Epidemiol. Infect. (2003), **130**, 221–226. © 2003 Cambridge University Press
DOI: 10.1017/S0950268802008233 Printed in the United Kingdom

Assessment of neonatal tetanus elimination in an African setting by lot quality assurance cluster sampling (LQA–CS)

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(*Accepted 9 December 2002*)

SUMMARY

Neonatal tetanus (NT) elimination, <1 case per 1000 live births (LB), was assessed at district level in Zimbabwe using a combined lot quality assurance–cluster sampling survey (LQA–CS). Three of the highest risk districts were selected. NT was considered eliminated if fewer than a specified number of NT deaths (proxy for NT cases) were found in the sample determined using operating characteristic curves and tables. TT2+ vaccine coverage was measured in mothers who gave birth 1–13 months before the survey and women aged 15–49 years. NT was considered as eliminated, TT2+ coverage was 78% (95% CI 71–82%) in women aged 15–49 and 83% (95% CI 76–89%) in mothers. The survey cost US$ 30 000 excluding costs of consultants. NT incidence was below the elimination threshold (<1/1000 LB) in the surveyed districts and probably in all districts. LQA–CS is a practical, relatively cost effective field method which can be applied in an African setting to assess NT elimination status.

INTRODUCTION

Neonatal tetanus (NT) is a vaccine preventable disease and globally it is estimated to be responsible for 215 000 (14%) of all neonatal deaths annually (WHO, 1998). Reducing deaths from NT is one of the simplest and most cost-effective means to reduce the neonatal mortality rate [1]. This disease is vastly underreported with an estimated case notification efficiency of 3% in 1997 [2]. NT occurs between the 3rd and 28th day after birth due to unhygienic birth practices. Case fatality is very high at 70–100%. Most of the deaths occur at home and often neither the birth nor the death is reported. NT can be prevented by vaccination of women of childbearing age with tetanus toxoid (TT).

Tetanus spores are ubiquitous and so eradication is not possible. The World Health Assembly called for the elimination of NT in 1989 and since then 104 of 161 developing countries have already achieved this goal. UNICEF, WHO and UNFPA agreed to set the year 2005 as the target date for worldwide elimination [1, 3]. Elimination is defined as the reduction of NT to <1 case/1000 live births (LB) in every district within a country.

The recommended approach for achieving NT elimination is to use the 'high-risk' strategy [4]. This

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approach involves the identification of high-risk districts (or areas within those districts); administration of three doses of TT to all childbearing women in those districts or areas; the use of proper disposal of auto-disable syringes and documentation of progress and achievements. When coverage of women with at least two doses of TT (TT2+) rises above 80% in a given area, rapid elimination of the disease is highly likely in that area [5]. A birth delivered under sanitary conditions, termed clean delivery (CD), is also protective against NT [6]. If trained attendants are assisting over 70% of births, the incidence of NT invariably wanes provided that appropriate equipment is available.

Although considerable effort has been made to eliminate NT, reliable data to document achievement of elimination is often not available, particularly in some of the most underserved districts where the risk of NT may be highest. Therefore, a simple, cost-effective method of measurement is needed to assess NT elimination in a country. This survey method checks for deaths attributable to NT rather than cases since verbal autopsy is reliable [7] and there is an assumed high case fatality among cases particularly in the high-risk areas where we use this method. NT mortality serves as a proxy for NT incidence. Once a country has reached elimination status, protection must be maintained and surveillance ongoing to avoid resurgence of the disease.

Since lot quality assurance sampling (LQAS) has the advantage of using a small sample size it has been proposed to assess the implementation and impact of various public health strategies [8–10]. In 1991, WHO identified LQAS as one practical rapid assessment method for monitoring the quality of health care services in developing countries. LQAS has been applied in different health settings, e.g. to assess immunization coverage [11–13] and quality of health care [14–15]. Lot quality assurance–cluster sampling (LQA–CS), which combines LQAS with cluster sampling, was developed to assess elimination of NT in selected districts and has been used in Bangladesh (1994), Indonesia (1995 and 2001) and India (2000). However, LQA–CS had not up until this survey been applied in an African setting. Namibia has since been surveyed (August 2001).

The three objectives of the study were to evaluate the use of the LQA–CS method as an assessment tool for the elimination of NT in an African setting; to determine if NT has been eliminated in Zimbabwe and to measure TT coverage among mothers who

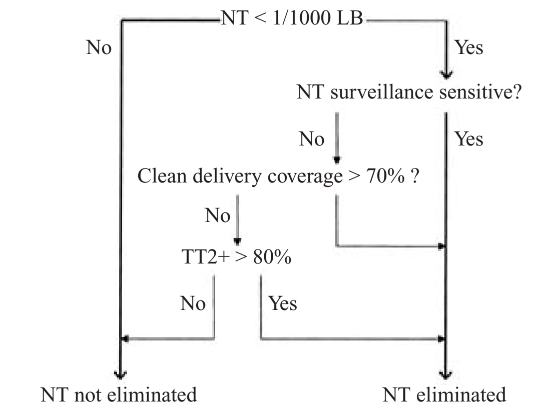

Fig. 1. WHO/UNICEF algorithm for assessment of neonatal tetanus elimination.

gave birth 1–13 months before the start of the survey and among women aged 15–49 years.

METHODS

Review of national surveillance data

Prior to conducting the survey, a review of data from the national surveillance system for each of the 58 districts in Zimbabwe was done to decide whether or not there was evidence that the basic criteria for NT elimination were met. District-specific data on NT incidence, proportion of LB with antenatal care (ANC) and CD, TT2+ vaccination in pregnant women and ANC, perinatal mortality and DPT3 uptake for the years 1998 and 1999 were available from the Ministry of Health (MoH). NT incidence, CD and TT2+ coverage were evaluated using the WHO–UNICEF algorithm. This algorithm specifies four core indicators for assessing elimination: the reported incidence of NT, surveillance sensitivity, % CD and the % of childbearing age women who have received doses of TT sufficient to provide passive protection to their offspring (Fig. 1) [16]. The algorithm also suggests several surrogate indicators that should be considered, particularly if they are considered more reliable than the data corresponding to the core indicators. ANC was added to the list of indicators because it is MoH policy in Zimbabwe that TT should be provided if needed during ANC visits. DPT3 coverage was also added to the list of indicators since it is a better indicator of routine immunization activity than other antigen doses (Table 1).

High-risk district selection

A high-risk district is one for which the incidence of NT (reported or estimated) is 1 case or more per

Table 1. *Summary of selected indicators, data obtained from National Surveillance system, Zimbabwe, 1998–1999*

Indicator	1998	1999
Reported cases of NT	8 (0·03/1000 LB)	12 (0·04/1000 LB)
Clean delivery* (%)	83	81
TT2+ in pregnant women (%)	75	70
Antenatal care (%)	79	77
DPT3 (%)	75	77

* In Zimbabwe, clean delivery is defined as delivery in a hospital or health centre.

1000 LB, coverage of women with TT2+ is less than 80%, or CD is reported for less than 70% of births or for which no data are available ('silent' districts). If a district reports less than 1 case per 1000 LB, it can be accepted as evidence of elimination provided the district has an efficient, well-documented system of NT surveillance or at least 80% TT2+ coverage or 70% CD coverage.

The rationale for identifying a district(s) at high NT risk is the assumption that if NT has occurred in the recent past, it will have occurred in such a district(s). If NT has been eliminated in a high-risk district(s) it is probable that it has been eliminated in lower-risk districts.

Districts were ranked by the reported values of the indicators to identify the districts with highest risk for NT. In the final selection of the high-risk districts to survey, administrative, financial and logistical issues were taken into consideration [16].

LQA–CS

LQA–CS was used to assess whether the number of NT cases in high-risk districts was less than 1/1000 LB during a recent 12-month interval (1–13 months before the start of the survey). The LQA–CS method combines industrial type LQAS with cluster sampling. This approach allows a population to be classified as acceptable ('pass' status) or unacceptable ('fail' status) for the presence of NT deaths amongst LB. A decision is made about the elimination of NT based on mathematical probabilities of obtaining less than a specified number of NT deaths in a sample of LB of a predetermined size. We chose a double sample plan, which would allow a decision to be made from the first sample to 'accept' if the rate of NT is sufficiently low, or to 'reject' if the rate is high. If a decision cannot be reached from the results of the first sample, survey of the second sample begins; if the 'acceptance number' of NT deaths is surpassed at any time during the second sample, the survey can be truncated with a decision to 'reject'. In other words, a double sample plan will reduce the sample size needed for a decision to accept, or reject, if the rate of NT is relatively low or high, in the population (lot) from which the sample is drawn [17].

The operating characteristic curves for the double sample plan used ($n1=1000$, $n2=2000$; $d1=0$, $d2=3$) with a total sample size of 3000 LB are shown (Fig. 2). The y-axis shows the probability of accepting the lot and the x-axis shows the rate (number of NT deaths/1000 LB) in the population. The three OC curves show the probabilities of acceptance if no deaths or more than three deaths are found in the first sample, and if three or fewer deaths are found in the combined first and second samples.

Small clusters of 20 LB were chosen to enable interviewer teams to complete a cluster each day, which allows a decision to be made daily on whether to continue the survey. The average number of households considered possible to visit during a day's work was estimated to be about 120. With a crude birth rate of 34·5/1000 per population and an average household size of 4·7 people per household, the estimated number of LB per cluster would be around 20.

The Central Statistical Office provided population data by ward and census enumeration unit (CEU) for the three districts, Goromonzi, Mutoko and Uzumba Maramba Pfungwe (UMP), which were selected for the survey. One hundred and fifty CEUs were systematically selected in the three districts to obtain starting locations for clusters of 20 LB each. Every third cluster, from a random start, was identified as a cluster for the first sample (50 clusters), the remaining clusters constituted the second sample (100 clusters). The clusters were plotted on district maps and subsequently assigned to supervisor and interviewer teams. Interviewers, mostly senior community health sisters, were recruited and trained to perform the interviews using role-play and practice interviews. In the field,

https://doi.org/10.1017/S0950268802008233 Published online by Cambridge University Press

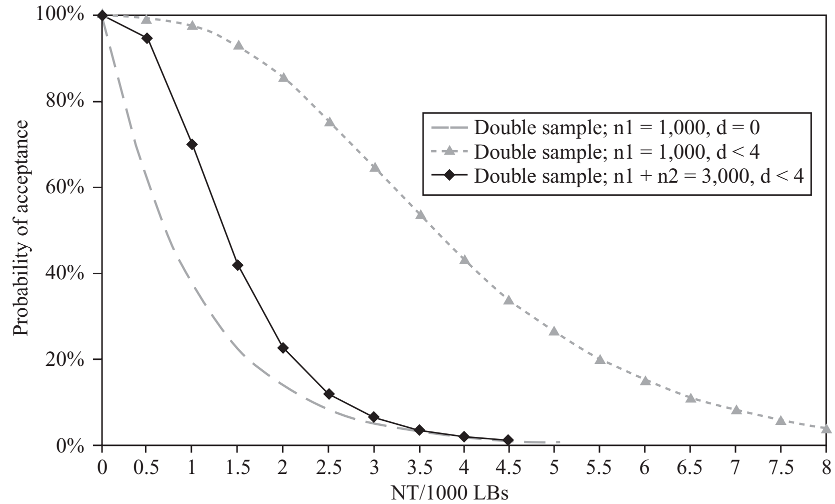

Fig. 2. Operating characteristic curves – double sampling plan with n1 + n2 = 3000 LB.

the teams started the survey of each cluster from a randomly selected household. The procedure of visiting neighbouring households until the quota of LB had been surveyed was followed (as in an EPI cluster survey). On each day, supervisors reported the number of NT cases, if any, found by their teams.

The sample was representative and so attributes other than neonatal deaths were measured on a subsample of selected women encountered in surveyed households. During survey of each cluster (of the first sample only) we collected information on TT2+ status on a sample of 8 women aged 15–49 years of age (400 total) and on 4 mothers of the LB surveyed (200 total).

Information was collected on LB delivered during the 13 months to 1 month prior to the commencement of the survey. For each LB, interviewers asked whether the child was still alive and if not, whether death occurred during the first 4 weeks after birth. A verbal autopsy form was completed for every neonatal death found. Questions were asked about the circumstances of birth and death of the child; the presence of signs of NT, whether the child was born at home with/without a trained birth attendant or in a health facility and whether care was sought.

Staff resources included 18 interviewing teams of 2 people each, 5 supervisors and 3 consultants. Fourteen vehicles were available with drivers.

RESULTS

The surveillance data by district for the years 1998 and 1999 showed 8 (0·03/1000 LB) and 12 (0·04/1000 LB) reported NT cases, respectively for the country as a whole; CD at national level was above 70 % but 15 districts reported coverage lower than 70 % and 2 reported CD lower than 50 % during that 2 year period. The national estimates of TT2+ coverage were 75 % in 1998 and 70 % in 1999 (Table 1).

Seven high-risk districts were identified for possible inclusion in the survey (Table 2). For logistical and administrative reasons, three neighbouring districts in the province of Mashonaland East (ME), close to Harare were selected. These were Uzumba Maramba Pfungwe (UMP), Goromonzi and Mutoko. There were 2410 visits made to households to complete the first sample of 1000 LB. Among the 1000 LB recorded in the first sample, there were nine neonatal deaths (9/1000 LB, 95 % CI 4·4/1000–16·5/1000 LB); with one neonatal death considered to be attributable to NT. A decision on whether NT was eliminated could not be made from the first sample results, and so the second sample was surveyed. During 4737 household visits in the second sample, six neonatal deaths were recorded. No deaths attributable to NT were found in the second sample. Males represented 50 % of the recorded LB.

The survey results on TT coverage (by recall and/or vaccination card) showed that 83 % of the mothers and 78 % of women aged 15–49 years had been vaccinated with at least two doses against tetanus (Table 3). Vaccination cards were available with 28 % of mothers of the surveyed LB and 13 % of women aged 15–49 years. It was reported that 14 % of the mothers and 13 % of women aged 15–49 had received five or more doses of TT.

Table 2. *Districts identified as being at highest risk for NT – reported values (%) for selected indicators, data obtained from National Surveillance system, Zimbabwe, 1998–1999*

	Reported cases of NT		Clean delivery		TT2+ coverage		ANC		DPT3 coverage	
District	1998	1999	1998	1999	1998	1999	1998	1999	1998	1999
UMP	NR*	0	NR	35	NR	87	NR	68	NR	31
Goromonzi	0	0	76	68	35	103	26	58	26	129
Lupane	0	0	58	57	49	54	76	71	65	65
Umguza	0	0	59	62	71	42	38	48	36	34
Umzingwane	0	0	58	55	53	49	64	62	61	64
Mutoko	0	0	88	85	24	61	36	79	24	97
Gweru	0	0	82	83	53	47	57	56	52	52

* NR, no report received.

Table 3. *Estimated card retention and TT coverage in three of the highest risk districts, Zimbabwe, November 2000 (%)*

	With card *	TT1	TT2	TT3	TT4	TT5
Mothers of LB	28	96	83	49	27	14
Women 15–49	13	89	78	48	26	13

* Percentage of women who had an immunization card at the time of the survey.

The local cost of the survey was US$ 30 000 including per diems of the interviewers and supervisors. There was an additional cost of US$ 27 000 for WHO consultants.

DISCUSSION

The LQA–CS method was developed to assess elimination of NT at district level in a rapid and economical way and has been used for this purpose in Asia. The method had not been applied in an African setting prior to this survey in November 2000. Zimbabwe was chosen for assessment of NT elimination because of the small numbers of NT cases notified with improved surveillance activities and high reported coverage with TT2+ and CD at national level. The survey results suggest that Zimbabwe had achieved NT elimination in 1998–9. However, it should be remembered that NT cannot be eradicated and elimination status needs to be maintained through continuous provision of antenatal care, clean delivery services and TT for childbearing women. As more African countries approach elimination of NT, efficient and least costly means of assessing elimination become more important. LQA–CS was an approach found to be practical and useful in assessing NT elimination in South East Asian countries. The method was slightly modified and tested in Zimbabwe to determine whether it could be useful in an African setting.

There are limitations with the LQA–CS design. Only a 'Yes' or 'No' decision is made. Point estimates can be calculated for the samples if completed but the confidence intervals (CI) are large; if a single case of NT is identified the 95% upper confidence limit will be $>1/1000$ LB. The method is useful when there is evidence that NT is probably eliminated in a country, and a point estimate of $<1/1000$ LB for the NT mortality rate in the highest-risk district(s) will be acceptable as an indicator that lower-risk districts have lower incidence of the disease. The sampling plan we used can be modified to increase the probabilities of rejection at rates above 0·001 by increasing the sample size(s) and/or reducing acceptance numbers. However, there is a trade-off between the acceptance and rejection probabilities, which is evident upon review of published tables and operating characteristic curves [17].

The use of LQAS with cluster sampling can reduce the workload and the cost of assessing a rare event such as NT, where the design effect is expected to be close to 1, i.e. the precision of the estimate with cluster sampling is close to the precision of the estimate if the survey had been completed on a random sample with the same number of LB.

The numbers of neonatal deaths recorded in the survey were lower than expected. Under-recording of neonatal deaths has been observed in past NT mortality surveys. Under-recording has been attributed to excluding early neonatal deaths as stillbirths and/or interviewers not recording early neonatal deaths, which were probably not attributed to NT. In this survey the lead-in questions to identify eligible LB were whether any woman in the household had been pregnant during the previous 2 years, if the delivery occurred during the 12-month period of eligibility and whether the baby cried, moved or gasped for breath. A possible improvement in obtaining better measurement of early neonatal deaths may be to record the outcome of all pregnancies, and evaluate the distribution of the survey measurements with other data. Reviews of verbal autopsies for various diseases have found that the NT verbal autopsy has excellent sensitivity [7] but specificity needs to be improved, particularly as disease incidence declines.

The total cost of this survey was approximately US$ 60 000 of which nearly half was for external consultants. This may sound expensive but it is certainly a cost effective method when compared to alternatives, which would involve huge sample sizes in order to measure a rare disease with precision. However, several shortcomings in this study led to an increase in costs. Non-productive time for staff on per diem accumulated, as maps were not available in time and funding was delayed. To improve the quality and reduce the cost of future assessments, selection of the highest-risk districts could be done in advance and detailed district maps and population estimates could be available prior to the arrival of an external evaluator(s). Furthermore, we expect that the cost of assessment of NT elimination will be lower in other African countries, as per diems are lower. We think it is important to further evaluate the LQAS–CS before using it on a wider scale in African countries. Although the design has proved to be useful in Asia, conditions are different.

The LQA–CS method was a relatively inexpensive and feasible method to assess NT elimination in Zimbabwe. The method may be useful in other African countries, in high-risk districts where routine monitoring of data may be less reliable to verify elimination status, provided that financial and logistical arrangements are in place. We recommend that the method be validated using a conventional survey design.

ACKNOWLEDGEMENTS

We greatly appreciate the time and effort contributed by the Ministry of Health, Zimbabwe, with particular mention to the interviewer teams and the team supervisors. We would like to convey special thanks to Catherine Shaw, Francois Gasse and Boniface Munyame of UNICEF for their assistance. This survey was funded and co-ordinated by WHO and UNICEF.

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