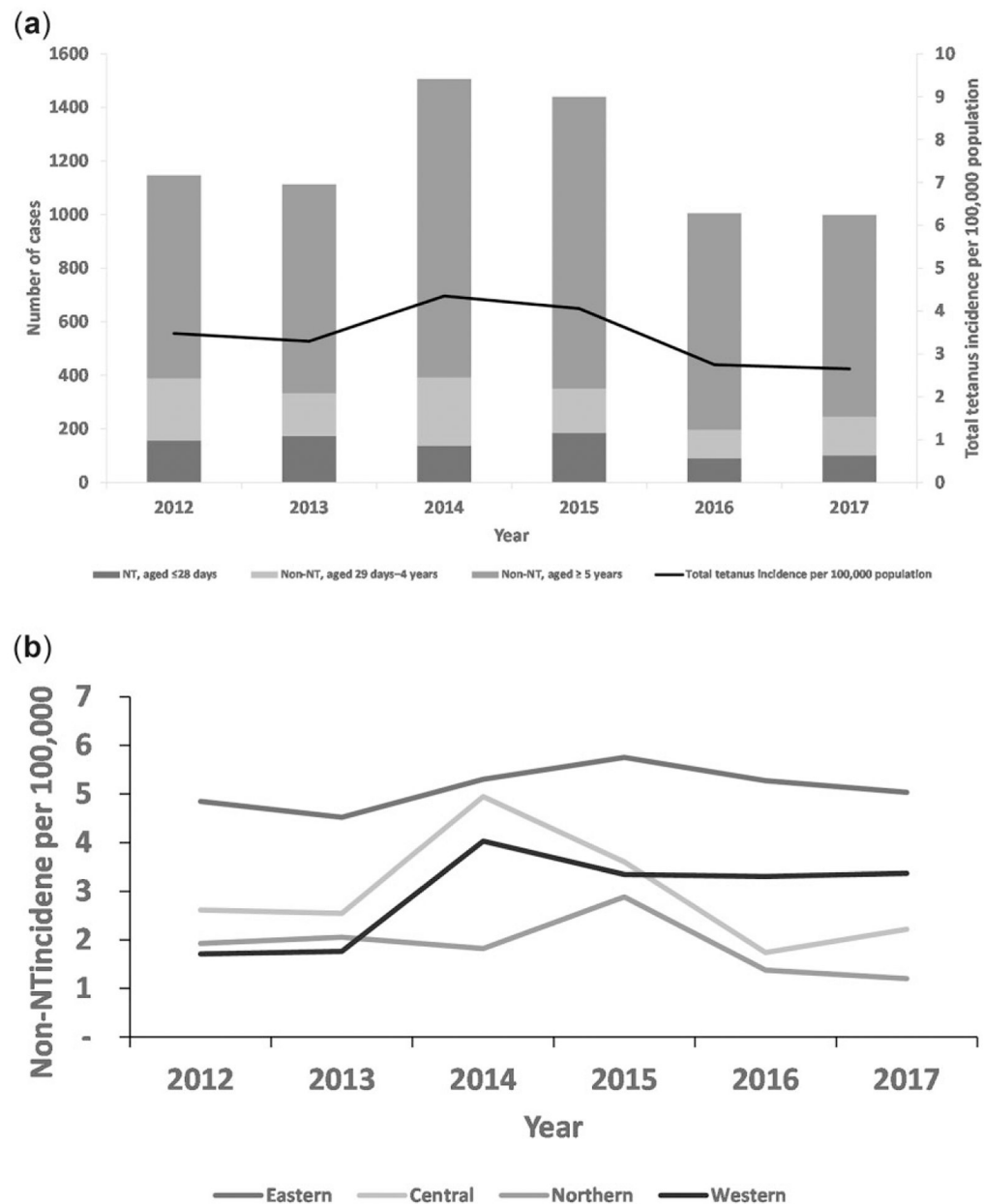
**Box 1****Summary of observed data errors and possible impact on non-neonatal tetanus reporting during the evaluation in Uganda, 2017**

- **Over-reporting:**
  - Data recording errors, e.g. tetanus vaccine doses recorded as cases
  - Electronic entry errors, e.g. female-predominant illnesses such as urinary tract infection and pelvic inflammatory disease being entered as tetanus (due to proximity to tetanus on the inpatient and outpatient reporting forms, respectively)
  - Misinterpretation of diagnosis by recorders, e.g. transient tachypnoea of the newborn recorded as tetanus
- **Misclassification in either direction:**
  - Use of provisional (admitting) vs final diagnosis for reporting, combined with missing patient files for further validation
  - Clinical diagnosis differs from surveillance case definition
- **Under-reporting:**
  - Lack of or delay in reporting/data entry in DHIS2, sometimes due to lack of DHIS2 access
  - Inaccurate zero reporting, e.g. 14 cases identified at two hospitals reporting zero cases
  - Other documentation challenges: lost registers, blank diagnoses, tetanus cases not entered in register



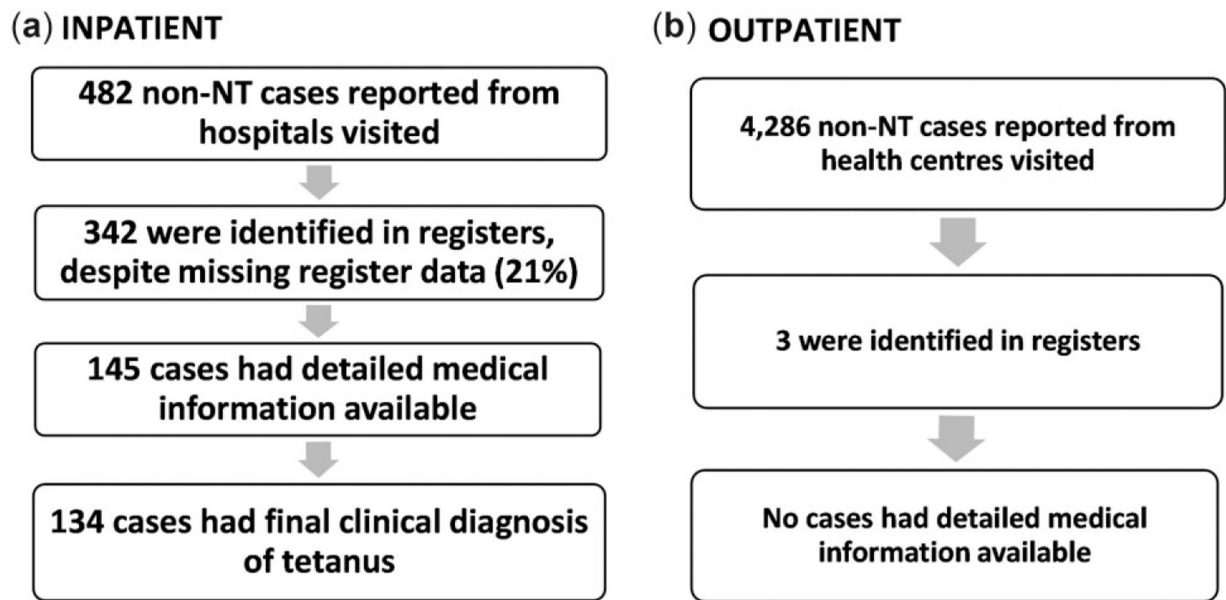


**Figure 1.**  
National reported number of non-neonatal tetanus (non-NT) cases reported from inpatient and outpatient departments by sex, Uganda, 2012–2017



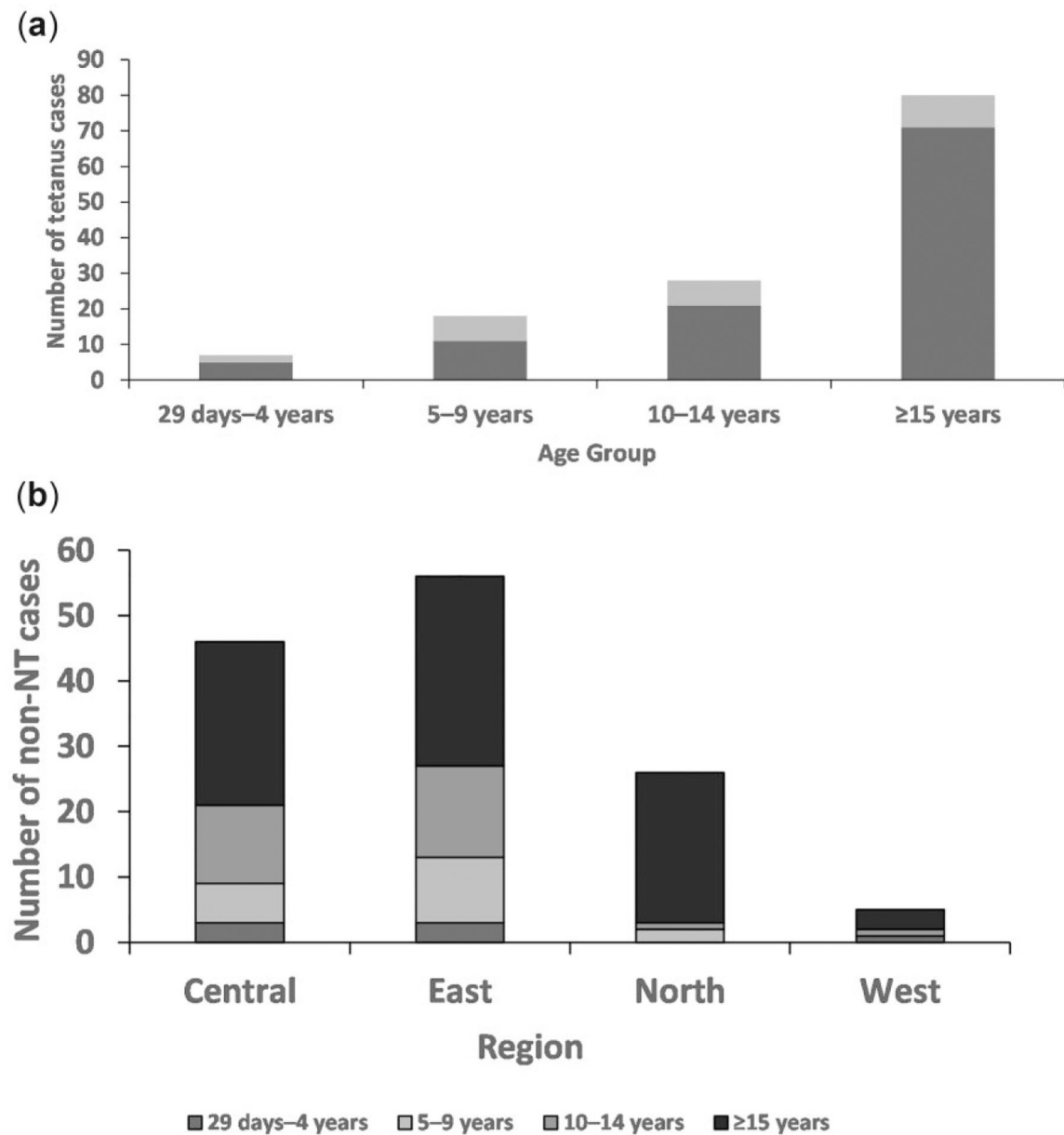
**Figure 2.**

Reported tetanus cases in Uganda, 2012–2017. (a) Number of reported inpatient neonatal tetanus (NT) and non-neonatal tetanus (non-NT) cases, and incidence of total tetanus (NT + non-NT) per 100 000 population. (b) Incidence of inpatient non-neonatal tetanus by region per 100 000 population



**Figure 3.**

Schematic of patient enrolment for medical records review: Uganda, 1 January 2016–30 June 2017. (a) Number of inpatient non-neonatal tetanus (non-NT) cases reported from hospitals compared with the number identified in the registers, the number with available medical records and documented final diagnosis of tetanus. (b) Number of outpatient non-neonatal tetanus (non-NT) cases reported from health centres compared with the number identified in the registers



**Figure 4.**

Clinically confirmed non-neonatal tetanus (non-NT) cases with available medical records ( $n = 133$ ),<sup>a</sup> Uganda, 1 January 2016–30 June 2017. (a) By gender and age group. (b) By age group and region. <sup>a</sup>One case record missing age or date-of-birth information

Total reported non-neonatal tetanus cases in Uganda 2015–2017<sup>a</sup> by age, sex and type of facility as reported through inpatient and outpatient reporting forms

Table 1

Gender	Age (years)	Number of cases (%)				
		Male<5	Female<5	Male 5	Female 5	Total
INPATIENT						
Total for health centres		20 (2)	22 (2)	277 (29)	651 (67)	970 (16)
Health centre Level I		0 (0)	2 (2)	33 (33)	64 (65)	99 (2)
Health centre Level II		1 (1)	1 (1)	51 (37)	84 (61)	137 (2)
Health centre Level III		11 (3)	3 (1)	113 (26)	309 (71)	436 (7)
Health centre Level IV		8 (3)	16 (5)	80 (27)	194 (65)	298 (5)
Total for hospitals		220 (11)	150 (7)	1018 (49)	691 (33)	2079 (34)
General hospital		116 (10)	68 (6)	532 (48)	395 (36)	1111 (18)
Regional referral hospital		73 (9)	63 (8)	417 (54)	217 (28)	770 (13)
National referral hospital		31 (16)	19 (10)	69 (35)	79 (40)	198 (3)
TOTAL INPATIENT		480 (8)	344 (6)	2590 (42)	2684 (44)	6098
OUTPATIENT						
Total for health centres		15 (0)	41 (1)	4184 (80)	1051 (20)	5229 (44)
Health centre Level I		2 (2)	3 (3)	26 (26)	68 (69)	99 (1)
Health centre Level II		6 (0)	18 (0)	4084 (87)	604 (13)	4712 (40)
Health centre Level III		5 (1)	19 (5)	56 (13)	338 (81)	418 (4)
Health centre Level IV		2 (3)	1 (2)	18 (29)	41 (66)	62 (1)
Total for hospitals		49 (8)	51 (8)	259 (41)	269 (43)	628 (5)
General hospital		38 (11)	38 (11)	168 (51)	88 (27)	332 (3)
Regional referral hospital		5 (2)	8 (3)	69 (27)	174 (68)	256 (2)
National referral hospital		6 (15)	5 (13)	22 (55)	7 (18)	40 (0)
TOTAL OUTPATIENT		128 (1)	184 (2)	8886 (75)	2640 (22)	11776

<sup>a</sup>Prior to 2015, disaggregated data by age and sex were not available for outpatient forms.

Clinical presentation, management and documented risk factors of cases with a documented clinical diagnosis of tetanus (N= 134), Uganda, 1 January 2016–30 June 2017

Table 2

Clinical presentation of cases	Number of patients <i>n</i>	Percentage of patients
Meets World Health Organization case definition <sup>a</sup>	129	96
Muscle spasms/contractions	107	80
Trismus (lockjaw)	90	67
Spasticity	89	66
Opisthotonos (arching of back)	55	41
Muscle rigidity	50	37
Dysphagia	50	37
Febrile ( > 37.5°C)	38	28
Risus sardonicus (sardonic smile)	31	23
Respiratory distress	24	18
Autonomic dysfunction	6	4
Ablett Classification <sup>b</sup>		
I	1	1
II	27	20
III	100	74
IV	6	4
60		45
Health facility visit prior to admission		
Risk factors documented in patient records		
Tetanus vaccination history		
Any prior tetanus vaccination	13	10
‘Up-to-date’	10	7
One dose received	1	1
Three doses received	1	1
Unknown number of doses	1	1
Occupation for ages 16 years (n = 77)		
Farmer, labourer	20	26
Other	11	14
Not documented	46	60
Any wound	114	85
Puncture	31	23



Clinical presentation of cases	Number of patients <i>n</i>	Percentage of patients
Laceration	28	21
Other	55	56
Prior herbal treatment for wound	9	8
History of infected wound	61	54
History of jagger bites	5	4
History of circumcision	5	4
Any type of circumcision	2	1
Traditional circumcision	1	1
Medical circumcision	2	1
Unknown type	4	3
History of ear or dental infection		
<b>Management of cases</b>		
Treated in intensive care unit (ICU)	32	24
Intubated	30	22
Nasogastric feeding	75	56
Treated in isolation facilities	97	72
Received human tetanus immunoglobulin (TIG)	32	24
Received equine anti-tetanus serum (ATS)	18	13
Received either TIG or ATSC	48	36
Received tetanus vaccination during admission	34	25
Treated with antibiotics	26	19
Any antibiotic	131	98
Metronidazole	125	93
Penicillin	103	78
Ceftriaxone	64	48
Flucloxacillin	1	1
Other	55	41
Diazepam	124	93
Chlorpromazine	60	45
Magnesium	15	11
<b>Outcome</b>		
Death	72	54

Clinical presentation of cases	Number of patients <i>n</i>	Percentage of patients
Discharged	33	25
Unknown (self-discharge, transfer, undocumented)	29	22

<sup>a</sup> A confirmed case is any person >28 days of age with acute onset of at least one of the following: trismus (lockjaw), risus sardonicus (sustained spasm of the facial muscles) or generalized muscle spasms (contractions), and clinically confirmed as tetanus by a physician/trained clinician.

<sup>b</sup> (I) Mild: mild to moderate trismus; general spasticity; no respiratory embarrassment; no spasms; little or no dysphagia. (II) Moderate: moderate trismus; well-marked rigidity; mild to moderate but short spasms; moderate respiratory embarrassment with an increased respiratory rate of >30; mild dysphagia. (III) Severe: severe trismus; generalized spasticity; reflex prolonged spasms; increased respiratory rate of >40; apnoeic spells; severe dysphagia; tachycardia of >120. (IV) Very severe: Level III and violent autonomic disturbances involving the cardiovascular system. Severe hypertension and tachycardia alternating with relative hypotension and bradycardia, either of which may be persistent.

<sup>c</sup> Two patients were documented as receiving one dose of ATS and one dose of TIG.