Validation of Maternal and Neonatal Tetanus Elimination

including a guide to the use of Lot Quality Assurance – Cluster Sample Surveys to assess neonatal tetanus mortality

World Health Organization

WHO/IVB/18.15

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DEPARTMENT OF IMMUNIZATION, VACCINES AND BIOLOGICALS

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TABLE OF CONTENTS

ABBREVIATIONS

ANC	antenatal care
BCG	Bacillus Calmette-Guérin
CBAW	childbearing-aged woman
CBR	crude birth rate
CS	cluster sample
DTP	diphtheria–tetanus–pertussis vaccine
HH	household
LB	live birth
LQA	lot quality assurance
MNT	maternal and neonatal tetanus
MO	medical officer
MOH	ministry of health
ND	neonatal death
NGO	nongovernmental organization
NT	neonatal tetanus
NMR	neonatal mortality rate
NTMR	neonatal tetanus mortality rate
PAB	protection at birth
PPS	probability proportionate to size
QA	quality assurance
SIAs	supplemental immunization activities
TBA	traditional birth attendant
Td	tetanus–diphtheria toxoid vaccine (adult formulation)
TT	tetanus toxoid vaccine; in this manual, "TT" also signifies either TT or Td
TT2+	2 or more TT doses at the time of the last pregnancy
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
WHO	World Health Organization

INTRODUCTION

In the 1980s, community-based surveys demonstrated that neonatal tetanus (NT) was one of the principle causes of global neonatal mortality, resulting in an estimated 770,000 deaths per year. In response to the recognition of this high NT burden, the 1989 World Health Assembly called for global NT elimination.

Neonatal tetanus elimination was defined as a neonatal tetanus mortality rate of less than 1 case per 1000 live births in every district. The principal strategies adopted for NT elimination were:

- routine and supplemental immunization with tetanus toxoid-containing vaccine (TT or Td)[1]
- clean delivery and cord care
- effective surveillance to identify areas where NT persists and to monitor elimination progress

By 2000, 104 developing countries had achieved NT elimination; estimated NT cases had declined to 238,000 annually. UNICEF, UNFPA and WHO reaffirmed their commitment to NT elimination in that year, adding maternal tetanus to the elimination goal (MNT elimination) and creating a revised strategic plan.[2]

To accelerate MNT elimination, the revised plan recommended the high-risk approach: women of childbearing age living in high-risk districts, or in high risk areas within districts, are immunized with 2 or 3 doses of TT through supplemental immunization activities (SIAs – i.e., community-wide campaigns). TT SIAs supplement the three strategies listed above, all of which continue to form the basis for achieving and sustaining MNT elimination.

Since the 2000 revitalization of the MNT Elimination Initiative, 34 countries, 18 of 35 Indian states, 29 of 34 Indonesian provinces and Ethiopia excluding the restive Somali Region have validated MNT elimination,[3] and many others are close to being able to demonstrate elimination.

The purpose of this guide is to describe the recommended process for assessing and validating MNT elimination in countries believed to have achieved that goal.

The companion *Statistical Supplement to the Guide for Validation of Maternal and Neonatal Tetanus Elimination* ("Statistical Supplement") describes in detail the statistical underpinnings of the recommended survey methods.

1 In this manual, the abbreviation TT represents either single antigen tetanus toxoid vaccine or adult formulation tetanus-diphtheria vaccine (Td).
2 UNICEF, WHO, UNFPA. Maternal and neonatal tetanus elimination by the year 2005: Strategies for achieving and sustaining elimination. WHO/V&B/02.09. Geneva: WHO, UNICEF, UNFPA, 2000
3 Count as of December 2013.

1.
Assessing MNT Elimination

1. ASSESSING MNT ELIMINATION

When a country believes it has eliminated MNT, it can proceed to validation of that claim, following the steps outlined in this guide. In most instances, WHO participates in the validation exercises to ensure adherence to recommended methods, and consistency of results among countries achieving elimination.

Definition of MNT Elimination: less than 1 NT case per 1000 live births in every district

1.1 REVIEW OF DISTRICT-LEVEL DATA

Countries can consider claiming MNT elimination when district-level indicator data suggest that NT has fallen below the threshold of 1 NT case per 1000 live births in all districts.

The first step in evaluating whether elimination has been achieved is a formal review of district-level data. There are 3 possible outcomes of this review:

1. The data clearly support elimination; elimination can be declared
2. The data clearly indicate that elimination has not been achieved (or is highly unlikely). Additional measures required to achieve elimination are then identified.
3. Elimination appears likely, but some doubt remains. Districts with data that lead to uncertainty, or are suggestive of continued NT risk, are identified for additional evaluation, including possible field visits or surveys.

The data review process

The district data review evaluates the core indicators: reported NT cases and incidence per 1000 live births, clean delivery coverage and TT2+ coverage, and supplemental indicators such as SIA TT coverage, ANC coverage, infant DPT coverage, and various socioeconomic indices. Typically administrative data are used, but when survey data are available, especially for TT2+, PAB, and DPT3, they should be included, even if available only at the provincial level.

The process is individualized for each country based on the indicators available, the quality of the indicator data, and the knowledge and insight of national and local representatives of the country under review.

A spreadsheet with a row for each district and columns for each core and supplemental indicator for the 2-3 most recent years must be prepared in advance. A template is available

from WHO/HQ (see example in Annex 1). At a minimum, the following variables should be included for each district, if available:

Core	Supplemental
Reported NT cases	PAB
Number of Live Births (LBs)	SIA TT coverage (TT1, TT2, TT3)
Reported NT rate/1000 LBs	ANC Coverage *(1 visit minimum)*
Quality of surveillance *(zero reporting, number and distribution of reporting sites, completeness and timeliness of reporting)*	DPT1 and DPT3 coverage
Clean Delivery Rate	DPT3-DPT1 dropout rate
TT2+ coverage	Urban vs. rural status

Other indicators used for the review have included: measles vaccine and/or BCG coverage, trained TBA coverage, women's literacy, human development indicators (life expectancy, adult literacy, gross school enrollment, population living in poverty), and health service access indicators (population per health center, health centers/km², difficulty of terrain). The most current district-level population estimates, including annual numbers of births, numbers of pregnant women and women of childbearing age, should be included in the spreadsheet, if available.

Once the spreadsheet has been prepared, a team of national and international staff including representatives of the MOH, WHO, UNICEF and, if appropriate, local NGOs, should review the data district-by-district. Ideally, the meeting should take place in-country with all team members present and an accurate district-level map at hand. If that is not feasible, the review can be conducted by telephone and e-mail.

The following is a summary of the major considerations involved in the data review:

1.1.1 The core indicators

1.1.1.1 Reported incidence of NT and review of the surveillance system

Most countries where NT continues to be a problem do not have uniform nationwide surveillance or vital event registration with medical certification of the cause(s) of death. Unreliable routine surveillance is most likely to be found in districts with higher risk for NT. Such districts may have active NT surveillance in district hospitals; however, if their reported NT rates are low, an evaluation of the sensitivity and reliability of the surveillance system is necessary before they can be accepted.

While a comprehensive evaluation of a surveillance system cannot be undertaken by the NT assessment team, the following parameters should be considered when evaluating the quality of surveillance data:

- The presence of an adequate number of reporting sites, with representative distribution
- Mandatory negative (or "zero") reporting.
- Completeness of reporting of at least 80%
- Annual reviews of hospital records and/or of active NT surveillance
- Active community surveillance in rural areas with limited health facility access to ensure that neonatal deaths are detected, reported and investigated to rule out NT

Because MNT elimination is defined as less than 1 NT case per 1000 LBs in *every district*, any district with a reported NT rate above 1 per 1000 live births, particularly in more than 1 year, has not met the definition of elimination and must be given close attention. The details of reported NT cases in such a district, or any district with a suspiciously high number of NT cases should be requested and reviewed to rule out misdiagnoses. Surveillance data for several years should be evaluated.

Because NT surveillance is frequently unreliable, reported NT rates must be interpreted with caution.

Effective evaluation of surveillance systems and data from a distance is very difficult. Reports of no NT cases can hide significant on-going NT. For that reason, surveillance data alone cannot be used to make a decision about the likelihood of MNT elimination - all available indicators must be considered.

1.1.1.2 Percentage of births with clean delivery

The indicator, "clean delivery" is usually defined as a delivery assisted by a medically trained health worker (physician, nurse, or midwife). Some countries define clean deliveries as those occurring in health facilities. For the data review, the nationally-accepted definition can be used, as long as it is clearly specified and used consistently for all districts.

Most developing countries have some type of hygienic delivery and/or safe motherhood promotion that includes providing clean delivery information to pregnant women, training traditional birth attendants (TBAs), and/or distributing safe delivery kits. These efforts can reduce NT incidence substantially, even if many deliveries still take place at home without medically trained attendants.

Districts with clean delivery coverage of at least 70% are generally likely to have achieved MNT elimination. This is both because the majority of deliveries occur in hygienic

conditions and because clean delivery concepts are likely to have reached subpopulations with limited access to professional care when clean delivery coverage is high.

However, in districts with clean delivery coverage below 70%, especially those with large rural, dislocated or slum populations, home deliveries may continue to take place under non-sterile conditions, and application of potentially infectious traditional substances to the umbilical stump may still be common. Such districts should be carefully evaluated as elimination may not yet have been achieved.

1.1.1.3 Percentage of pregnant women immunized with TT

Immunization of childbearing-aged women (CBAW) with tetanus toxoid (TT) provides maternal anti-tetanus antibodies, which are transferred from the mother to the developing fetus during pregnancy, thereby protecting infants against tetanus during the first several months of life. Because tetanus immunity wanes with time, women must receive a series of doses during their reproductive years to maintain protection (Table 1).

Table 1. TT vaccination schedule for pregnant and childbearing-aged women who have not received previous immunization against tetanus.

TT or Td Dose	Optimal Dosing Interval	Minimum Acceptable Dosing Interval	Estimated Duration of protection
1	At first contact or as early as possible in pregnancy	At first contact or as early as possible in pregnancy	None
2	6-8 weeks after TT1*	At least 4 weeks after TT1	1-3 years
3	6-12 months after TT2*	At least 6 months after TT2 or during subsequent pregnancy	At least 5 years
4	5 years after TT3*	At least one year after TT3 or during subsequent pregnancy	At least 10 years
5	10 years after TT4*	At least one year after TT4 or during subsequent pregnancy	All childbearing age years; possibly longer

*optimally given at least several weeks before due date if administered during pregnancy

If a high proportion of pregnant or childbearing-aged women in a district have received enough TT to ensure protection, MNT most likely has been eliminated.

The standard indicator to measure TT coverage, "TT2+", is the proportion of pregnant women who received their second or higher TT dose during pregnancy in a given year. This indicator is based on district administrative data that tend to underestimate the true level of protection in mothers and their newborns. The reasons why administrative estimates of TT2+ coverage may not reflect actual protection include:

- Pregnant women already may have received 5 TT doses before their last pregnancy, and therefore do not need additional TT doses. However, the administrative computation of TT2+ will count them as pregnant women who did not receive TT. This problem is most common in countries with longstanding, well-functioning immunization systems.
- If TT immunization records for pregnant women are unavailable, health workers may re-start the TT series in every pregnancy. A single dose is reported as TT1, while in reality it might represent a third (or higher) dose. The actual protection again would not be captured by the TT2+ indicator
- In areas where TT SIAs have been performed, the supplemental doses are not included in the routine TT2+ count.
- As young women who received DTP in infancy enter their childbearing years, they require fewer TT boosters to achieve protection, a fact not captured by "TT2+". Similarly, booster doses given later in childhood or adolescence are not reflected in TT2+.

The indicator "Protection at Birth (PAB)" is used by some countries to complement TT2+. PAB is the proportion of children protected against NT at the time of birth based on their mothers' complete TT immunization history. PAB is often registered at the DTP1 contact. If PAB data are available, they should be included in the district review.

1.1.2 Supplemental indicators

When high quality data are available for the reported NT rate, clean delivery coverage, and TT2+/PAB coverage, assessment of MNT elimination is straightforward. However, more commonly, data are incomplete or unreliable. Additional information on "supplemental indicators" are used to create a series of data which, when taken together, help complete the picture of whether each district is likely to have eliminated MNT, and to identify districts which are still at relatively high risk for NT.

The most frequently used supplemental indicators are:

- The proportion of pregnant women having made at least one visit for antenatal care (may complement data on clean delivery)
- DPT1 coverage (indicates access to immunization services and may indicate access to other health care)
- DPT3 coverage (may indicate a well-managed immunization program and complements TT2+ coverage estimates)
- DTP1 to DTP3 drop-out rate (calculated as: [(DTP1– DTP3) / DPT1] x 100%; also provides an indication of the management of immunization services)
- The proportion of women in the district having received 2 or 3 doses of TT during SIAs - only for districts with SIAs
- Urban or rural status of a district; difficulty of terrain

As mentioned above, other indicators used for the review have included: measles vaccine and/or BCG coverage, trained TBA coverage, women's literacy, % population living in poverty and other Human Development Indicators, and health service access indicators such as population per health center and health centers/km². The choice of supplemental indicators is country-specific and depends on data availability and reliability. Supplemental indicator data for each district should be incorporated into the data review spreadsheet (Annex 1).

1.1.3 Supplemental Data

In addition to core and supplemental indicator data, other helpful information may be available for the district review. Examples are reports of surveys of coverage or serological status, neonatal death investigations, annual record reviews, etc. Such reports can be useful in evaluating the likely elimination status of the districts involved or the status of specific population subgroups.

The assessment team may also decide, if necessary, to carry out field visits to clarify uncertainties, for example: to better understand the NT reporting system, to discuss the limitations of the immunization program with health workers and women utilizing the health system, to explore the circumstances under which "clean deliveries" are performed, etc. Such additional information may resolve concerns about questionable data.

At the completion of the data review, the group should come to unanimous decisions about:

- **The likelihood that MNT is eliminated, given the available data**
  If the data and information indicate that MNT is likely eliminated, the reviewers should judge whether or not additional information is needed (e.g., field visits to resolve doubts and inconsistencies, and/or whether to conduct a survey to validate MNT elimination)
  If the data seem to show that MNT has not been eliminated, the actions necessary to achieve elimination should be determined (e.g., conduct SIAs in high risk areas, strengthen outreach services to increase routine immunization coverage, etc.)
- **The selection of the highest-risk district(s) for a survey**
  If MNT elimination is likely, a confirmatory survey is usually recommended.
  The assessment team must then select the district, or districts to be surveyed (selection methods are discussed below).

1.2 DISTRICT FIELD VISITS

When there are problematic data or program issues that leave the MNT elimination status of districts in doubt, field visits may be indicated. Examples of situations that might prompt field visits are: districts that report NT rates above 1 per 1000 LB; districts with very low or very high TT2+, or large TT2+ fluctuations over time; or large inconsistencies among the core and supplemental indicators.

Activities during field visits may include:

- Examination of reports of NT cases to see if there have been misdiagnoses, or if the cases belonged to other districts (e.g. referral cases)
- Review of the NT surveillance procedures, including if and how hospital record reviews are performed; if there is active/community-based surveillance and community sensitization in rural areas
- Review of registers, micro plans, vaccine stock records to assess whether TT2+ is over- or underestimated
- Interviews with a sample of childbearing aged women to get a rough idea of TT coverage, the frequency of missed opportunities for TT administration, typical delivery conditions, cord care practices, use of ANC services, and perceptions about service availability and reliability
- Discussions with local health workers and authorities, including hospital pediatric ward staff, to get an impression of the general state of health services in the area and to obtain any additional reports and information
- Review of earlier reports on district performance (surveys, service or surveillance evaluations, etc.)

At the end of a field visit, if the MNT elimination status of the district remains unclear, the assessment team should consider what else needs to be done. For example, a small coverage survey may help to determine TT2+ and/or clean delivery coverage.

Once all additional information has been collected, the assessment team should consider again whether it is likely that MNT elimination has been achieved, and if a confirmatory survey is required.

1.3 SELECTION OF DISTRICTS FOR THE SURVEY

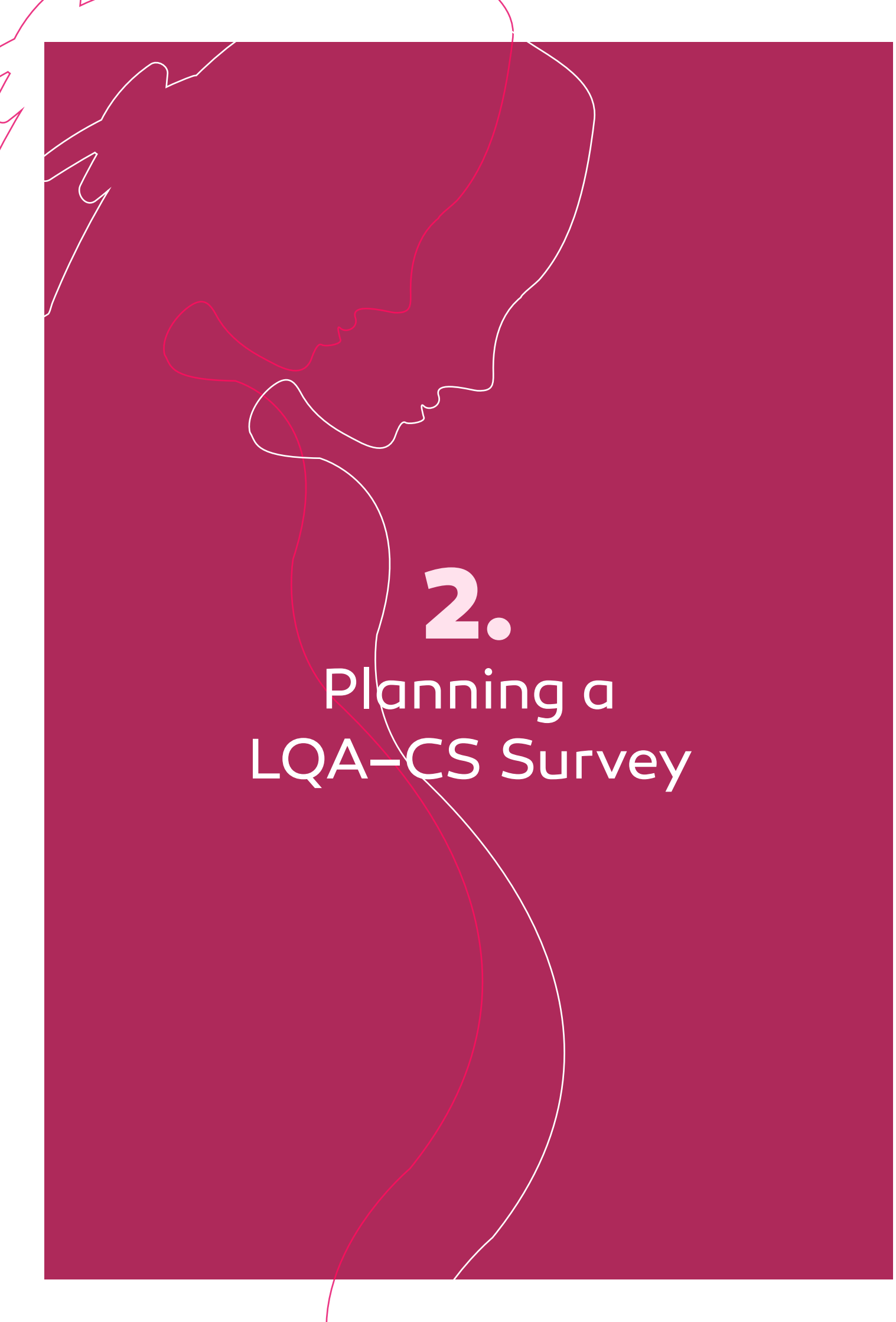
(See also Section 1 of the Statistical Supplement)

If, after reviewing the district level data, the assessment team agrees that MNT is likely eliminated, but that the available data are not conclusive, the team may decide that a survey is required. Because surveys are labor-intensive and expensive, they should only be performed when little doubt remains that MNT elimination has been achieved.

The survey should be carried out in one or a few districts that are judged to be at highest risk for on-going NT compared with the other districts in the country. The basis for surveying only those districts at highest risk is the assumption that if NT has been eliminated in the highest risk districts, it is reasonable to assume that the disease also has been eliminated in districts at lower risk, i.e., in the rest of the country.

The spreadsheet prepared for the data review (Annex 1) also is used to select the survey district. A shortlist of districts with the weakest performance levels is created using the indicators which the assessment team thinks are most reliable for judging performance. This short list is then carefully reviewed by the team. The final district selection should depend not only on indicator performance levels, but also on local knowledge, "gut impressions", and consideration of other public health, logistical and financial factors.

Normally, only one district is surveyed, however when the poorest performing districts have very small populations, the survey may combine several high-risk districts or encompass an entire province. More details can be found in the section "Sample Size Determination" below.



2.
Planning a LQA–CS Survey

2.
PLANNING A LQA-CS SURVEY

Part 2 outlines the steps required for planning a survey to validate MNT elimination once the decision to perform a survey has been made and the district(s) to be surveyed has been selected. WHO-HQ will review the objectives, specific terms of reference, survey protocol and required preparations with the national core team of MOH, WHO and UNICEF representatives. The core team should agree on individual team member responsibilities and the activities timeline.

2.1 SURVEY PREPARATIONS – OVERVIEW & SUGGESTED TIMELINE

2.1.1 Preliminary planning

1. National team briefing on LQA-CS survey
   - Review summary of required preparations; assign responsibilities; adopt timeline (sample checklists in Annex 2; budget calculator in Annex 3)
   - WHO/HQ to ensure the team understands the tasks ahead and is prepared to complete them

2. Appoint a National Focal Point
   - Ideally an MOH representative who assumes overall responsibility for coordinating the survey

3. Notify the selected district(s) and obtain approval(s) for the survey
   - The district team leader(s) should be identified and briefed
   - Security conditions should be reviewed

4. Decide on dates for the survey (with district team leader(s))
   - Consider access, weather and local customs (religious events, seasonal migration, planting/harvesting times, etc.)
   - Notify WHO/HQ

2.1.2 Determine survey design, micro plan & budget

1. Determine sample size, cluster size and number of clusters (pp 13-15 & Annex 4)
   - Decide on a single or a double sample plan
   - Determine total sample size; calculate cluster size and number of clusters

2. Select cluster locations (pp. 16-17)
   - A list of district villages/wards with populations *in hand* is required

3. Prepare micro plan based on actual clusters to be surveyed.[1]
   - Who, what, where, when, how - as prepared for SIAs and/or other surveys
   - Develop a micro plan *with district representatives*
   - The micro plan should be detailed and designed specifically for local conditions - staffing ratios and transport needs may vary depending on population density and terrain within the district(s).

4. Calculate budget based on the micro plan.
   - A rough budget calculator is available from WHO (see Annex 3 -- modify as appropriate)
   - Prepare budget *with input from district representatives* (local costs may vary)
   - Include all anticipated expenses based on micro plan and past experience

5. Submit micro plan and budget request to WHO/HQ
   - Funds are available from WHO HQ for most surveys, but in some cases countries have contributed to the costs.

6. Provide district team(s) with final micro plan and timeline
   - (District-level checklist sample in Annex 2)

7. Identify the survey staff (see section on Roles & Responsibilities below)
   - WHO/HQ will identify the consultant(s)
   - The national team typically identifies the monitors
   - The district team(s) should identify supervisors, surveyors, local guides, and MOs with assistance from national team if needed

2.1.3 Training

1. National-level training for monitors
   - For national team, monitors (and supervisors if possible) who will conduct district training workshop(s)
   - Usually conducted by the WHO consultant in the capital city during the week before the survey; lasts 2-3 days
   - Follows standard training package available from WHO/HQ; must include a field-exercise

2. National team arrives in district(s)
   - Preferably 1-2 days before district workshop to review preparations and assist with final tasks

3. District training workshop for entire survey staff

1 While early selection of clusters creates risks of falsification, it is impossible to do proper microplanning and budgeting without knowing where teams are going – this is of crucial significance for difficult-to-access areas. Microplanning could be done with trusted local informants (perhaps people who are not directly involved with the MNTE program or survey) or using general target areas that include the specific clusters but without naming the actual villages/wards.

- Training conducted by monitors in the local language of the survey district(s)
- Usually held in the district capital just before the survey start; usually 2-3 days long
- Follows standard training packages for different staff roles; must include a field-exercise

2.2 DESIGNING THE COUNTRY-SPECIFIC SURVEY

The community-based survey method recommended in this manual uses a combination of lot quality assurance (LQA) and cluster sampling (CS) techniques to judge whether the neonatal tetanus mortality rate, or NTMR, is probably greater than 1 NT death/1000 live births or not.

The structural elements that must be determined for each specific survey are:

- Single vs. double sample plan
- Survey sample size – the total number of live births to be identified and surveyed
- Cluster size – the number of live births per cluster (sampling unit)
- Number of clusters – the total number of clusters to be surveyed
- Duration of survey – depends on sampling plan, average time required to complete clusters and staff availability

The following sections describe the LQA-CS survey and how to determine the structural elements required for each survey. See the Statistical Supplement for greater detail.

2.2.1 Background

The LQA-CS survey method is appropriate for selected populations in the final stage of MNT elimination when there is evidence suggesting that NT has been reduced to less than$_1$ case/1000 live births and only occurs sporadically (not in clusters). The method was developed because conventional surveys to measure low NTMRs require very large sample sizes - tens of thousands of live births. The LQA-CS method uses samples of 3000 live births or less, making surveys feasible and affordable in countries ready to demonstrate MNT elimination.

- The statistical basis and technical aspects of the LQA-CS methodology is described in detail elsewhere.[2] The following summarize basic survey assumptions and structure.

  The NT LQA-CS is a type of *neonatal mortality survey* in which identified neonatal deaths are investigated by verbal autopsy to determine if the death was caused by tetanus (see "Neonatal Death Investigations" below for the NT case definition).

2 Hund L and Pagano M. Statistical Supplement to the Guide for Validation of Maternal and Neonatal Tetanus Elimination. 2014.

While MNT elimination is defined as less than 1 NT *case* per 1000 live births, the survey measures NT *deaths* per 1000 live births. Because NT mortality is very high (>80%), especially in areas without intensive care medical facilities, the NT mortality rate is assumed to approximate NT incidence.[3]

The primary elements sampled are live births delivered during a 12-month *eligibility period* that ends at least 4 weeks before the start of the survey. The 4-week interval between the end of the eligibility period and the start of the survey is to ensure that the outcome for all eligible live births can be determined for the entire neonatal period.

- The LQA-CS survey assesses whether the NTMR in the survey area probably exceeds 1/1000 live births during the 12-month eligibility period, or not. It is not designed to provide a point estimate of the NTMR for the surveyed area.

  The number of NT deaths detected during the survey is compared to a pre-determined maximum *acceptance number* of NT deaths that defines whether the district "passes" (NTMR probably does not exceed 1/1000) or "fails" (NTMR is probably greater than 1/1000). This pass/fail design comes from LQA methodology.[4]

  The acceptance number is calculated to ensure that there is a high probability that a district given a "pass" did not have an actual NTMR greater than 1/1000 live births during the 12 month interval covered by the survey.

- A *double sample* procedure divides the total sample in two parts to be surveyed sequentially. The double sample plan has the advantage of allowing a decision to be made from the results of the first sample if the number of NT deaths detected is very low (0), or very high (more than the acceptance number). When results of the first sample fall in between, the second sample is needed (see "Survey Procedures – Overview" below).

  When the second sample is required, a decision can be made before completing the second sample if the number of detected NT deaths surpasses the acceptance number (fail). Thus, a double sample plan can reduce the total sample size needed to reach a decision, and decrease the amount of field work and costs associated with the survey.

- The cluster selection method used for the LQA-CS survey is the same as that used for a standard 30 x 7 cluster survey for immunization coverage,[5] except that more clusters are used. The larger number of clusters increases the representativeness of the sample and the precision of point estimates for variables other than NT mortality.

3 Ad Hoc Committee on Maternal and Neonatal Tetanus: Meeting Report, Geneva, 25-26 March 2003 (WHO/IVB/04.11)
4 LQA is a technique which originally was developed for quality control in manufacturing to ensure that lots (batches) of products do not have an unacceptable proportion of defective items.
5 Immunization Coverage Cluster Survey - Reference Manual (WHO/IVB/04.23); available at: http://whqlibdoc.who.int/hq/2005/WHO_IVB_04.23.pdf.

- TT coverage, clean delivery coverage and cord care practices are measured during the survey as well.

2.2.2 Sample Size Determination

The survey sample size is determined by the population size of the survey district(s), and the sampling scheme chosen.

Originally, the surveys were designed as double sample surveys for populations with at least 30,000 births per year. In that case, the total sample size required is 3000 live births: 1000 live births in the first sample with an acceptance number of 0 NT deaths; 2000 live births in the second sample with a maximum acceptance number of 3 NT deaths.

Modifications to the original design were made to enable double sample surveys of smaller populations and use of single sample surveys. In 2012, the statistical basis and assumptions of the method were thoroughly reviewed. Recommended sample sizes were refined. Sample sizes and acceptance numbers were determined for single and double sample surveys for both large populations (at least 50,000 live births) and smaller ones, with similar probabilities of acceptance for all, thereby maintaining comparability among surveys

See Annex 4 for a table that provides the required sample sizes for double or single sampling in populations with different numbers of annual live births.

Note: sample sizes were determined based on the assumptions that NT mortality is approximately 80% and that 90% of all NT deaths will be identified (see Statistical Supplement). If these assumptions are not appropriate for a given survey, the required sample sizes can be recalculated with the "LQASdesign" package written for the computer program R.[6]

Sample size for populations of less than 50,000 births per year, using a double sample plan

Annex 4 provides sample sizes and acceptance levels for surveys of populations with fewer than 50,000 live births per year. For example, a population with 15,000 live births requires 1340 live births for the first sample and 1220 live births for the second. NT can be considered eliminated if 0 NT deaths are found upon completion of the first sample, or if 2 or fewer NT deaths are identified in samples 1 and 2 combined.

6 Contact Dr. Nasir Yusuf, Senior Health Specialist - Monitoring, MNTE & GVAP, for the necessary statistical package and instructions: yusufn@who.int

Sample size for single sample surveys

Adjusted sample sizes and acceptance levels for single sample surveys also can be found in Annex 4. For example, if a district has 30,000 live births, a single sample survey requires a sample size of 2470 live births. NT can be considered eliminated if 2 or fewer NT deaths are identified. In a district of 10,000 live births, the recommended single sample size is 1730 live births; NT is considered eliminated with 0 or 1 NT death.

Sample size for districts with very small populations

When districts have fewer than 3000 live births, two or more districts at high NT risk can be combined in the same survey to increase the total population size. The results will be interpretable only for the group of districts, not for each district separately. Strictly speaking, a pass for the combined districts does not validate MNT elimination at the *district* level, but this is considered an acceptable limitation.6 See also Section 1 of the Statistical Supplement.

Single versus double sample surveys

Double sample surveys are usually chosen when it is expected that NT elimination can be demonstrated with the first sample alone, that is, when a country is confident that NT has become so rare that it is likely that no NT deaths will be found in the first sample. In such cases, NT elimination status can be determined from the relatively small first sample of a double sample plan, or before finishing the survey of all second sample clusters. See also Section 2.4 of the Statistical Supplement.

Single sample plans are appropriate when logistics are too complicated and/or communications inadequate for a double sample plan. Double sample surveys are more complicated to organize because arrangements (transport, per diems, etc) must be made for both samples in advance, even if it is possible that only the first sample will be required. Communication among teams is critical in double sample surveys, as the decision to implement the second sample depends on timely receipt of all results from the first sample. In addition, results from second sample clusters must be monitored continuously to determine whether the number of identified neonatal deaths has exceeded the acceptance number, yielding a “fail” and allowing the survey to be terminated. Single sample surveys are thus indicated when logistics and communications infrastructures cannot support a double sample survey.

2.2.3 Determination of the size and number of clusters

Once the total sample size of live births required for the survey is determined, the cluster size and number of clusters can be calculated.

Ideally one cluster should be completed in 1 day or less. Thus the **cluster size**, or number of live births per cluster, is equal to the number of live births that can be surveyed in a day.

To calculate the cluster size, calculate the number of live births that can be surveyed in 1 day by multiplying:

- the average number of households that can be visited in 1 day

  by

- the average household size *(this gives the number of people that can be surveyed in 1 day)*

  by

- the crude birth rate or CBR *(this gives the number of live births surveyed in 1 day)*

Cluster size = (#HHs) x (HH size) x (CBR)

For example: if 100 households can be visited in 1 day, the average household size is 5.5, and the CBR is 0.036, the cluster size will be: 100*5.5*0.036 = 19.8, or 20 live births per cluster.

To calculate the total number of clusters required, divide the total sample size by the cluster size.

Number of clusters = sample size / cluster size

Continuing the example from above, if the total sample size is 3000 live births, the number of clusters required is: 3000/20 = 150. For a double sample survey, this total number of clusters is divided into those required for the first and second samples based on the respective sample sizes.

District specific data for average household size and crude birth rate should be used whenever possible. If district data are not available, provincial or national data are acceptable substitutes.

A realistic estimate of the average number of households that can be visited in a day (or 2 days for especially hard-to-reach populations) is critical for determining realistic cluster sizes and therefore realistic workloads for survey teams.[7]

District authorities should be consulted about past local experience with other surveys or door-to-door vaccination campaigns to determine an appropriate estimate.

7 The estimated number of households that can be visited in one day is ONLY used to compute cluster size and number. Surveyors must visit households until they reach the pre-set number of live births for each cluster (20 in the example above), regardless of the number of households it takes to find the required number.

In districts with low population densities and/or difficult terrain, it may be necessary to complete clusters in more than 1 day. The cluster size and number of clusters should be calculated as above, but the days required to complete the clusters can be increased.

In districts with a wide range of conditions, some surveyors will be able to complete clusters in less than 1 day, while others will need more than 1 day. Allocation of survey staff should reflect differences in conditions (e.g., extra staff assigned to difficult areas, or more clusters assigned per surveyor in easy areas).

The size of every cluster must be the same; the time to complete clusters can vary.

2.2.4 Sample Size for TT2+, Clean Delivery and Cord Care Assessment

At least 250 mothers of eligible live births are asked about their TT immunization history, the circumstances of delivery and the application of traditional substances on the umbilical cord.[8]

When a double sample plan is used, the first 5-8 mothers with an eligible live birth in each cluster of the first sample are asked the additional questions. The number of mothers surveyed per cluster depends on the number of clusters to be surveyed. In a single sample survey, usually only the first 3 mothers per cluster are asked the additional questions because the number of clusters is larger.

To calculate the number of mothers per cluster who will be asked the additional TT, clean delivery and cord care questions, divide the total number of mothers to be surveyed (250) by the number of clusters, and round up to the next whole number if necessary:

Mothers per cluster = 250 / #clusters

For example, in a double sample survey, if there are 50 clusters in the first sample, the number of surveyed mothers per cluster would be: 250/50 = 5 mothers per cluster. For a single sample survey with 110 clusters, 250/110 = 2.5 or 3 mothers per cluster.

The number of mothers surveyed in each cluster must be the same; the total number must be 250 or more.

2.2.5 Cluster selection

Once the number of clusters required for the survey is determined, the locations of the clusters are randomly selected from a list of the smallest population units available, e.g., villages, towns, and wards / census blocks of larger cities in the district(s) to be surveyed.

8 The sample size recommended here (250) should provide estimates with narrower confidence intervals than the + 10% maximum assumed for a 30 x 7 cluster survey because a larger number of clusters are surveyed and coverage is usually higher than 50%. There is no advantage to increasing the number of mothers surveyed per cluster unless a subset analysis is desired (e.g., comparing coverage in different age groups) or greater precision is required.

A complete list of population units with current populations is essential.

Cluster selection is performed in the same manner as in the 30 x 7 cluster survey method, and like the 30 x 7 cluster survey, uses "probability proportionate to size" (PPS) so that all individuals in the population have an equal probability of being selected.8 The procedure is most easily performed with a computer spreadsheet program, although it can be done by hand if necessary. Refer to the example in Table 2 below.

1. The first step is to obtain a complete list of all villages and urban population units (wards, census blocks, etc.) with the best estimates of the population for each in a second column. An up-to-date list is essential and must be compiled if not available from district authorities.

2. Next, calculate the cumulative population for each community on the list and place it in a third column. This is done by adding the population of the first community on the list to the population of the second community – the sum is shown as the cumulative population of the second community. Continue by adding the population of the next community on the list to the cumulative population of the preceding community for each listed community. The cumulative population of the last community on the list should equal the total population for the district(s) to be surveyed.

3. Calculate the *sampling interval* by dividing the total population to be surveyed by the total number of clusters; round off the result to the nearest whole number. This sampling interval is the number used to systematically select clusters from the list. In Table 2, an example is shown in which 30 clusters will be sampled, the sampling interval is: 139,324/30 = 4644

4. Choose a random number to determine the starting point on the list. The number should be less than or equal to the sampling interval, and have the same number of digits. The random number can be obtained from a random number table or computer program, or from the serial number on a currency note. In the example, it is 3311.

5. Select the location of the clusters. The first cluster is the community on the list with a cumulative population that is equal to or more than the random number. Write "1" beside this community in a column for listing cluster numbers. As 3311 falls in the cumulative population of the first community on the list (11,627), the first cluster is located in the first community.

   To select the location of the second cluster, add the sampling interval to the random number and find the community with a cumulative population that equals or exceeds that sum. Write "2" besides the community. In the example, 3311+4644 = 7955; 7955 also falls within the cumulative population of the first community.

The location of the rest of the clusters is determined in the same way - the community in which the cumulative population equals or exceeds the sum of the previous total plus the sampling interval is the next location of a cluster. This procedure is continued until all cluster locations are identified. (Note: it is possible that some large communities will have several clusters).

If the survey has a double sample plan, the final step is to allocate the selected cluster locations to the first and second samples. This is done by selecting the cluster locations for the first sample by one of the two methods described below. The remaining cluster locations will be used for the second sample if needed.

First, re-number all the selected cluster locations (from 1 to the total number).

Method 1 - systematic allocation of clusters to first and second samples:
(This is the preferred method as the allocation will be PPS):

In the case of surveys in large districts, if the second sample size is twice the size of the first (e.g., n_1 = 1000; n_2 = 2000), every third cluster location should be selected for the first sample.

- Select a random number from 1 to 3. The community with the cluster number equal to the random number is the first cluster location for the first sample. The second cluster location is that with the number equal to the random number plus three. Continue sequentially adding 3 (selecting every third cluster number) until all clusters for the first sample have been identified.
- The remaining cluster locations constitute the second sample.

Method 2 - random allocation of clusters to first and second samples:
(for surveys in smaller districts when the size of the second sample is not a multiple of the first.)

- Generate random numbers between 1 and the total number of clusters in the survey. The quantity of random numbers required is the same as the number of clusters in the first sample.[9]
- The communities with numbers corresponding to the random numbers will be the cluster locations for the first sample. The remaining cluster locations will be used for the second sample (if needed).

  For example, if the total number of clusters is 168, and 60 are required for the first sample, then 60 random numbers between 1-168 (inclusive) are needed. The 60

9 Epi Info 7 is a small, easy-to-use computer application that will generate a list of random numbers based on specifications entered into the program "random number list" found in EPITABLE. The software is freely available at: http://www.cdc.gov/epiinfo. Many other statistical software packages have similar programs.

communities with numbers corresponding to the random numbers will be the first sample; the rest are second sample clusters.

Table 2. Example of systematic cluster location selection proportionate to community size

Column 1	Column 2	Column 3	Column 4	Column 5
	Community/Area	Population	Cumulative population	Cluster numbers
1	Al Naser South	11 637	11 637	1,2
2	Al Naser North	18 181	29 808	3,4,5,6
3	Al Sinet	2 000	31 808	7
4	Hakib Alah	9 800	41 608	8,9
5	Arkaweet	4 000	45 608	10
6	Awoda	13 726	59 334	11,12,13
7	Helat Hasan	6 000	69 334	14,15
8	Al Dubasin	3 363	72 697	
9	Al Omal	12 727	85 424	16,17,18
10	Al Qatati	2 000	87 424	19
11	Al Muneera	1 500	88 924	
12	Al Mattar	2 000	90 924	
13	Al Sudani	950	91 874	20
14	Al Shartta	9 000	100 874	21,22
15	Al Muwazafin	1 500	102 374	
16	Al Zamalik	2 000	104 374	
17	Dardig	11 000	115 374	23,24,25
18	Hai Nasir	9 800	125 174	26,27
19	Al Maki	4 350	129 524	28
20	Al Gazeera	9 800	139 324	29,30
	TOTAL	139 324		
	Sampling interval		139,324/30 = 4644	
	Random number		3311	

(Source: Immunization coverage cluster survey – Reference manual, WHO/IVB/04.23)

2.3 SURVEY STAFF – ROLES & RESPONSIBILITIES

The success and validity of the survey depends on the performance of the staff involved. Survey personnel should be chosen on the basis of their qualifications and willingness to participate. Roles and responsibilities must be clearly delineated.

The following summarizes the categories of survey personnel and their general duties.

Surveyors

- Usually 1 per cluster (often responsible for more than 1 cluster)
- Responsible for:
  - going house-to-house, interviewing residents
  - collecting survey data and completing survey forms
  - notifying supervisors/MOs when neonatal deaths are identified.
- Should be health care workers, public health staff or medical/nursing students with experience in communicating with families about the sensitive issues of pregnancy, childbirth and child deaths. Teachers may be acceptable alternatives if sufficient health workers are not available.
- Must know the local language and be familiar with local customs. Women surveyors are preferred because of the sensitive nature of some questions
- Surveyors should NOT be assigned clusters in the areas where they normally live and/or work. If possible, surveyors should come from outside the survey district.
- Several back up surveyors should be hired and trained to cover for drop-outs

Local guides

- 1 per surveyor (for a given cluster area)
- Responsible for introducing the surveyor / other survey personnel to community leaders and household residents, and helping the surveyors identify and navigate the cluster localities
- Should be selected /approved by the village/ward head; preferably well-known to the community; often are auxiliary community health workers.

Supervisors

- Usually 1 for 3-5 surveyors; ideally able to visit all surveyors in the field each day. In areas with exceptionally scattered population and/or difficult terrain might be assigned to only 2 surveyors.
- Are preferably Medical Officers (doctors) who can conduct neonatal death investigations
- Responsible for:
  - providing/arranging transport for surveyors to and from clusters

  - supervising surveyors in the field to ensure that household selection and data collection are properly performed (daily if possible)
  - Responsible for investigation of all neonatal deaths identified in the survey in their assigned areas, including completion of the neonatal death investigation form (Form 3)
  - contacting MOs when neonatal deaths are identified (if supervisor is not an MO)
  - reviewing data collection forms at the end of the day, tallying cluster results and checking Quality Assurance indicators (QA Section, p. 30), and informing monitors of results
  - troubleshooting any problems that arise
- Usually recruited from district-level supervisory/senior staff; ideally from another district. Should NOT be assigned areas where they normally live/work.

Exceptionally, when there are no MOs available in the country, NDs could be investigated by paramedics or midwives, but to be verified by the monitors based on the clinical history.

Monitors

- Usually 3-5 per survey – more may be required for widely dispersed populations / difficult terrain.
- Responsible for:
  - district-level training of surveyors, supervisors and MOs
  - second level supervision during the survey, including visits to as many surveyors and supervisors in the field per day as possible
  - helping trouble-shoot any problems that arise
  - reviewing data with supervisors at the end of each day to ensure correct procedures are being followed
  - monitoring survey quality indicators, especially NDs; providing feedback to supervisors and surveyors
  - re-investigating and confirming any identified NT deaths in assigned area
  - assisting with data entry (optional – depends on circumstances)
- Usually national and provincial staff; may include district heads

International consultant

- 1 per survey (or more when several districts are covered)
- Responsible for:
  - acting as main technical advisor; ensuring adherence to global protocol
  - leading / participating in national training workshop; assisting with district training
  - serving as monitor during the survey
  - assisting with data entry & analysis
  - helping draft first survey report

Coordinators - "Core Team" for survey

- Usually consist of national-level team and the international consultant; often also serve as monitors. One national member serves as the overall survey coordinator and main contact with WHO/HQ
- Make ultimate decisions about survey outcome, the need to repeat portions of the survey if procedures are not followed, etc.
- Finalize survey report.

Data Manager

- 1 per survey (optional – data management may be performed by coordinators)
- Assists with data entry of cluster-level data and/or compiling data entered by monitors; might assist with district-level survey preparations and worksheets, and with monitoring.
- Usually a district IT staff member or data manager; may be provincial or national level

2.4 TRAINING

Good training ensures a well-executed survey.

When procedures are not followed correctly, survey results are invalid – survey staff must be retrained and the survey repeated.

An LQA-CS survey training kit is available from WHO/HQ. The kit contains:

- 2 sets of PowerPoint presentations designed for national-level monitors and supervisors training, and one for district-level surveyors training. Subjects covered include:
  - MNT elimination and the purpose of the survey
  - Survey staff roles and responsibilities
  - Survey procedures, including how to use the data collection forms
  - Survey quality issues and indicators
  - Understanding survey results
- A role-play board game that takes trainees through survey procedures and a range of situations they are likely to encounter.
- Instructions for a mandatory field exercise
- Sample workshop agendas, surveyor instructions and scripts, and survey forms (Annexes 7-10).

The materials should be adapted for the local setting and specific survey before use; slides, handouts and forms used by surveyors must be translated into the local language.

Training should be well-organized, practical and participatory to ensure that survey personnel are provided with all the preparation they need to conduct the survey properly and collect high quality data.

For the role-play game and field exercise, trainees should be divided into small groups. Organizing groups by survey assignments is preferred. (Surveyors, supervisors and monitors who will work together also should train together). At the end of the field exercise, all trainees should return for a large group discussion of encountered problems and questions.

At the end of the training, the following areas of understanding are critical:

- Surveyors must be knowledgeable on:
  - How to choose households and why no household can be skipped
  - How to find ALL eligible live births and ALL eligible neonatal deaths
  - How to complete Forms 1 and 2
  - How and when to contact their supervisors
- Supervisors must be knowledgeable on:
  - All survey materials
  - How to tally Forms 1 and 2 when clusters are completed
  - How to supervise effectively and monitor quality indicators
  - What to do if problems are identified
  - What is the NT case definition; what supplemental factors can be useful in diagnosing NT?
  - How to decide if a neonatal death was caused by NT
  - How to complete Form 3
- Monitors must be knowledgeable on:
  - All aspects of the survey including all surveyor, supervisor and monitor materials.

3.
Survey Implementation

3.
SURVEY IMPLEMENTATION

3.1 SURVEY PROCEDURES - OVERVIEW

Note: Supervisors and Monitors must all have independent transportation for optimal supervision and prompt investigation of neonatal deaths.

Start of survey day:

- Supervisors drop their surveyors at the assigned cluster sites.
- (When distances between clusters are large, supervisors may arrange for independent transportation for some of the surveyors assigned to them.)
- Surveyors meet the local guides; visit the head of the cluster area (village chief, head of ward, etc.) to explain the purpose of the survey and obtain permission to work in the area
- Monitors help ensure that survey personnel have transport and can begin work in a timely manner.

During the survey day:

- After the introduction to the cluster area head, surveyors select the first household of the cluster (see below) and proceed with interviews and data collection as described in section 2 and annex 6.
- If questions/problems arise, and when NDs are identified, surveyors contact their supervisors.
- Supervisors return to the clusters being covered by their surveyors to check the progress of the work, ensure that procedures are being followed properly (observe surveyors at work; recheck several houses), solve any problems that arise, and investigate identified neonatal deaths.
- Monitors visit clusters being covered by the groups of surveyors and supervisors assigned to them, independently checking the work and ensuring proper procedures are adhered to.
- Monitors (core team) should re-check neonatal deaths that are thought to be due to tetanus.
- Throughout the day, the number of identified neonatal deaths and neonatal tetanus deaths should be communicated to the survey coordinators so that progress of the survey can be monitored.
- A cluster is completed when the pre-set number of live births have been identified, regardless of the number of HH visited, or the number of ND identified.

End of survey day:

- Supervisors pick up their surveyors, review the data sheets and, with their group of surveyors, discuss any questions/problems that arose. When the clusters are completed, supervisors collect all forms and tally the cluster results.
- Monitors meet with (or talk by telephone) with their supervisors to learn of the day's progress, noting the number of clusters completed, neonatal deaths identified and if any cases of NT have been found.
- Completed data forms should be collected and all quality assurance indicators checked as soon as possible (see QA Section, p. 30).
- Monitors meet with supervisors to review ND investigations at the end of the day, or as soon as possible.
- Monitors meet as a group each evening to review survey progress and discuss/resolve any problems that arose. This coordinating meeting also should include staff responsible for survey logistics.
- (When monitors are based in geographically dispersed areas, they may need to call in the progress of their teams to the head survey coordinator.)
- Surveyors and supervisors should be given feedback about survey progress (number of clusters completed, numbers of identified neonatal and NT deaths, etc.) at the end of each day or before starting work the following morning. Observed problems must be discussed and solutions be proposed.
- If major flaws in survey implementation have surfaced by the end of the first day, the survey may need to be stopped, and surveyors/supervisors retrained on Day 2, before restarting the survey.

Survey completion:

- **Single sample survey:** work proceeds as above until all clusters are completed.
- **Double sample survey:** work proceeds as above until all clusters in first sample are completed.

  The results of the first sample will determine whether the second sample must be performed. After all clusters in the first sample have been completed:

  - If no NT deaths are detected, NT elimination can be accepted (pass) without surveying the second sample. The survey can be stopped.
  - If more than the maximum acceptance number of NT deaths is detected, NT elimination is rejected (fail); the second sample is unnecessary. The survey can be stopped.
  - If any NT deaths have been identified, up to and including the maximum acceptance number, a decision about NT elimination cannot be made; the second sample of clusters must be started.

When the second sample of clusters is required, work continues in the same manner as described above. Identified neonatal deaths and neonatal tetanus deaths must be reported as soon as possible to the coordinators so that progress of the survey is continuously monitored.

– If the total number of identified NT deaths (both samples combined) remains less than the maximum acceptance number, all clusters in the second sample must be completed.

If the total number of identified NT deaths exceeds the maximum acceptance number at any time, the second sample can be stopped, even if not all clusters are completed.

3.2 SURVEY PROCEDURES - SPECIFICS

Essential definitions

- A household is defined as a group of people sharing the same kitchen.
- Eligible live births are those delivered by eligible mothers between __/__/__ and __/__/__
- Any birth between __/__/__ and __/__/__ to an eligible mother is eligible,
- even if the birth was at a different location.
- Eligible mothers are mothers who delivered during the eligible period and who reside in a household at the time of the survey – **not visitors**.
- If a mother is temporarily away at the time of a survey, she is still eligible.
- A neonatal death is a death in the first 28 days of life

3.2.1 Procedures for Surveying Clusters

- Upon arrival at the cluster location, first visit the head of the area (village chief, head of ward, etc.,) to explain the purpose of the survey, general procedures (choice of first HH, which HHs will be visited, what kinds of questions will be asked) and request permission to perform the survey.

  If a local guide was arranged in advance, meet the guide who can then introduce the head of the area.

  If a local guide has not been arranged, ask the area head to appoint a guide (local health worker or administrative assistant who is familiar with the residents)

- Select the first household as described below.
- The local guide should make the introductions; then briefly explain the purpose of the survey.

- Explain that survey participation is not obligatory and that refusal to participate will not result in any negative consequences. Then ask if the household members are willing to participate, i.e., to give verbal informed consent.
- Interview the head of the household / resident women with eligible live births as described in Annex 6, completing Forms 1 and 2 as directed.
- Proceed to subsequent households, repeating the introduction, explanations, interviews and data collection, until the required number of live births for the cluster has been surveyed.
- If a neonatal death is identified, the supervisor should be contacted immediately. If the supervisor cannot be reached, the monitor should be contacted.
- Forms 1 and 2 should be submitted to the supervisor once a cluster has been completed – usually at the end of a work day when meeting with the supervisor and fellow surveyors.

Selection of the First Household in each Cluster

The first house to visit in each cluster should be selected at random. Several methods can be used:

Method 1: Areas where household lists are available.

The ideal situation is one in which there is a complete list of households in the cluster area that can be used to randomly select the first household to be surveyed. If such a list is available:

- Number the households on the list.
- Select a random number from 1 to the highest numbered household on the list (inclusive). Do this by using a table of random numbers or the serial number on a currency note.
- Find the household on the numbered list whose number corresponds to the random number selected. This is the first household to visit.

Method 2: Rural areas and urban subdivisions where household lists are not available.

In cluster sites where no there is no list of households (the most common situation):

- Select a central location in the village, town or ward, such as a market, a mosque or church. The location should be near the approximate geographical centre of the area.
- Randomly select a direction from the centre by throwing a pen spinning in the air. When the pen falls on the ground the point indicates the direction to be taken.
- Walk in the selected direction, counting all the houses passed until the edge of the area is reached.
- Select a random number between 1 and the total number of houses counted. The house with the corresponding number is the first house to visit. For example, if the randomly

selected number is 9, the ninth house from the central location is the first household to visit.

Note: if a village where a cluster is begun is known to have fewer HHs than will probably be needed to complete the cluster, surveying can start at any household because all households will be visited

Method 3: Choosing subdivisions in urban areas and large rural towns

Often urban cluster sites are too geographically large and/or contain too many households to use Method 2 without first selecting a smaller portion of the cluster area. If the area already has official or locally recognized geographical or political subdivisions with approximately equal populations (or which can be grouped to obtain equal populations) these should be used. If such subdivisions don't exist, use a map or sketch of the area and create subdivisions of approximately equal size (e.g., blocks of about 100 houses) with the help of local authorities.

- Number each subdivision and select a random number between 1 and the total number of subdivisions. The selected number indicates the subdivision in which the first household is located.
- If a household list exists for the subdivision identified, select the first household to visit by following the procedure described for Method 1.
- If a household list is not available, use Method 2 to identify the first household.

This subdivision method can also be used when more than 1 cluster site is located in a single urban ward or large rural village. To select the cluster locations within the ward or village:

- Use the pre-existing subdivisions or create them with the help of a map/sketch and local authorities. Ideally, there should be at least 2-3 times as many subdivisions as clusters to be surveyed in the ward or village.
- Number the subdivisions
- Choose random numbers (between 1 and the total number of subdivisions) to identify the subdivision for each cluster to be surveyed in the ward or village. The random numbers can be obtained using a table of random numbers or currency note serial numbers.
- If a household list exists for the subdivision identified, select the first household to visit by following the procedure described in Method 1.
- If a household list is not available, use Method 2 to identify the first household

A household is defined as a group of people sharing the same kitchen. In urban areas, there may be many households in a single building. To ensure an unbiased selection of households in such buildings, choose one floor at random. Number the households on the selected floor and randomly select the first household to visit.

Selection of Subsequent Households

The second (or next) household to visit is *the one that is nearest to the first*.

The next nearest household is the one whose front door is closest to the front door of the household just visited (see the figure below).

If the front doors of 2 households are at equal distances from the first, but one can be reached more quickly, go to that household next; otherwise, flip a coin to determine the next household.

In apartment buildings, the second household to visit is the door nearest to the first. After all the households on the floor have been visited, randomly choose a direction up or down to determine the next floor to visit. Visit all the households on that floor. Continue from floor to floor, visiting the next nearest floor which has not been visited previously. After all households in the building have been visited, go to the nearest door of the nearest building, and repeat the process.

Identifying the nearest household in hilly terrain with highly scattered dwellings can be difficult. If there is no map showing household locations, surveyors must rely on their local guides to direct them to the nearest household.

All households must be visited and counted for the survey to be valid.

3.2.2 Neonatal Death Investigations

Neonatal deaths are investigated using standardized verbal autopsy methods to determine if the death was caused by tetanus. The investigations must be conducted by trained physicians or other clinically-trained personnel (by the supervisor, or if he/she is not a trained physician, by the monitor).

Careful, thorough neonatal death investigations are critical for valid survey results.

NT is a clinical diagnosis; there is no confirmatory laboratory test.

The NT case definition is:

A neonate who feeds and cries normally for at least the first 2 days of life,

and, between 3 and 28 days of life

Stops sucking normally

and

Develops stiffness/rigidity and/or spasms

For a diagnosis of NT to be made, the criteria in the case definition must be met.

Additional information that supports the diagnosis of NT:

- Hypersensitivity to touch, sound and/or light, setting off spasms
- Presence of risk factors associated with NT such as lack of maternal TT immunization and/or unhygienic delivery and/or umbilical cord care

NT can be ruled out in cases where death occurs in the first 2 days of life.

Specific instructions for conducting the investigation and completing Form 3 can be found in Annex 7.

3.2.3 Collection of Survey Information

The information collected during the survey should be limited to data that are essential for evaluating the NTMR, TT and clean delivery coverage of mothers, and occasionally a few other epidemiological factors related to NT risk. Collection of non-essential information should be avoided as it may have a negative impact on the quality of the essential data.

Examples of data collection forms and instructions for surveyors and Medical Officers are provided in Annex 6 and 7. These forms must be translated into the local language before the survey starts.

The following summarizes the forms and essential data to be collected:

Form 1 – Household data (one per cluster):

- The number of residents in each household visited - used to verify the actual number of household visits needed to complete each cluster, and to calculate the total population surveyed and average household size. These estimates can be compared with other sources of data to validate the quality of the survey data.
- The number of pregnancies in the previous 2 years in each household, the outcome of those pregnancies, and the number of live births that occurred in the eligible period of the survey.[1]

Form 2 – Live birth data (one per cluster):

- Information about each eligible live birth is recorded on a line on Form 2 - date of birth, survival status and, if the baby died, whether the baby died before reaching 28 days of age. (Eligible births are those occurring 1-13 months before the survey.)
- In addition, information about the delivery conditions, TT status and the use of traditional substances on the umbilical cord, of a sub-sample of mothers of the eligible live births is collected in first sample clusters of a double sample survey, and in all clusters in a single sample survey.

1 While the information about the number of miscarriages and stillbirths is not used in final data analysis, it is collected on Form 1 as part of information gathering about pregnancy outcomes. Because it is not uncommon for babies who expired shortly after birth to be misclassified as stillbirths or late miscarriages, completion of the pregnancy outcome section of Form 1 helps remind the surveyors to try to ensure that early neonatal deaths are not missed. If a survey identifies fewer live births or neonatal deaths than expected, the information on Form 1 can be used to revisit households with stillbirths

(A simplified version of Form 2 without columns for clean delivery and TT status is used for the second sample in a double sample plan.)

Form 3 – Neonatal death investigations (6-10 per Medical Officer, depending on assignment):

All neonatal deaths that occurred in identified eligible live births (i.e., the death of an eligible live birth that occurred in the first 28 days of life), must be investigated by an MO. Form 3 is used to record the information collected in the investigation, and the investigator's conclusion about whether the death was caused by NT.

Form 4 – Informed Consent – optional (one per interviewee or group of interviewees):

Form 4 is a consent form (Annex 10). However, if the surveyor instructions presented in Annexes 8 and 9 are followed, informed consent can be obtained without the need for Form 4.

3.2.4 Survey Quality Assurance

The survey results are not valid unless the data collected are complete and accurate.

Common survey quality problems and the indicators used to monitor data quality are summarized, and then discussed in detail below.

Quality Problem	Indicator
Not all HHs visited	survey CBR, compared to reference CBR
	CBR = (#LBs / #residents) x 1000
	% locked houses
	%locked = locked HHs / all HHs x 100
Incomplete LB information	#LBs: #eligible LBs
	Compare # total LBs to # eligible LBs – should be ~1.5x
NDs missed	# NDs found, compared to the expected #NDs
	expected NDs = (reference NMR)(sample size)/1000
Not following the correct methodology	Surveyors finishing early (very fast)

1. Skipped Households / High Crude Birth Rate & % Locked Houses

Occasionally, surveyors do not follow correct procedures and only visit households with young living children, skipping the other households. By skipping houses, the count and composition of all households and residents in the surveyed area is skewed, and households where neonatal deaths have occurred may be missed. This problem is most common when:

- Surveyors are focused on identifying live births but do not fully understand the goal of finding neonatal deaths. The tendency to focus on live children may be a consequence of past participation in vaccination campaigns and coverage surveys for which only live children are identified.

  When surveyors work in familiar areas (areas where they live or normally work), the tendency is greater to try to save time by only visiting houses with known young children.

- Local guides lead surveyors preferentially to houses with live children (for the same reasons mentioned above)

Indicator: a) CBR in the surveyed population compared with the reference CBR

(district or regional CBR reference preferred; national CBR if local values unavailable)

Survey CBR = (#LBs / #total residents) x 1000

If the survey CBR is substantially higher than the reference CBR, it suggests that HHs with young children might have been preferentially visited, while HHs without young children were skipped. In that case:

- Supervisors and monitors should recheck surveyed areas with the responsible surveyors, making sure that all HHs were visited (and that correct interview procedures were followed).

Note: it is not uncommon to find higher CBRs in poorer, more remote communities like those in districts selected for the LQA-CS survey. Thus, while rechecking must take place when survey CBRs are higher than expected, the conclusion may be that the high CBR is valid for the survey area.

Indicator: b) % locked/missed houses (residents away temporarily) ≤10%

%locked = locked HHs / all HHs x 100

To avoid bias, information should be obtained from at least 90% of HHs with residents who are residing there at the time of the survey. If many residents are away at the time that the surveyor arrives at their house (at the market, working in their fields) the houses must be revisited later, even if it means that surveyors must return to a cluster location a second time. Exclude HHs that are away long-term.

2. Incomplete Live Birth Information

If the total number of LBs is *not* more than the number of eligible LBs, surveyors may be going only to houses with young children (or where guide knows a baby was born in the

eligible period), or simply not recording information on LBs that took place outside of the eligibility period.

Indicator: low ratio of total LBs: eligible LBs

Compare # total LBs to # eligible LBs – should be ~1.5x

If the number of total LBs is similar to the number of eligible LBs:

- Supervisors and monitors should recheck surveyed areas with the responsible surveyors, making sure that correct interviewing technique was followed and that all HHs were visited.

Note: if the birth rate in the survey area is very high, it is possible that almost every house will have an eligible live birth. However, this must always be double-checked.

3. Missed Neonatal Deaths

The biggest and most common survey quality problem has been a failure to detect the expected number of neonatal deaths. If NDs are missed, it is possible that NT deaths also are missed.

Historically, the failure to detect neonatal deaths has undercut the results of many neonatal morality surveys (including LQA-CS surveys and other forms of NT mortality surveys). Evaluations performed to identify the reasons that neonatal deaths are missed have identified the following causes:

- Discussion of infant/child deaths is culturally unacceptable, or so painful that parents avoid mention of such deaths
- Very early neonatal deaths are described as stillbirths (neonates dying within hours of birth are not considered live births)
- Recall bias – neonatal deaths occurring more than 6 months prior to the survey have been shown to be increasingly forgotten (or not recalled as having occurred during the survey eligibility period).
- Surveyors have preferentially visited houses with live young children, thereby skipping households where there was a neonatal (or infant/child) death.

Indicator: #NDs found in the survey compared to the expected #NDs

Calculate the expected #NDs using the reference NMR – preferably the district or regional NMR:

Expected NDs = NMR x (sample size) / 1000

For example, if the known NMR = 35/1000, then 35 NDs would be expected for a sample size of 1000

If the sample size is 1320, the expected NDs = (35 x 1320)/1000 = 46

The expected number of NDs per supervisor or per monitor also can be followed:

– Calculate the expected NDs per cluster (usually a fraction)

Expected NDs per cluster = total expected NDs / total clusters

– Then calculate the expected NDs per supervisor (or monitor) by multiplying expected NDs per cluster by the number of clusters assigned to the supervisor.

Expected NDs per supervisor = (expected NDs/cluster) x #clusters per supervisor

For example, if the expected #NDs = 46, and total #clusters = 100, then 0.46 ND (~0.5 ND) would be expected per cluster; a supervisor responsible for 5 clusters would expect to find 2-3 NDs.

Monitors can calculate the number of NDs expected in their areas in the same way - multiply the #expected NDs per cluster by the total #clusters in their area of responsibility.

If the number of survey NDs is significantly below the expected (approximately 70% or less), several things should be done:

- Supervisors and monitors should recheck surveyed areas with the responsible surveyors, making sure that correct interviewing technique was followed and that all HHs were visited
- Mothers reporting stillbirths should be re-interviewed to be sure that none of the stillbirths were actually early neonatal deaths. This re-interviewing must be performed gently, with awareness that repeated questioning about a tragic event is painful for the mother.
- **If serious lapses in survey protocol or deficiencies in interviewing technique are identified, the cluster(s) must be re-surveyed.**

  If no problems with survey procedures are identified, monitors should talk to local health personnel or community leaders to verify that known neonatal deaths occurring in surveyed households have not been missed. If they have, the reasons they were missed should be identified, and corrective measures taken before the personnel involved proceed to their next survey areas.

4. Not following the correct methodology/ finishing early

When surveyors finish much faster than expected (based on past local experience or the experience with other surveyors), it is possible that corners are being cut – houses are being skipped, not all questions are being asked, complete information is not being recorded.

Indicator: surveyor requires the expected time to finish a cluster

If a surveyor finishes very early, the supervisor or monitor should first check the completed data collection forms to ensure they are complete and that the data look appropriate. Note:

if the household size in the area is very large, fewer houses need to be visited to complete a cluster and the work goes faster.

If the data forms look complete and plausible, recheck the surveyed area to see whether the houses have been marked systematically. Visit several households to verify the surveyor's visit and that the information recorded for that household is correct. Observe the surveyor conducting several interviews to see if any systematic mistakes are being made.

While cutting corners is relatively common, falsification of data is rare, but has occurred.

3.2.5 Survey Data Entry

A customized excel spreadsheet is provided by WHO/HQ for data entry and analysis for every LQA-CS.

The summary data for each cluster (tallied by the supervisor and re-checked by a monitor) is entered into the survey analysis spreadsheet. The data entry can be shared by some or all monitors, or completed by a single designated data manager.

Once the data for every cluster has been entered into the analysis spreadsheet, survey results and statistical parameters are automatically calculated for the variables of interest.

A second spreadsheet for neonatal death investigation data is also available.

3.2.6 Analysis of Survey Data

The LQA-CS survey method is designed to assess whether the surveyed district(s) has an NT mortality rate that is greater than 1 NT death per 1000 live births. It is not designed to provide a point-estimate for the NT mortality rate and should not be used to calculate one.

The results of the NT LQA-CS are interpreted as follows:

- **if no NT deaths are identified** among the live births surveyed in the first sample of a double sample survey, or all clusters in a single sample survey, NT can be considered to have been eliminated in the district(s) surveyed.

  if the number of identified NT deaths is less than or equal to the maximum acceptance number after both the first and second samples in a double sample survey, or all clusters in a single sample survey are completed, NT has been eliminated in the surveyed district(s).

  If NT has been eliminated in the districts at highest risk for NT in the country under evaluation, it can be assumed that NT has been eliminated throughout the country.

- **If the number of identified NT deaths is more than the maximum acceptance number,** NT has not been eliminated in the survey district(s), Therefore the definition of NT elimination has not been met by the country being evaluated.

Point estimates for TT coverage of surveyed mothers are calculated by dividing the number of mothers immunized with a particular dose of TT by the total number of who have been sampled.

%TT-x = (#mothers with TT-x / #mothers-total) x 100

For example, if a TT vaccination history was obtained from a subsample of 250 mothers, of whom 220 had received TT1 and 200 TT2, then TT1 coverage is 220/250 = 88% and TT2 coverage is 200/250 = 80%.

Point estimates for all other variables or subsamples (e.g., health facility deliveries, skilled attendance at birth; TT coverage in CBAW, use of traditional substances on the umbilical cord) are calculated in the same way.

Calculation of confidence intervals for the point estimates must take the cluster sample design of the survey into account. A data analysis spreadsheet prepared by EPI-WHO is available to assist with the necessary calculations. Survey personnel enter the data collected from each cluster into the spreadsheet, and, once all data are entered, the spreadsheet automatically provides the point estimates and 95% confidence intervals for each variable.

ANNEXES

ANNEX 1.

EXAMPLE OF DISTRICT-LEVEL DATA SHEET

(spreadsheet shown in halves, normally is continuous)

Country:

S.No.	District	Coverage Data								surveillance		
		Target Population under 1yr	Live births reported	DTP1 reported	DTP3 reported	DPT 3 Survey data	Measles Survey data	TT2+ coverage Preg Women reported	TT2+ coverage Preg Women survey data	Reported NT cases	monthly report %	Reported NT rate per 1000 LBs
		number	number	%	%	%	%	%	%	number	%	rate
a	b	c	d	e	f	g	h	i	j	k	l	m
1												
2												
3												
4												
5												
6												
7												
8												
9												
10												

Year (Use separate sheet for each year):

System Indicators											
ANC (≥ 1 visit) reported by state	1 or more ANC visit survey data	3 or more ANC survey data	institutional delivery rate (reported by state)	Institutional delivery rate (survey)	Clean Delivery Rate reported by State	Safe Delivery: Doctor/Nurse/TrainedBirth Attendant (Survey)	Urban or rural (majority of pop'n)?	Drop-Out Rates DTP1-DTP3	TT SIA coverage (IF HELD)	Other indicator (add columns as needed)	Conclusion: NT Risk Status/ ranking
%	%	%	%	%	%	%	Urban / Rural	(DTP1-DTP3)/ DTP1	% TT2 SIA Coverage Reported		
n	o	p	q	r	s	t	u	v	w	x	y

ANNEX 2.
PLANNING CHECKLISTS

National Checklist (generic - modify as needed)

Checklist of preparations	Name of person responsible	Date completed
Preparations to be completed well in advance		
Protocol, objectives, and expected outcome discussed with national staff		
Objectives, terms of reference & dates agreed upon with MOH		
Village-level population data obtained from selected districts		
Clusters selected		
Microplanning (with district(s)):		
Detailed maps obtained of selected clusters		
Number of required staff calculated (surveyors, supervisors, MOs)		
Surveyors, supervisors, MOs, drivers identified and contracts prepared / signed (as required - all must agree to dates, responsibilities, conditions of work)		
Vehicles/source of petrol identified and reserved		
Budget calculated		
Financial resources identified		
Financial resources mobilized so that they can be rapidly accessed		
Training dates set (all levels)		
Training locations (s) identified & reserved (including field exercise site) - all levels		
Accommodations & meals for trainers & trainees set?		
Interview forms prepared (adapted to the local situation; translated & field tested)		
Clearance obtained from districts where the survey will be conducted		
Preparations to be completed just before the start of the survey		
Money accessed to pay per diems and petrol		
Staff trained (including field exercise)		
Interview forms and other stationary prepared for each interview team		
Means and frequency of communicating with survey teams established		

MNTE Survey: District Level Check list

(generic - modify for specific survey site as needed)

Ground work preparation by the district before pre visit of the team.		
	Activities	**Check (√)**
1	Discuss plan, time line and itineraries	
2	Maps of the district and all villages / wards	
3	Listing of subdivisions and villages /wards in each subdivision.	
3	Letter from district head to supervisors of all staff identified for the validation exercise (one week before)	
4	List of available health workers (interviewers) in each subdivision with names and place of postings	
5	List of available teachers / other potential interviewers in each subdivision with names and place of postings	
6	List Village Guides (for each village/cluster) to be surveyed	
7	List of Health Supervisors in subdivision with names and place of posting	
8	Discuss team and supervisor allotments and route maps/ movement plan	
10	List of Doctors in each block with names and place of posting	
11	List of Pharmacists in each block with names and place of posting	
12	List of any Medical College in the district.(Contact details of Principal, Vice Principal, SPM deptt)	
13	Names of District data handler/ statistician/ Computer assistant (identify the computer he will work on)	
14	identify reserve / floater staff for absent teams (train them along with the identiied staff)	
15	Identify agencies who could carry out the validation survey in case of manpower shortage.	
16	Identify the agency/ firm that can provide vehicles for hiring (vehicles reqmt will depend on microplanning). Use Govt. vehicles whenever possible. Gasoline expenses can be paid from the budget	
17	Identify the place for stationary products (with contact edtails)	
18	List of closest identified photo copy points in each subdivision	
19	Site(s) for training of identified Health workers, supervisors, doctors	
20	Is generator back up present at the site of training? If NO, identify the place from where to hire this for 2-3 days	
21	Identify the place from where the refreshments will be ordered for the trainers and trainees.	
22	Identify the hotels for the stay of the State /National level staff (with contact details)	
23	Identify the sites where the teams can stay at the district and subdivision levels (training center, hostel, hotel, etc)	
24	Identify sites for training field exercise(s)	
25	Explain budget assumptions- plan for effective fund flow. Identify the staff who will deal with fund flow and documentation.	
26	Briefing of role of data handlers/ statistician/ steno	
27		
28		
29		
30		

ANNEX 3.
BUDGET CALCULATOR

(available as an excel spreadsheet from WHO/HQ)

BUDGET CALCULATION MNT LQA		
Parameters/Assumptions regarding the NT survey		
	is the average number of HHs that a surveyors can visit in 1 day	
	is the average number of people per HH	
	is the average crude birth rate	
	is the total sample size of LBs needed for the survey (use table to decide)	
	is the desired number of days of field work (all samples combined, excluding training)	
	is the desired number of surveyors per supervisor (usually 3-5 depending on conditions)	
	is the desired number of spare surveyors (usually ~2)	
	is the desired number of surveyors per medical officer (if supervisors are not MOs)	
	is the estimated number of days for training of national monitors (usually 2)	
	is the estimated number of days for training of surveyors & supervisors (usually 2-3)	
	is the estimated per diem in USD for national/provincial monitors during national training	
	is the estimated per diem in USD for national/provincial monitors during field implementation	
	is the estimated perdiem in USD for surveyors	
	is the estimated perdiem in USD for local guides	
	is the estimated perdiem in USD for supervisors	
	is the estimated perdiem in USD for medical officers - if supervisors are not MOs or paramedics (doing ND investig)	
	is the estimated perdiem in USD for drivers	
	is the estimated cost in USD of vehicle rental per day - modify if motorcycles required (add rows or itemize separately)	
	is the estimated cost in USD of petrol per car per day	
Survey characteristics based on assumptions above		
	live births can be found by one team in one day	
	clusters in the survey	
	surveyors needed (including spare teams)	
	local guides needed (survey=1 per cluster, plus 4 for training field exercises - adjust if needed)	
	supervisors needed	
	medical officers - if supervisors are not MOs; adjust based on expected NDs per supervisor	
	national/provincial monitors (usually 3-5 per survey)	
	Number of international consultants	
	vehicles needed per day of activity for Monitors (including int'l consultants) - in general 1 vehicle per monitor	
	vehicles needed per day of activity for supervisors - in general 1 vehicle per supervisor - add rows for motorcycles/boats	
	vehicles needed per day of activity for medical officers (if needed) - in general 1 vehicle per MO	
	vehicles needed per day of activity for teams - add rows for motorcycles/boats	
Budget item	**Cost**	**Comments**
Perdiem monitors		During national training
Perdiem monitors		During survey implementation
Perdiem-surveyors		For training plus implementation
Perdiem-local guides		For implementation - add on additional cost of guide(s) for training field exercise
Perdiem-supervisors		For training plus implementation
Perdiem-medical officers		For training plus implementation if supervisors are not MOs or paramedics doing ND investigations too
Perdiem-drivers		Only if car rental does not include driver
Vehicle rental		All - if motorcycles or boats are required, add rows or itemize separately and add to grand total
Petrol		Only if car rental does not include petrol
Training Facility		For training of monitors (all days of "national training")
Training Facility		For training of surveyors/supervisors/MOs (all days of training; include cost of meals & breaks)
Transport capital - field		For monitors / other staff, round trip, if not included in car rental days.
Administrative support		
Communications		E.g., phone cards for all survey personnel
Stationary		
Incidentals		Use approx 5-10% of total
Total		

ANNEX 4.

TABLE OF SINGLE & DOUBLE SAMPLE PLANS

(for populations with the indicated numbers of annual live births; sample sizes have similar probabilities of acceptance)

	Single Sampling Plan				Double Sampling Plan							Upper & lower Limits†	
Pop. (LBs)	Sample size (n)	d*	α	β	1st sample size (n_1)	d_1*	2nd sample size (n_2)	d_2*	α_1	α	β	p_l	p_u
3,000	1,360	1	0.099	0	1,050	0	380	1	0.049	0.099	0	0.33	2.33
4,000	1,480	1	0.098	0	1,140	0	410	1	0.049	0.099	0	0.25	2.25
5,000	1,560	1	0.098	0	1,200	0	430	1	0.049	0.1	0	0.2	2.2
6,000	1,610	1	0.099	0.072	1,240	0	450	1	0.049	0.1	0.074	0.33	2.17
7,000	1,650	1	0.1	0.056	1,270	0	470	1	0.049	0.099	0.057	0.29	2.14
8,000	1,690	1	0.098	0.045	1,300	0	470	1	0.049	0.099	0.045	0.25	2.13
9,000	1,710	1	0.099	0.095	1,320	0	480	1	0.049	0.099	0.097	0.33	2.11
10,000	1,730	1	0.1	0.079	1,330	0	490	1	0.05	0.1	0.081	0.3	2.1
15,000	2,370	2	0.099	0.031	1,340	0	1,220	2	0.049	0.099	0.034	0.33	2.13
20,000	2,440	2	0.099	0.043	1,380	0	1,250	2	0.049	0.099	0.048	0.35	2.1
25,000	2,440	2	0.099	0.036	1,380	0	1,240	2	0.049	0.1	0.039	0.32	2.12
30,000	2,470	2	0.1	0.043	1,400	0	1,260	2	0.049	0.1	0.047	0.33	2.1
40,000	2,490	2	0.099	0.052	1,400	0	1,290	2	0.05	0.099	0.057	0.35	2.1
50,000	2,500	2	0.099	0.05	1,410	0	1,280	2	0.049	0.1	0.054	0.34	2.1

*Acceptance number
†Upper and lower NTMR thresholds - see Statistical Supplement

Note: sample sizes were determined based on the assumptions that NT mortality is approximately 80% and that 90% of all NT deaths will be identified (see Statistical Supplement).

If these assumptions are not appropriate for a given survey, the required sample sizes can be recalculated with the "LQASdesign" package written for the computer program R.[1]

1 Contact Dr. Nasir Yusuf, Senior Health Specialist - Monitoring, MNTE & GVAP, for the necessary statistical package and instructions: yusufn@who.int

ANNEX 5.
SAMPLE TRAINING WORKSHOP AGENDAS

National-level workshop for monitors

9:00 - 9:15	Opening Session: • Greetings • Self-Introduction • Purpose of the workshop
9:15 - 09:30	Address by dignitaries
9:30 - 10:15	Neonatal tetanus (NT) and NT elimination • Global Overview & Regional Overview • Country Update
10:15 - 10:30	Tea Break
10:30 - 11:00	Assessing MNT Elimination: an overview of the validation methodology
11:00 - 11:30	Summary of process to select districts for LQA
11:30 - 11:45	Sample Size Determination
11:45 - 12:00	Determination of number of clusters and cluster size
12:00 - 12:15	How to select the clusters
12:15 - 12:30	Finding the first and subsequent households
12:30 - 13:30	Lunch
13:30 - 14:30	Review of the forms / questionnaires
14:30 - 15:30	*Group Work: role play on using the forms*
	Working Tea
15:30 - 16:00	Frequently encountered problems and issues
16:00 - 16:30	Quality Issues related to the LQA
16:30 - 17:00	Survey Preparations : things to consider
17:00 - 17:30	Summary and clarifications
08:00 – 11:00	*Field Work in the city: Example of real-.life survey implementation*
11:00 - 13:00	Feedback from Field work and clarifications
13:00 - 14:00	Lunch
14:00 - 14:30	Data Entry, data analysis, report writing
14:30 - 15:00	Practical arrangements for the LQA(s): Staffing, funding, accommodation, transport, supplies, communication.
15:00 - 15:30	Final wrap-up
15:30 - 15:45	Tea Break

15:45 – 16:45	*Preparation for field work: training surveyors, schedule, assignments, administrative and logistical matters*

District-level workshop for surveyors and supervisors

		Opening session and welcome	Focus on:
Day 1		Objectives of the training session Introduction of facilitators and participants	
	1	Background of Neonatal Tetanus Disease, its prevention, definition, etc.	Understand the disease
	2	Neonatal tetanus incidence survey: Purpose, clusters selected, cluster size, etc.	Understand the basics of the survey
	3	Starting the Survey: • Introduction to the Village Chief • The starting-point in the cluster: first and subsequent HH • Eligible HH respondents	How to start and move around in the villages
	4	The use of the forms: • form 1: demographics • form 2: live-births	Asking the right questions: focus initially on past pregnancy, how to identify neonatal deaths
	5	Role-play and/or game: • finding the starting-point in the cluster • completing forms	Use Game provided
Day 2	6	Field exercise (in nearby village)	
	7	Review of the training and field exercise	
	8	Logistics and assignment of teams and supervisors	Understand where to go, who to contact when, etc.
	9	Last questions and answers	
		Teams covering distant clusters should leave the same day as the training	

ANNEX 6.
EXAMPLES OF FORMS & SURVEYOR INSTRUCTIONS[2]

1. Find the first household (HH) in the village/ward as explained in the training. Introduce yourself and collect the survey information following the script below.

2. Proceed to the nearest household and repeat; continue *until you have identified the total Live Births (LBs) to be surveyed in the cluster.*

3. If the village you are visiting has insufficient live births **after you have visited all the HHs**, continue to the next village. The "next" village is the one nearest to the first.

Remember: the purpose of this survey is to find the neonatal deaths from among all babies who were born in the eligible period. Do not look for living children – look for pregnancies to find ALL live births and ALL neonatal deaths. Make sure to ask specifically if any girls were born, especially in cultures where high emphasis is placed on male children.

2 Note: The forms provided at the end of this Annex, and the instructions for their use, should be modified to fit the needs of the specific country and survey. The forms should be translated into the local language. Please note that the instructions are meant for training and as references only - they are too exhaustive to be used during the survey itself.

Completing Form 1

In each HH, ask all of the following questions and mark the answers on the relevant forms (only take information from adults). First, introduce yourself:

I am [NAME] and I work at the [ORGANIZATION NAME] in [CITY]. We are conducting a survey to find out how many children in this area still die because of neonatal tetanus [USE LOCAL NAME IF IT EXISTS] so that the government can have a better idea whether any specific action is needed.

We would like to ask some questions to as many women who have been pregnant recently as possible. Are you willing to talk with us? If the answer is yes, proceed.

How many people live in this household? Write the number on *Form 1* (one line per household).

Are there any women living in this household whose age is between 15 and 49 years old (even if they are not here right now and depending on the age range used by the country for women of reproductive age)? Ask specifically if there is more than 1 woman.

- **If No,** mark 0 for "#Resident women" and all the other columns; thank the person for his/her time and explain that they are not the target group for the survey. Mark the HH number from Form 1 on the door with chalk; go to the next HH.
- **If Yes,** mark the number in the column for "#Resident women" and ask:

Were any women pregnant in the past 2 years?

- **If No,** mark 0 for #Resident women pregnant during last 2 yrs" and the other columns; thank the person; mark the HH number on the door; go to the next HH.
- **If Yes,** mark the number in the column for "#Resident women pregnant", and ask:

May I speak to her/them? Interview each woman who was pregnant in the past 2 years (see next page). If unavailable, obtain the information from another adult HH member.

- If a woman normally is a resident in the HH, but is absent temporarily, include her in the survey
- Resident women who have gone somewhere else to deliver (e.g., parent's house) should be included in the survey
- Women who normally live elsewhere, but are visiting, should NOT be included in the survey. (Visitors are those whose residence has been elsewhere in the past year, and whose presence is temporary)

Were you pregnant in the past 2 years? (Explain that you are asking about *any pregnancy*, regardless of the outcome or if the child is still alive).

- **If No,** revise count in Form 1 if necessary; thank her for her time; mark the HH number on the door; go to the next HH

- **If Yes,** ask: What was the outcome of the pregnancy?
  There are 4 choices for pregnancy outcome on Form 1: still pregnant, Live Birth, or Abortion/Miscarriage and Stillbirth.
  - If the woman is still pregnant, ask if she has been pregnant earlier as well during the last 2 years. Fill the forms and thank her for her time. Continue with other women in the HH who were pregnant during the last 2 years.
  - **In the case of a reported stillbirth, it is very important to make sure that the baby was not alive at birth** and then died shortly thereafter. First let the mother know that you understand how painful her loss must be and extend your sympathy. Then try to gently confirm that there were no signs of life when the baby was born (no spontaneous movement, breathing, or crying) to rule out the possibility of an early neonatal death.
  - **If there was a live birth,** ask:

Was the child born between __/__/__ and __/__/__? (inclusive). Ask the child's immunization card to verify the date of birth.
(Note that this includes children who have since passed away, not just children still alive).

- **If No**, thank her for her time; mark the HH number on the door; go to the next HH
- **If Yes,** mark the number of eligible live births on *Form 1*, and complete one line for each on Form 2

Note: before leaving a HH, try to make sure a neonatal death was not missed, ask if the household ever lost a child, and if yes, if that child was born during the eligible period.

- **Be sensitive to the fact that child deaths cause the family great pain and grief. Always be respectful, sympathetic and gentle when probing for sensitive information.**
- **Before leaving a HH with a live birth born in the Eligible Period, make sure you filled in all the necessary information in Form 2.**
- **No index entries found. If there was a NEONATAL DEATH, did you call your supervisor?**
- **When the HH is completed, mark the HH number on the door before proceeding.**

Completing Form 2

Form 2 is for all live births in the Eligible Period (__/__/__ to __/__/__, inclusive).

Each line should be completed for every eligible Live Birth.

Note the HH number (from Form 1) *in the first column, then ask the following questions:*

What is your (the mother's) name? Alternatively, ask for the child's name or father's name.

When was the child born? Write the date as day-month-year. Double-check that the date is within the Eligible Period.

Was it a boy or a girl? Write "M" if it was a boy, "F" if it was girl.

Did the child die?

- **If No,** mark "N" in the column "Died".
  If you are talking with one of the first few women in your cluster, (usually 3 or 4, with the number being determined by the total number of clusters to be surveyed in a single sample survey design or the total number of clusters for the first sample in a double sample design), continue with the questions about delivery and TT status (see below)

  Otherwise, thank the person for her time and continue with any other mothers of eligible live births in the household. When finished with all live births, mark the HH number on the door; go to the next HH.

- **If Yes,** (the baby died), first read the following text, or explain in your own words:
  I am sorry that your child has passed away. We understand that this must cause you great grief. However, we would like to ask you some more questions about the circumstances under which your child died.

Did the baby die when he/she was 28 days old or less? (in first 28 days of life)

- **If No**, double-check by asking how old the child was at death. Obtaining correct information *is very important.* If not 28 days or less, write "N" in the column "died when < 28 days old?".
  For the first few mothers as agreed continue with the questions about delivery and TT status. For the other mothers, thank the person for her time. Mark the HH number (Form 1) in chalk on the door and go to the next HH.

- **If Yes,** mark "Y" in the column "died when less than 29 days old", and **immediately call your supervisor** to let them know you have identified a neonatal death.

  Explain to the mother that a doctor will come to ask her some additional questions to try to understand what caused the baby's death.

  For the first few mothers as may be determined, continue below

The following questions are for the first agreed number of mothers per cluster only:

Did you deliver in a Health Facility? Mark "Y" or "N".

If you did not deliver in a health facility, was there a medically trained person with you to assist with the delivery? (includes doctors, nurses, midwifes; but excludes TBAs)

Mark "Y" if there was a medically trained attendant. (Note: for mothers who delivered in a health facility, this question is automatically "Y".)

Do you have an immunization card (mother's card)?

- If she can show her card:
  - mark "Y" in the column "Mothers Imm Card Available", and
  - write the dates of TT doses listed on the card in the relevant columns.
- If she cannot show her card or says she does not have a card:
  - mark "N" in the column "Mother's Imm Card Available";

Have you received any doses of Tetanus Vaccine (a vaccine given in the upper arm) during a pregnancy, during a vaccination campaign, after an accident, or on any other occasion? If yes, how many times did you receive a dose (total during your life)?

- Mark a "Y" in the first column under TT1 if one dose was received; mark "Y" in the first column under TT1 and TT2 if 2 doses were received; mark "Y" under TT1, TT2, and TT3 if 3 doses were received, etc.
- Write the date in the second column of the concerned dose when the immunization card is available. If no card is available and information is based on history only, mark "-" in the second column of the concerned dose.
- When there is a card but no date is mentioned, only "V", mark "V" in the second column of the concerned dose.

When finished, quickly check that you have filled in all the necessary information, thank the mother (or other respondent) for her time; mark the HH number (Form 1) on the door; go to the next HH.

Form 1: Household Tally - *use one line per household*

Cluster No: _____ **Village:** _____ **District**

Location 1st HH: _____ **Eligibility Period for Live Births: d/m/y to d/m/y**

Interviewer's name(s) _____ **Date:** _____

HH #	# residents	# Women (age 13-49)	# Women pregnant (last 2 years)	Outcomes of pregnancies (last 2 years)				# Eligible Live Births (born between d/m/y and d/m/y?) → Form 2	Ever loose a child? If yes, born d/m/y and d/m/y?
				Still Pregnant	Live Births	Miscarriage, Abortion	Stillbirth		
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
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24									
25									
26									
27									
28									
29									
30									
31									
32									
33									
34									
35									
Subtotal									

Form 2 - Live Births, Conditions at Birth and Mother s' TT Status

Eligibility Period for Live Births: _ _/_ _/_ _ to _ _/_ _/_ _

Cluster No: _____ **Interviewer's name:** _____ (_____ Live Births per Cluster)

Supervisor's name: _____ **Supervisor's phone number:** _____

Part A. Identifier			Part B. Baby's information				Part C. Mother's information related to this Live Birth													
										TT1		TT2		TT3		TT4		TT5	
Serial No	# HH	Mother's or Father's Name	Date of Birth	Sex	Died?	Died when ≤28 days old? If Y: call supervisor / MO	Birth in Health Facility	Birth attended by MD, Nurse, Midwife? (exclude TBA)	Mother's Imm Card Available?	received (card or hist)?	If card, date:	rec'd?	date	rec'd?	date	rec'd?	date	rec'd?	date	rec'd?	date
			dd/mm/yy	M / F	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N / U	(mm/yy)	Y / N / U	(mm/yy)	Y / N / U	(mm/yy)	Y / N / U	(mm/yy)	Y / N / U	(mm/yy)	Y / N / U	(mm/yy)
1																				
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7																				
8																				
9																				
10																				
11																				
12																				
13																				
14																				
15																				
Totals - to be tabulated by the Field Supervisor			**# LB:**	Males # M:	Deaths # Y:	NDs # Y:	(HF) # Y:	(Skilled) # Y:	(Card) # Y:	TT1 # Y:	with date #:	TT2 # Y:	with date #:	TT3 # Y:	with date #:	TT4 # Y:	with date #:	TT5 # Y:	with date #:		

ANNEX 7.
EXAMPLE OF FORM 3 AND INSTRUCTIONS

Form 3 - Neonatal Death Investigation Form – to be completed by a Medical Officer

This form needs to be completed for all eligible children who died in the neonatal period, that is, in the first 28 days of life (between birth and the end of the 28th day).

It should NOT be completed for children who are still alive, who were stillborn, or who died on or after their 29th day of life.

If you (the investigating MO) conclude that the cause of death was NT, one of the survey monitors or coordinators must be contacted immediately. In case of any doubt, consult a monitor!

NT is a clinical diagnosis; there is no confirmatory laboratory test.

The NT case definition is:

A neonate who feeds and cries normally for at least the first 2 days of life,

and, between 3 and 28 days of life

Stops sucking normally

and

Develops stiffness/rigidity and/or spasms

For a diagnosis of NT to be made, the criteria in the case definition must be met.

Additional information that supports the diagnosis of NT:

- Hypersensitivity to touch, sound and/or light, setting off spasms
- Presence of risk factors associated with NT such as lack of maternal TT immunization and/or unhygienic delivery and/or umbilical cord care

NT can be ruled out in cases where death occurs in the first 2 days of life.

Before beginning your interview with the mother (or available family member), Introduce yourself, express empathy with her grief and willingness to answer additional questions.

If the mother (or family member) agrees to the interview:

First complete the initial sections of Form 3 covering the child's identity and information about the mother's TT vaccination history, antenatal care, and delivery condition.

Then ask the mother to provide the history of the child's birth, illness and death in her own words. This narrative history should be recorded on the blank box of Form 3. The specific questions on the form in the section about the child's history of illness and death should be asked afterwards. The questions should NOT be read to the mother; leading questions should be avoided.

In the final section of the form, record the respondent's understanding of the child's cause of death, followed by your own impression ;then provide your judgement as to whether the child died of NT or not.

If there is uncertainty about whether a death was caused by NT, and the child was taken to a health facility or private medical office, the facility or consulting medical provider must be contacted to obtain the diagnosis given at the time of assessment.

When finished, ask again if there are any questions. Thank the mother for her willingness to participate.

Form 3: Neonatal death investigation form

(To be completed by the Medical Officer)

District: _____

Cluster No: _____ **Household no (Forms 1&2):** _____ **Medical Officer's name:** _____

Case identification & household location

Name of respondent: _____ Relationship to beby: _____
Address of respondent: _____ Village/Ward: _____
Baby's date of birth: ___ / ___ / ___ Baby's date of death: ___ / ___ / ___
Age at death in days: _____ Sex of baby: M ☐ F ☐

Mother's immunization status

Did the mother have an immunization card (circle)? Yes ☐ No ☐
Immunization history by: card ☐ memory ☐ both ☐ unknown ☐
How many TT doses did the mother receive **in the last pregnancy**: _____
How many TT doses has the mother received **before the last pregnancy**: _____ (on any occasion)
Dates (**all TT doses**): ___ / ___ / ___ ___ / ___ / ___ ___ / ___ / ___ ___ / ___ / ___ ___ / ___ / ___ ___ / ___ / ___ ___ / ___ / ___

Mother's antenatal car history

How many antenatal care visits were made during this pregnancy? _____

Delivery practices

Where was the baby delivered? Health facility ☐ Home ☐ Unknow ☐ Other: ☐ _____
Who assisted with the delivery? Doctor ☐ Nurse ☐ Midwife ☐ TBA ☐ Relative ☐
Nobody ☐ Unknow ☐ Other: ☐ _____
On whate surface was the baby delivered? _____ Clean? Yes ☐ No ☐
What was used to cut the cord? _____ Clean? Yes ☐ No ☐
Was any substance put on the cord stump? Yes ☐ No ☐
If yes, specify _____

Baby's signs/symptoms: ask respondent to describe the symptoms and the history (use open-ended questions)

At birth, did the baby seem normal? Yes ☐ No ☐ Unknown ☐
At birth, did the baby suck normally? Yes ☐ No ☐ Unknown ☐
How old (in days) was the baby when signs of illness began? ___ days Unknown ☐
Did the baby stop suckling? Yes ☐ No ☐ Unknown ☐ If yes, how many days after birth? _____
Did the baby have spasms, or stiffness? Yes ☐ No ☐ Unknown ☐
Did the baby have the following signs of illness:
Spasm when stimulated by touch, sound or light? Yes ☐ No ☐ Unknown ☐
Become rigid or stiff as illness progressed? Yes ☐ No ☐ Unknown ☐
Developed "pursed lips" and/or clenched fists or feet? Yes ☐ No ☐ Unknown ☐

Treatment & outcome

Was the sick baby taken to a health facility? Yes ☐ No ☐ Unknown ☐
If yes, record name of health facility: _____
(Visit the health facility if there is doubt whether the case died of neonatal tetanus)

Health Facility Confirmation - if symtoms suggest tetanus - call monitor

Conducted? Yes ☐ No ☐ If no, why not? _____
Facility Name: _____ Date Visited: ___ / ___ / ___ (dd/mm/yy)
Location: _____ Attending doctor's name: _____
Baby's medical record available: Yes ☐ No ☐
Admitting date: ___ / ___ / ___ (dd/mm/yy)_____ Admitting diagnosis: _____
Discharge date: ___ / ___ / ___ (dd/mm/yy) _____ Discharge diagnosis: _____
Comments:

Conclusion

What does the respondent say was the cause of the baby's death? _____
Your impression of cause of death? _____
Based on the information you received, was this a case of neonatal tetanus? Yes ☐ No ☐ Unknown ☐
Comments:

Signature & Date: _____ (Medical Officer and/or other medical personnel investigating the case)

ANNEX 8.
FORM 4 - INFORMED CONSENT

The surveyor instructions as outlined in annex 8 and 9 contain a series of questions to obtain informed consent from the respondents. In case it is decided to change these surveyor instructions, the informed consent form below can be used instead.

Informed Consent Form for Neonatal Tetanus Mortality Surveys

[INSTITUTIONAL LETTER HEAD]

[Name of Principle Investigator]
[Name of Organization]
[Name of Sponsor]

Information Sheet for the Group of Individuals Participating in the Research "Assessment of Neonatal Tetanus Mortality" in [COUNTRY]

[PART 1: To be read to the person opening the door of the house: Introduce yourself and what you are doing]

I am [NAME] *and I work at the* [ORGANIZATION'S NAME] *in* [CITY NAME]*. We are conducting a survey to find out how many children in this area still die because of neonatal tetanus* [USE LOCAL NAME IF IT EXISTS] *so that the government can have a better idea whether any specific action is needed. For this, we would like to ask some questions to as many women as possible who have been pregnant recently.*

How many people live in this household? Are there any women in this household aged between 15 and 49 years old? If yes, was any of them pregnant between [DATE] *and* [DATE]*?* [Record responses on form1] *If so, may we ask them if they would they be prepared to take part in this survey, which will consist of a number of questions only?*

[If yes, continue below. If no, explain that they are not the target group for the survey and thank the person for their time. Move to the next house*].*

[PART 2: To be read to the women who was pregnant between [DATE] and [DATE]]

[Introduce yourself and what you are doing]

I am [NAME] *and I work at the* [ORGANIZATION'S NAME] *in* [CITY NAME]*. We are conducting a survey to find out how many children in this area still die because of neonatal tetanus* [USE

LOCAL NAME IF IT EXISTS]*, so that the government can have a better idea whether any specific action is needed.*

This study involves asking some questions in two parts.

In the first part of the study we will ask you 4 or 5 questions related to your pregnancy and its outcome covering the period of up to one month after delivery. This will not take more than 10 minutes. After the first part of the study, if it is necessary to ask you more questions,, we will give you more information about the second part of the study and take your permission again to continue.

This household was selected by chance. You can refuse the interview, stop it at any time, or ask questions, without any negative effect. By participating, you personally will not gain any direct benefit. The information you give will be kept confidential to the group conducting the survey only.

The person accompanying me [Give name of the person] *will sign on your behalf to certify that you have agreed to take part in this study, after having been provided with the above information.*

Do you have any questions now? -- If later you have more questions, you can contact [name and address – add telephone number and e-mail if available]

Do you agree to take part in the study?

Is it OK to continue with the questions now?

[Ask the questions related to the survey, including the questions on TT immunization, and complete the form 2 as explained in the training]

[If the respondent's child is still alive, complete the tables and at the end thank the person for her collaboration]

[If the respondent's child (born between the dates stated above) has died, proceed to part 3 before asking questions about the circumstances of the child's deaths]

[PART 3: To be read only in a situation where the child has passed away]

I am sorry to hear that your child has passed away. We understand that this must cause you a lot of grief. However, we would like to ask you some more questions about the circumstances under which your child died. Some of these questions may cause you grief and pain. As said above, you are under no obligation to continue and you can stop this interview at any time without any loss of benefits that you may be getting from your health centre. Your responses will not be divulged to anyone, except [NAME AS APPLICABLE] *and the form on which we take down your answers will not have your name on it, only a code that will be known only to the researchers.*

We would like to do this interview in a place that guarantees privacy. No one else needs to be present with you at this interview. Do you have any questions now?

If you have any questions in the future, you may contact the person whose name is given above.

Is it OK that we continue?

[If yes, complete the question on whether the child died within 29 days, and if yes, also the neonatal death investigation form (form3)]

[At the end, thank the person for her cooperation]

ANNEX 9.

STATISTICAL SUPPLEMENT TO THE GUIDE FOR VALIDATION OF MATERNAL AND NEONATAL TETANUS ELIMINATION[3]

By Lauren Hund and Marcello Pagano[4]

INTRODUCTION

For a country to declare maternal and neonatal tetanus elimination (MNTE), a lot quality assurance cluster sampling survey is conducted to confirm whether the nation achieved that goal. In this supplement to the survey guide, we discuss technical issues in the design of the MNTE LQA-CS survey (hereafter referred to as the 'MNTE survey'). In Section 1, we describe issues with identifying the target population, or highest risk district, for the survey. In Section 2, we introduce the lot quality assurance sampling (LQAS) methodology and discuss extensions of this methodology that are used in surveys to validate MNTE, including cluster sampling, finite population adjustments, and double sampling designs. In Section 3, we discuss the sensitivity of the survey instrument to detect neonatal tetanus (NT) cases and the implications of measuring a marker for NT incidence, namely the NT mortality rate (NTMR). In Section 4, we describe the statistical calculations used to construct the survey design and the metrics used to evaluate the properties of the design. Finally, in Section 5, we present a recommended survey design for validation of MNTE.

9.1 SELECTION OF DISTRICTS FOR THE SURVEY

Surveys to validate MNTE are conducted at district-level (third administrative level) in keeping with the definition of MNT elimination: less than 1 NT case per 1000 live births in every district. As discussed in the body of this manual, the first step in the design of the survey is deciding which district in a country is likely to have the highest NT incidence. This district will be the target population for the survey.

The implications of this definition are important to consider when designing an MNTE survey. NT rates less than 1 in 1000 live births must be achieved in *every* district. The survey is only conducted in the highest-risk district, under the logic that if the rates of NT are less than 1 in 1000 in that district, then the rates are also below this threshold in all the lower risk districts. This reliance on a prior ranking of NT risk among districts should

3 WHO. 2014. **Validation of Maternal and Neonatal Tetanus Elimination** including a guide to the use of Lot Quality Assurance – Cluster Sample Surveys to assess neonatal tetanus mortality. Updated Field Version.

4 Both authors are in the Biostatistics Department of the Harvard University School of Public Health, Boston MA, USA

be emphasized since the validity of subsequently declaring a country as having achieved elimination depends on this ranking. If it is not possible to choose between highest risk districts, then all high-risk districts must be surveyed to avoid running the risk of failing to select the district that has not achieved elimination.

The smaller the district to be surveyed, the more precise we can be in our classification of elimination within that district because, in small districts, we sample a large fraction of all live births. However, if a district population is too small, it may not be logistically feasible to survey only that district due to an insufficient number of live births. In such a situation, the target population can be redefined by combining multiple small high-risk districts into one survey. However, by combining districts, *we are changing the definition of elimination,* which should be clearly stated and approved by the assessment team before the survey is conducted. The revised definition of elimination for the country is now "an average NT incidence rate < 1 in 1000 live births among the worst performing districts in the country."

It is important not to overlook the implications of pooling information across multiple districts and changing the definition of elimination. For instance, consider a situation in which we identify three high risk districts with a low number of live births. We decide to conduct one survey, sampling from all three districts combined. Even if one of the three districts has an NT incidence rate greater than 1 in 1000 live births (definition of MNTE not met), the country will be declared as having achieved elimination if the *average* incidence rate across the three high risk districts is less than 1 in 1000, which is possible.

9.2 INTRODUCTION TO THE LQA-CS SURVEY METHODOLOGY

The LQA-CS survey method is appropriate for selected populations in the final stage of MNT elimination when there is evidence suggesting that NT incidence has been reduced to less than 1 case/1000 live births and only occurs sporadically (not in clusters).[a] The method enables a binary decision: has MNT elimination occurred, yes or no? No further requirement is made to also provide an actual estimate of the NTMR. In contrast, conventional surveys designed to estimate the NTMR with any degree of confidence require very large sample sizes - tens of thousands of live births - due to the extremely low incidence of NT in the final stages of MNT elimination.[b] The LQA-CS method requires relatively smaller sample sizes than the traditional estimation surveys,[c] making the survey feasible and affordable in countries ready to demonstrate MNT elimination.

In an LQA-CS MNTE survey, the number of NT deaths detected during the survey is compared to a pre-determined maximum *acceptance number* of NT deaths that defines whether the district "passes" (elimination achieved) or "fails" (elimination not achieved). The acceptance number is calculated to ensure that there is a high probability that a district with a high NT incidence rate during the 12-month interval covered by the survey does not "pass", and that districts with truly low NT rates do not "fail".

While NTMR point estimates and confidence intervals can be calculated using LQA-CS data, this is not recommended because the estimates have large variances (resulting in not very informative, really wide confidence intervals). If a survey is stopped before all clusters are completed (in a double sampling survey, see below), the estimate is susceptible to selection bias and must not be used. Instead of calculating NTMR point estimates and confidence intervals, the number of sampled live births and observed NT deaths should be reported. Lot quality assurance sampling (LQAS) survey designs in public health have been described extensively in the literature [*e.g.*,Valadez[c] and Robertson and Valadez[d]]. We briefly describe the LQAS methodology to aid in the interpretation of the final survey design.

9.2.1 Review of LQAS methodology

To declare MNTE in a district, we need to decide whether the NTMR during the 12-month interval covered by the survey is sufficiently low. We denote the district-level NTMR as p. In the district, we sample n live births, and let X denote the number of NT deaths.

Assuming the population size/annual number of live births in a district is large (> 50,000), we can model X using a binomial distribution, specifically X ~ Binomial (n,p). For some number d (the acceptance number), if X > d, we conclude that elimination has not occurred; if X ≤ d, we conclude elimination has been achieved. In choosing a sampling design for an LQAS survey, the goal is to select a sample size n and corresponding acceptance number d such that we run as small a risk as possible of misclassifying districts as having achieved or not achieved elimination. The lot quality assurance sampling (LQAS) survey design is determined by the following two equations, which control the error of the classification procedure:

$$P(X \leq d \mid n, p_u) \leq \alpha$$

$$P(X > d \mid n, p_l) \leq \beta$$

For a given choice of n and d, α is the probability that we classify a district as having achieved elimination when the NTMR is greater than or equal to p_u; and β is the probability that we classify a district as not having achieved elimination when the NTMR is less than or equal to p_l. To select an appropriate sample size n and decision rule d, we first need to decide what the appropriate choices of p_l, p_u, α, and β are.

As an example, if we choose α = 0.1 and β = 0.1, we then find a sample size n and acceptance number d such that we can make the following statement about our survey:

"In an area with a true NTMR equal to 0.0021 (p_u) or more, if we repeat the MNTE elimination survey a very large number of times, we would incorrectly conclude that neonatal tetanus has been eliminated at most 10% (α) of the time. In an area with a true NTMR equal to 0.00035 (p_l) or less, if we repeat the MNTE survey a very large number of

times, we would incorrectly conclude that elimination has not occurred at most 10% (β) of the time."

If a district has a true NTMR between p_l and p_u, we say that the NTMR lies in the "grey region." We do not restrict the classification errors within the grey region. Within this region, the risk of misclassification is higher than the smaller of α and β. To fully understand classification properties for districts with true NTMR in the grey region, we must examine the operating characteristic curve or the risk curve (see Section 4 below).

For MNTE surveys, we have selected p_l and p_u such that some districts with true NTMRs in the grey region may not have technically met the definition of elimination, but have achieved low enough NTMRs that it is not a serious error to declare elimination if that mistake were to occur. Validation surveys are only conducted when we have some confidence that elimination has been achieved; ideally, most survey districts will not have true NTMRs that lie within the grey region. However, it is important to understand the inherent risk in the classification procedure.

In an LQAS survey, decreasing the width of the grey region (narrowing the distance between p_l and p_u) results in more precise classifications. However, the size of the grey region is directly related to the sample size of the survey. When searching for a rare event in the population, required sample sizes are generally large, and we must balance precision against feasibility in our selection of p_l and p_u.

Table 1 below illustrates the impact of decreasing the grey region, lowering p_u when $p_l = 0.00035$, $\alpha = 0.1$ and $\beta = 0.1$ (as above). To convert the NTMR thresholds in Table 1 back to NT incidence rates, see the discussion about sensitivity and specificity in Section 3. Assuming sensitivity is 70% and specificity is 100%, these upper thresholds for NTMR correspond to NT incidence rates of 3, 2, 1.5, and 1 cases/1000 live births; the lower NTMR threshold corresponds to an incidence rate of 0.5 cases/1000 live births.

Table 1: Shows the impact of the width of the grey region on the sample size. Single and double sampling plans are presented for large populations (> 50,000 live births per year) and a population with 5,000 live births per year.

	>50,000 live births						5,000 live births					
	Single Sampling		Double Sampling				Single Sampling		Double Sampling			
p_u	n	d	n_1	d_1	n_2	d	n	d	n_1	d_1	n_2	d
2.1	2,540	2	1,430	0	1,310	2	1,560	1	1,200	0	430	1
1.4	4,780	3	2,140	0	4,070	4	2,270	1	1,740	0	650	1
1.05	8,840	5	2,860	0	8,000	6	2,560	1	1,970	0	720	1
0.7	28,760	14	4,280	0	29,870	16	3,400	1	2,640	0	920	1

9.2.2 Finite population size effect

When the number of live births in a district is not sufficiently large (<50,000 live births in the population), we model X using the hypergeometric distribution, X ~ Hypergeometric(n, N, m), where n once again denotes the number of live births sampled; N is the total number of live births; and m = Np is the number of NT deaths in the district over the 12-month survey period for a given NTMR p. When N is large, the binomial and hypergeometric distributions are equivalent; the sample size and acceptance number for the survey will be identical regardless of which distribution is used for the calculations.

To design an LQAS survey, we calculate the parameter m using p_u and p_l. *The consequences of searching for a rare event in a finite population on the survey design are not trivial.* The NTMR p can only take on a finite number of values, since m is an integer by definition (m being the number of NT deaths). For example, consider a population of 2,500 live births. The NTMR can only take on certain values in the population: p = 0 with 0 NT deaths; p = 0.4/1000 live births with 1 NT death; p = 0.8/1000 live births with 2 NT deaths; p = 1.2/1000 live births with 3 NT deaths; and so on.

Thus, in practice, the grey region in an LQAS survey usually is not truly from p_l to p_u, but is wider because p can only take on a finite number of values. For instance, in the example above with a population size of 2,000, if we select p_l = 0.0005 and p_u = 0.002, then the true grey region spans from 0.0004 to 0.002, because p cannot take on the value 0.0005.

The widening of the grey region impacts smaller population sizes more than larger ones where p can take on a wider range of values. It is important to consider the appropriateness of the grey region when designing a survey with finite population sizes. For instance, if only 500 live births occur in a district, designing an elimination survey based on p_l and p_u is difficult. Elimination has only been achieved if 0 NT deaths occur in the district. The narrowest possible grey region is from 0 to 0.002, as p can only take on the values 0,

0.002, 0.004, etc. It is more intuitive and more appropriate to discuss absolute numbers of events, instead of focusing solely on rates, when dealing with very rare events in a finite population.

Lastly, because tetanus cannot be eradicated, NT cases can occur sporadically even when MNTE has been achieved. The size of the target population should be sufficiently large to allow for an occasional random case without triggering the conclusion that elimination has not been achieved. For example, with a population of 1,000 and an NT rate of 0.9/1,000, the probability of observing one or more NT cases is better than 59%. Therefore, the total number of eligible live births in a district should exceed 3,000 to conduct a meaningful MNTE survey.

9.2.3 Cluster Surveys

Standard LQAS surveys usually select a simple random sample from the target population. Simple random sampling requires an enumeration of the entire population in the district, sampling from this list, and then locating the sampled individuals. Because it is impractical to implement simple random sampling for MNTE surveys, the logistically easier cluster sampling method is used instead.

The cluster sampling method used for MNTE surveys, "probability proportional to size" (PPS), is the same method used for standard 30 x 7 cluster surveys to measure immunization coverage.[e] With PPS sampling, the probability of selecting a sampling unit (e.g., village, census tract, etc.) is proportional to the size of its population. Larger sampling units have a larger probability of being selected and each cluster consists of the same number of sampled individuals (live births for MNTE surveys). Using this design, each individual has the same probability of being sampled, yielding a probability sample that is random and representative.[f,g] Note that the total number of clusters and households to visit within each cluster are different in the MNTE survey than in a 30 x 7 cluster survey.

Usually, cluster sampling increases the amount of variability in a survey because outcomes are more likely to be similar for individuals in the same cluster than for individuals in different clusters. To obtain a representative snapshot of the population, one needs to sample from many clusters. This within-cluster similarity is often quantified using the intracluster correlation coefficient (ICC or ρ). The relative size of the variability in the survey estimators is measured by the design effect (DEFF), defined as the ratio of the variance of the survey using cluster sampling to the variance using simple random sampling. DEFFs are usually greater than one.

To obtain the same level of precision with a cluster sample as one would have with a simple random sample, one needs to sample n x DEFF individuals for the survey (often referred to as the effective sample size). When the number of clusters is large, and the population

size within each cluster is large and approximately equal across clusters, DEFF ≈ 1+ (c-1) ρ, where c is the number of individuals sampled in each cluster.

When ρ is small relative to m, such that DEFF ≈ 1, we can treat the cluster sample like a simple random sample. Historically, low design effects have been observed in surveys estimating NTMR.[h] Additionally, MNTE surveys are only conducted when there is sufficient evidence that districts have low NT rates *without any clustering of cases*, adding credibility to the operative assumption that the DEFF approximates 1[a]. Lastly, in 41 MNTE surveys conducted from 2000–2011, only 42 neonatal deaths attributable to tetanus were identified in a total of 4,571 clusters and no cluster had more than one NT death. Thus, based on the strong evidence that clustering effects are negligible in MNTE surveys, a cluster survey is conducted but the data is analyzed by treating it as a simple random sample without adjustment.

9.2.4 Double sampling

A *double sample* procedure divides the total sample into two parts; these parts are then surveyed sequentially. Whether the second sample is carried out is conditional on the results of the first sample. This sampling procedure is analogous to interim monitoring in clinical trials, for example. For additional sequential LQAS designs, see the examples described in Myatt and Bennett[i] and Olives[j].

The double sampling plan has the advantage of allowing elimination to be declared from the results of the first sample if the number of NT deaths detected is very low (e.g. 0). The second sample is necessary if the number of NT deaths in the first sample is not low enough to declare elimination and not high enough to confirm failure to achieve elimination (does not exceed the acceptance number). This design has the potential to save on the total sample size required to reach a decision.

To construct a double sampling survey plan, we again specify thresholds p_l, p_u, α, and β. We also need to specify an additional parameter, α_1, which is the probability of declaring elimination after the first sample given p_u. This additional parameter does not affect the overall α level of the survey design, but instead serves as a guide to select the sample size and decision rule for the first sample. Based on these parameters, we can find the minimum sample sizes for the first and second samples, n_1 and n_2, and the corresponding acceptance numbers d_1 and d_2, to meet our survey design specifications.

The proposed double and single sampling plans are designed using identical overall survey parameters p_l, p_u, α, and β. Therefore, as discussed in the main MNTE survey guide (Section_2.2.2), to decide between a single and double sampling plan, we evaluate cost-effectiveness and feasibility and are not concerned about the statistical precision of double versus single sampling (as they have the same precision, by design). The main reason that

one would use a double sampling design is to reduce the amount of money/time spent conducting the survey.

Regardless of whether a single or double sampling plan is used, 'failure to achieve elimination' can be declared at any point in the survey if the number of detected NT deaths surpasses the acceptance number. However, to collect accurate, representative data on NT risk factors (TT coverage, proportion of deliveries conducted in health facilities and assisted by medically trained birth attendants, and use of traditional substances on the umbilical stump), data collection from all planned clusters should be completed for a single sampling survey or the first sample in a double sampling survey, even if the number of NT deaths detected exceeds the acceptance number. The second sample in a double sampling survey can be stopped early if the acceptance number has been exceeded because sufficient representative data was collected in the first sample.

Double sampling is only more cost-effective if we expect that the district has achieved elimination with a high level of confidence. If the second sample is required, the total sample size required for a double sampling survey is always greater than the sample size for a single sampling survey. That is because we perform two data analyses during the survey period and thus have 2 different opportunities to declare elimination. This is often referred to as "multiple comparisons"; we must adjust the classification errors to account for the fact that we look at the data twice. To obtain the desired classification errors α and β, we must sample more individuals in the double sampling plan to account for the inflated classification errors caused by looking at the data twice. As a general rule, we want to minimize the probability that we will need the second part of the sampling.

When choosing between a single versus double sampling plan, the deciding factor should be: "Is the cost/time savings that are potentially associated with double sampling worth the additional logistics that go into planning a double sampling survey and the *potential* extra cost of the second part?" If we are uncertain about whether or not elimination has been achieved, then we should choose a single sampling plan to save both time and money. In addition, logistical constraints such as lack of communication infrastructure and/or difficult terrain and a highly dispersed population often make a double sampling survey infeasible.

9.3 SENSITIVITY, SPECIFICITY AND SELECTION BIAS IN MORTALITY SURVEYS

The definition of NT elimination is < 1 case of NT per 1000 live births. *However, it is operationally easier to monitor NT deaths accurately, rather than to try to detect all cases of NT* (deaths and survivors). Historically, NT mortality has been very high in areas where NT most commonly occurs (>80%), making NT mortality a suitable marker for what we ideally

would like to measure, i.e., NT incidence. Nonetheless, we must consider the implications of measurement error produced by measuring a proxy of the outcome of interest.

We can rephrase this issue in terms of the sensitivity and specificity of the survey instrument/protocol. In an MNTE survey, sensitivity is the probability that an NT case is detected given that the NT case is included in the sample. Alternatively, we can state the sensitivity as the proportion of NT deaths in the sample that are detected by the survey instrument. An NT *case* can fail to be detected in several ways:

1. the case is not fatal,

2. the case is fatal, but NT is not identified as the cause of death, or

3. a neonatal death caused by NT is not detected.

NT deaths are diagnosed using the verbal autopsy method for all identified neonatal deaths.[k] If we can assume that all deaths due to NT are diagnosed correctly, then the sensitivity for our survey is equal to the case fatality rate (CFR; %deaths) among cases of NT in the population. If the NT CFR is low, then sensitivity will be further decreased and we will need to adjust the survey parameters accordingly. Low sensitivity can result in declaring that elimination has been achieved when it truly has not.

Selection bias and recall bias are also common issues in retrospective neonatal mortality surveys.[l,m,n,o] Omission of live births and subsequent deaths for children who are not living at the time of the interview is a common source of non-sampling error in surveys of live births; children who die in early infancy are the most commonly omitted births. Additionally, there is a tendency on the part of local guides assisting with surveys to lead to households with live young children; houses with potential infant deaths are consequently bypassed. Some surveys have found that post-neonatal infant mortalities may be incorrectly displaced into the neonatal period when there is pressure to find neonatal deaths. Poor quality in the reporting of age at death also can lead to underreporting of infant deaths. Lastly, in some surveys, mothers with children were more likely to be at home at the time of the survey, as opposed to women without children, increasing the potential to miss some live births and neonatal deaths.[p] Selection bias could result in declaring that elimination has occurred when it has not.

To obtain accurate survey results, it is important to recognize the potential for selection and recall bias to result in an underestimation of NT mortality, and therefore of NT incidence. We can adjust the assumed sensitivity of the survey instrument downward to account for underestimation caused by these biases.

Specificity is the probability that a live birth included in the survey is correctly classified as not being an NT case. The specificity of the survey is a function of the neonatal mortality

rate and the specificity of the verbal autopsy method; specificity should be very high for MNTE surveys. If the verbal autopsy method for detecting NT deaths correctly confirms all non-NT deaths, the specificity of the survey instrument is 1 and no neonatal deaths are misclassified as NT cases. Low specificity could result in declaring that elimination has not occurred when it truly has.

To adjust the survey design parameters p_l and p_u for the sensitivity and specificity of the survey instrument, we can exploit the relationship:

$$p = pi \times sensitivity + (1- pi) \times (1\text{-}specificity) ,$$

where p is the measured NTMR using current survey protocol, and pi is the true incidence rate of NT in the population.

The mortality rate (CFR) among live births with NT sets an upper bound for the sensitivity. For example, if we assume that the NT CFR is 80%, then the highest possible sensitivity for the survey is 80%. In this case, we assume that NT mortality is high (80%), all NT deaths in the sample are detected, and selection and recall biases are not an issue. When NT mortality is lower, e.g., a CFR of 50% and we expect that only 80% of NT deaths would ever be detected (due to selection and recall bias), then the sensitivity is 80%*50% = 40%. In that case, we need to adjust p_l and p_u downward by 40%. It is unreasonable to assume that recall and selection bias will not cause downward bias in NTMR estimates since they have been shown repeatedly to affect the results of retrospective child mortality surveys. Thus, the assumed sensitivity of MNTE surveys should be adjusted accordingly to reflect these biases.

Underestimating sensitivity is more conservative (*i.e.*, harder to declare elimination) than overestimating sensitivity. Failing to adjust for sensitivity of the survey instrument will produce survey results that are difficult to interpret. It is much more likely that NT elimination could be incorrectly declared if the potentially low sensitivity of the survey instrument is ignored.

9.4 AN EXPLANATION OF PROBABILITY CALCULATIONS FOR OPERATING CHARACTERISTIC CURVES

The LQA-CS method is considered the most practical method for assessing whether MNTE has been achieved; if districts at highest risk are surveyed and a PASS decision is made, we conclude that other districts at lower risk have also achieved MNTE (as discussed in Section 1).

The operating characteristic (OC) curve is defined as the probability of finding no more than d NT deaths (the acceptance number) as a function of the true NTMR in a survey district.

OC curves for both the single and double sampling plans are shown in Figures 1 and 2. They were generated using the Binomial distribution to model the number of NT deaths.

For a single sampling plan with a sample size n and acceptance number d, and where p is the true NTMR in the district, the points on the OC curve are calculated as follows:

$$\mathrm{OC(p)} = \mathrm{P(X \leq d \mid p)} = \sum_{k=0}^{d} \binom{n}{k} p^k (1-p)^{n-k}$$

To construct the graphs in Figures 1 and 2, OC(p) is calculated for a range of p for the values of n and d selected in Section 5 below and the results are plotted. The objective in survey design is to make the right tail of the curve as small as possible (minimize the probability of declaring elimination when p is large) and the left tail as large as possible (maximize the probability of declaring elimination when p is sufficiently small).

Sample OC curves

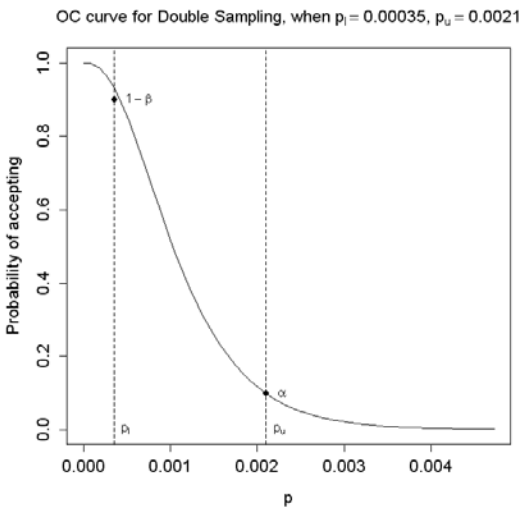

Figure 1: OC curve for single sampling plan. Sample size n = 2,540, acceptance number d = 2. Declare elimination if X ≤ d. Sample size and acceptance number calculated based on the parameters: p_l = 0.35 NT deaths/1000 live births and p_u = 2.1 NT deaths/1000 live births, α = 0.1 and β = 0.1.

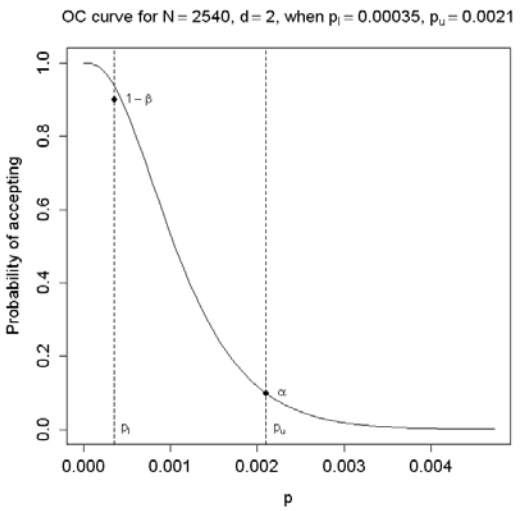

Figure 2: OC curve for double sampling plan. Sample size n_1 = 1,430, n_2 = 1,310 acceptance number d_1 = 0, d_2 = 2. Declare elimination if $X_1 \leq d_1$ or $X_1 + X_2 \leq d_2$. Sample size and acceptance number calculated with parameters: p_l = 0.35 NT deaths/1000 live births and p_u = 2.1 NT deaths/1000 live births, α = 0.1 and β = 0.1.

Given the very low incidence of NT in countries seeking validation of MNTE, if the number of live births in the district is less than 50,000, the hypergeometric distribution is used to calculate the OC curve to take into account the finite population size. (The hypergeometric distribution is otherwise identical to the binomial distribution which assumes an infinite population size). For populations with fewer than 50,000 live births, the OC curve is calculated as follows:

$$OC(p) = P(X \leq d \mid N, m = Np) = \sum_{k=0}^{d} \frac{\binom{m}{k}\binom{N-m}{n-k}}{\binom{N}{n}}$$

where p = m/N. Note that p can only take on a finite number of values when we use the hypergeometric distribution, since m = {0, 1, 2, …,N} is finite.

Calculations for the OC curve using a double sampling plan are slightly more complex. The surveys are designed so that the probability of declaring elimination when $p > p_u$ is approximately the same for the single and double sampling plans. Equivalently, the α-error of the single sampling plan is equal to the α-error of the double sampling plan. We also ensure that these plans have approximately equal β-errors.

To calculate an OC curve for a double sampling plan, we again calculate the probability that we declare elimination (pass) for a given NTMR in the population, but need to consider the fact that we can declare elimination at two different time points. We calculate (1) the probability of passing at the first stage of sampling; and (2) the probability of passing at the second stage of sampling given that we did not pass at the first stage (first sample result indeterminate). To obtain the total probability of passing a district when using a double sampling plan, these two probabilities are added (because the events are mutually exclusive).

$$\begin{aligned} OC(p) &= P(\text{pass} \mid p) \\ &= P(\text{pass at stage 1} \mid p) + P(\text{pass at stage 2 and not at stage 1} \mid p) \\ &= OC_1(p) + OC_2(p), \end{aligned}$$

where

$$OC_1(p) = P(X_1 \leq d_1 \mid p) = \sum_{k=0}^{d_1} \binom{n_1}{k} p^k (1-p)^{n_1-k}$$

$$\begin{aligned} OC_2(p) &= \sum_{k=d_1+1}^{d_2} \{P(X_1 = k \mid p) P(X_2 \leq d_2 - k \mid p)\} \\ &= \sum_{k=d_1+1}^{d_2} \left\{ \binom{n_1}{k} p^k (1-p)^{n_1-k} \sum_{j=0}^{d_2-k} \binom{n_2}{j} p^j (1-p)^{n_2-j} \right\} \end{aligned}$$

Note that we first calculate the first stage sample size and acceptance number, n_1 and d_1, using thresholds p_l, p_u, α_1, and set $\beta_1 = 1$ (because we use the first sample to `stop early' if we can declare elimination). Then, to finalize the second-stage sampling design, we calculate OC(p) over a range of n_2 and d_2, fixing n_1 and d_1, searching for a sample size and acceptance rule with the pre-specified design properties. Using OC(p), we examine whether the selected sample sizes and acceptance numbers meet the design specifications (governed by p_l, p_u, α, and β).

Similar to the single sampling plan, we can use the hypergeometric distribution to calculate the OC curve for a double sampling plan when the annual number of live births in a district is less than 50,000. In this case, we would calculate OC_1 (p) and OC_2 (p) using the hypergeometric as follows:

$$OC_1(p) = P(X_1 \leq d_1 \mid p) = \sum_{k=0}^{d_1} \frac{\binom{m}{k}\binom{N-m}{n_1-k}}{\binom{N}{n_1}}$$

$$OC_2(p) = \sum_{k=d_1+1}^{\min(n_1,d_2)} \{P(X_1 = k \mid p) P(X_2 \leq d_2 - k \mid p)\}$$

$$= \sum_{k=d_1+1}^{\min(n_1,d_2)} \left\{ \frac{\binom{m}{k}\binom{N-m}{n_1-k}}{\binom{N}{n_1}} * \sum_{j=0}^{d_2-k} \frac{\binom{m-k}{j}\binom{N-n_1-(m-k)}{n_2-j}}{\binom{N-n_1}{n_2}} \right\}$$

9.4.1 Risk Curve

A closely related concept to the OC curve is the risk curve. The risk curve is a function that gives the risk of making a mistake in the classification. Its definition requires the same values as the OC curve plus a cut-off point, p^*, to demarcate the acceptable NTMR from the unacceptable. Minimization of the risk curve is essential to a good design. Plotting the risk curve clearly indicates the true NTMR at which we are most likely to "make an error" in declaring that elimination has or has not occurred. Adjusting p^* for the imperfect sensitivity and specificity of the survey, we define p^* = sensitivity * 1/1000 + (1-specificity)*1/1000 = 0.7/1000 NT deaths per 1000 live births when sensitivity = 70% and specificity = 100%.

Figures 3 and 4 below show the risk curves corresponding to the OC curves in Figures 1 and 2 when p^* = 0.7 deaths/1000 live births. Using these figures, it is clear that the risk of misclassifying a district as having achieved elimination is high when the true NTMR in a district is between 0.7 and 2 NT deaths/1000 live births. We are willing to accept this risk, because an NTMR in this range is very close to meeting the formal definition of elimination; for practical purposes, the goal of eliminating MNT as a public health problem has been achieved.

Sample Risk Curves

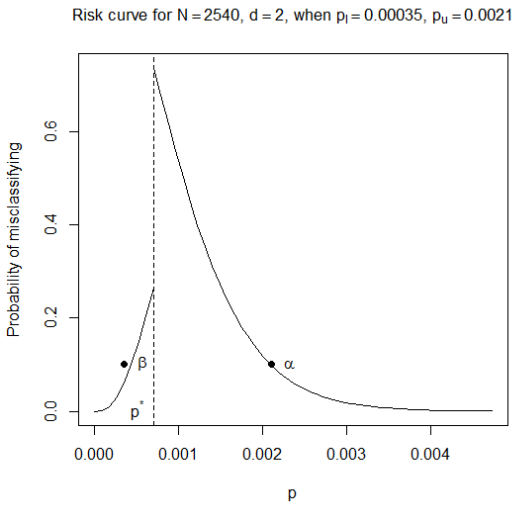

Figure 3: Risk curve for single sampling plan. Sample size n = 2,540, acceptance number d = 2. Declare elimination if X ≤ d. Sample size and acceptance number calculated based on: p_l = 0.35 NT deaths/1000 live births and p_u = 2.1 NT deaths/1000 live births, α = 0.1 and β = 0.1.

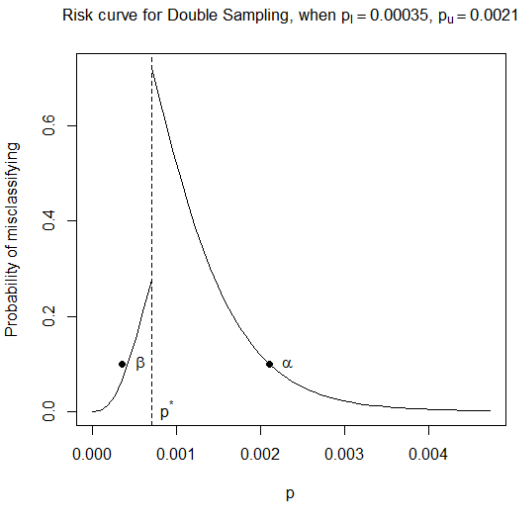

Figure 4: Risk curve for double sampling plan. Sample size n_1 = 1,430, n_2 = 1,310 acceptance number d_1 = 0, d_2 = 2. Declare elimination if $X_1 \leq d_1$ or $X_1 + X_2 \leq d_2$. Sample size and acceptance number calculated based on : p_l = 0.35 NT deaths/1000 live births and p_u = 2.1 NT deaths/1000 live births, α = 0.1 and β = 0.1.

The risk of declaring that a country has not achieved elimination when it truly has remains relatively low (<30%). This property of the survey design is a consequence of choosing a value of p_l that is closer to p^* than p_u. If we select p_l and p_u such that they are equidistant from p^* (and choose α = β), the risk of incorrectly declaring that a country has or has not achieved elimination should be close to 50% when the true NTMR p is very close to p^* (irrespective of whether it is higher or lower).

9.5 CHOOSING A SAMPLING PLAN

To design a specific LQA-CS survey for MNTE, we progress through the following steps, with a specific example in bold letters:

1. Select p_l^i and p_u^i, the relevant upper and lower thresholds for an LQA-CS survey based on NT *incidence*.
   We select p_l^i = 0.5 cases/1000 live births and p_u^i = 3 cases/1000 live births.

2. Select error rates α and β. **We select α = 0.1 and β = 0.1.**
   The choice of p_l^i, p_u^i and α and β is equivalent to stating: "In a district with a true NT rate equal to **0.003** (p_u) or more, if we repeat the MNTE elimination survey a number of times, we would incorrectly conclude that neonatal tetanus has been eliminated less than or

equal to **10%** (α) of the time. And in a district with a true NT rate equal to **0.0005** (p_l), if we repeat the MNTE survey a very large number of times, we would incorrectly conclude that elimination has not occurred **10%** (β) of the time."

3. Adjust the thresholds p_l^i and p_u^i for the estimated sensitivity and specificity of the survey instrument (includes adjustment for CFR), to obtain new thresholds p_l and p_u.
   We assume the sensitivity is 0.7 and specificity is 1, resulting in mortality thresholds p_l = 0.35 NT deaths/1000 live births and p_u = 2.1 NT deaths/1000 live births.

4. Calculate the required sample size based on α, β, p_l and p_u. If the size of the target population is known and is less than 50,000 live births, we use the formulas based on the hypergeometric distribution for the calculations. Otherwise, we use the binomial distribution. Usually, the hypergeometric distribution will be more appropriate, as the target population of live births is usually substantially less than 50,000.

For a large target population (> 50,000 live births), we arrive at the following designs:

- When using a single sampling plan, we need to sample **2,540** live births, and declare elimination if we observe less than or equal to **2** NT deaths.
- With a double sampling plan, we should initially sample **1,430** live births.
  - If we do not observe **any** NT deaths, we declare elimination.
  - If we observe **more than 2** NT deaths, we declare failure to eliminate.
  - If we observe **1 or 2** NT deaths, we sample an additional **1,310** live births. If a total of **2 or less** NT deaths are identified among all **1,430 + 1,310 = 2,740** live births, then we declare elimination. Otherwise, we conclude NT elimination has not been achieved.

For a smaller target population (< 50,000 live births), see section 5.1 below.

The OC curves and risk curves corresponding to these sampling designs are plotted in Figures 1-4 above. Single sampling plan curves are in Figures 1 and 3; double sampling curves are shown in Figures 2 and 4. Note that the single and double sampling curves appear nearly identical, reflecting the fact that the single and double sampling plans were designed to have comparable statistical classification properties.

In Table 3 below, we list the probability of declaring that elimination has occurred for various values of p (these are plotted in the OC curves, but are listed below for reference).

Table 3: OC calculations for single and double sampling plans. Upper and lower thresholds are denoted with a *. Sample size and acceptance number calculated based on the parameters: p_l = 0.35 NT deaths/1000 live births and p_u = 2.1 NT deaths/1000 live births, α = 0.1 and β = 0.1.

Probability (NT deaths/1000 live births)	OC Single Sampling	OC Double Sampling
0	1.000	1.000
0.1	0.998	0.997
0.2	0.985	0.984
0.35*	0.939	0.934
0.5	0.864	0.855
0.7	0.737	0.723
1.0	0.533	0.518
2.0	0.118	0.117
2.1*	0.099	0.099
3.0	0.018	0.022
4.0	0.002	0.004
5.0	0.0003	0.001

9.5.1 Finite Sample Size Plans

In Table 4, we present sample sizes and decision rules using the design parameters in the above section, when the target population size is less than 50,000 live births.

Table 4: Sample sizes for finite population sizes. p_l = 0.00035; p_u = 0.0021; α = 0.1; β = 0.1; α_1 = 0.05. In single sampling plan, sample N live births and denote number of NT deaths detected as X. Declare elimination if X ≤ d. In the double sampling plan, sample Ni live births at stage i and denote number of NT deaths as Xi. Declare elimination when $X_1 \leq d_1$ and when $X_1 + X_2 \leq d_2$.

			Single Sampling Plan				Double Sampling Plan						
Pop.	p_l	p_u	d	N	α	β	d_1	n_1	d_2	n_2	α_1	α	β
3,000	0.33	2.33	1	1,360	.099	0	0	1,050	1	380	.049	.099	0
4,000	0.25	2.25	1	1,480	.098	0	0	1,140	1	410	.049	.099	0
5,000	0.20	2.20	1	1,560	.098	0	0	1,200	1	430	.049	.100	0
6,000	0.33	2.17	1	1,610	.099	.072	0	1,240	1	450	.049	.100	.074
7,000	0.29	2.14	1	1,650	.100	.056	0	1,270	1	470	.049	.099	.057
8,000	0.25	2.13	1	1,690	.098	.045	0	1,300	1	470	.049	.099	.045
9,000	0.33	2.11	1	1,710	.099	.095	0	1,320	1	480	.049	.099	.097
10,000	0.30	2.10	1	1,730	.100	.079	0	1,330	1	490	.050	.100	.081

			Single Sampling Plan				Double Sampling Plan					
15,000	0.33	2.13	2	2,370	.099	.031	0	1,340	2	1,220	.049	.099	.034
20,000	0.35	2.10	2	2,440	.099	.043	0	1,380	2	1,250	.049	.099	.048
25,000	0.32	2.12	2	2,440	.099	.036	0	1,380	2	1,240	.049	.100	.039
30,000	0.33	2.10	2	2,470	.100	.043	0	1,400	2	1,260	.049	.100	.047
40,000	0.35	2.10	2	2,490	.099	.052	0	1,400	2	1,290	.050	.099	.057
50,000	0.34	2.10	2	2,500	.099	.050	0	1,410	2	1,280	.049	.100	.054

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