Application of lot quality assurance sampling for leprosy elimination monitoring—examination of some critical factors

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Accepted 28 August 2003

Background The concept of elimination of an infectious disease is different from eradication and in a way from control as well. In disease elimination programmes the desired reduced level of prevalence is set up as the target to be achieved in a practical time frame. Elimination can be considered in the context of national or regional levels. Prevalence levels depend on occurrence of new cases and thus could remain fluctuating. There are no ready pragmatic methods to monitor the progress of leprosy elimination programmes. We therefore tried to explore newer methods to answer these demands. With the lowering of prevalence of leprosy to the desired level of 1 case per 10 000 population at the global level, the programme administrators’ concern will be shifted to smaller areas e.g. national and sub-national levels. For monitoring this situation, we earlier observed that lot quality assurance sampling (LQAS), a quality control tool in industry was useful in the initially high endemic areas. However, critical factors such as geographical distribution of cases and adoption of cluster sampling design instead of simple random sampling design deserve attention before LQAS could generally be recommended. The present exercise was aimed at validating applicability of LQAS, and adopting these modifications for monitoring leprosy elimination in Tamil Nadu state, which was highly endemic for leprosy.

Methods A representative sample of 64 000 people drawn from eight districts of Tamil Nadu state, India, with maximum allowable number of 25 cases was considered, using LQAS methodology to test whether leprosy prevalence was at or below 7 per 10 000 population. Expected number of cases for each district was obtained assuming Poisson distribution. Goodness of fit for the observed and expected cases (closeness of the expected number of cases to those observed) was tested through \( \chi^2 \). Enhancing factor (design effect) for sample size was obtained by computing the intraclass correlation.

Results The survey actually covered a population of 62 157 individuals, of whom 56 469 (90.8%) were examined. Ninety-six cases were detected and this number far exceeded the critical value of 25. The number of cases for each district and the number of cases in the entire surveyed area both followed Poisson distribution. The intraclass correlation coefficients were close to zero and the design effect was observed to be close to one.

Conclusions Based on the LQAS exercises leprosy prevalence in the state of Tamil Nadu in India was above 7 per 10 000. LQAS method using clusters was validated for monitoring leprosy elimination in high endemic areas. Use of cluster sampling makes this method further useful as a rapid assessment procedure. This method needs to be tested for its applicability in moderate and low endemic areas, where the sample
Smallpox, poliomyelitis, guinea worm disease, tuberculosis, and leprosy are some of the diseases that have been targeted for eradication or elimination. The concept of eradication is clear as it aims at removal of the disease-causing agent and hence total absence of infection or disease. Theoretically it is conceivable to plan for evaluation of an eradication programme. Elimination is just a higher level of control, with the expectation that the disease will disappear in due course when the force of infection is brought below a threshold level. However, there is hardly any scientific evidence to predict what this threshold level, in terms of prevalence, should be for diseases like leprosy or tuberculosis. Measurements for elimination programmes are therefore not easy. In the context of leprosy, rapid and standard methods are needed to monitor progress towards the goal of elimination, at the country level in smaller countries and at sub-national levels in large countries, where leprosy has been endemic. Once low levels of prevalence of leprosy are reached, the health administrators’ concern will shift to targeting smaller areas such as a state or region with high leprosy prevalence for necessary intervention and programme strengthening. Programme-based case detection data may not identify these areas. Traditional sample surveys in each state or region are laborious, expensive, and time-consuming. Programme managers need rapid assessment techniques for monitoring the programmes through an independent mechanism.

Using real life data, we have earlier demonstrated that lot quality assurance sampling (LQAS) could be of particular value in initially high endemic areas for leprosy elimination monitoring. There are certain methodological issues to be addressed before it could be recommended for implementation. We assumed that leprosy cases were more or less evenly distributed in high endemicity situations and the number of cases followed Poisson distribution (curve for rare events). Random sample selection of individuals for leprosy examination is operationally inconvenient in the field. We considered a two-stage survey with households as the sampling units for operational convenience. The above critical factors needed to be examined using real life data before considering the applicability of LQAS for monitoring progress towards leprosy elimination.

LQAS is a quality control tool in industry. Items or goods of the same type, size, or grade in a production process are grouped to form homogeneous lots. A simple random sample of n items from each lot is taken for inspection to identify the number of defectives. If the number of defectives is less than or equal to maximum acceptable number (critical value) then the lot is regarded as having defective items within acceptance limits. On the other hand if the number of defectives exceeds the critical value on or before the complete examination of all the items in the sample, further examination of the sample items is discontinued and the lot is rejected. A lot in the health field may be a sample of people. More details of LQAS are available elsewhere.

The use of LQAS has gained importance in the health field over the last 15 years. However, its use for leprosy elimination monitoring has been limited only recently. After the introduction of leprosy elimination programmes, based on fixed duration multidrug therapy (MDT), a rapid decline in leprosy prevalence has been documented in high endemic regions. For example, in Tamil Nadu state in south India leprosy reportedly dropped from 53 per 10 000 in 1990 to 4 per 10 000 in 2001. The objective of this paper is to examine the validity of LQAS by using real life data from an initially highly leprosy endemic state, for leprosy distribution and for the design effect (enhancing factor for the sample size) if a two-stage cluster sample survey is employed.

Materials and Methods

Hypothesis

Reported prevalence in Tamil Nadu, a state in India endemic for leprosy, was 4 per 10 000 in December 2001. The state leprosy authorities anticipated a certain level of underestimation in the prevalence. They expected the leprosy prevalence in the state to be about 7 per 10 000. The null hypothesis to be examined was thus whether the prevalence of leprosy in the state was at or below 7 per 10 000.

Sample size, definitions, and examination procedures

The sample size that we provided for was adequate to conclude that the prevalence levels could be between 4 and 7 per 10 000 for the state. Details of the design are available from our earlier work. The sample size, assuming Poisson approximation, with 5% level of significance and a power of 90% required to test the hypothesis, was determined as 53 000 people. Allowing 20% as the margin of non-response, a sample of 64 000 people in the state was considered sufficient. The maximum allowable number of leprosy cases (d, critical value) in this sample was 25. If the number of cases in the sample exceeded the critical value (d) of 25, prevalence in the state was to be regarded as above 7 per 10 000.

For the purpose of sampling, Tamil Nadu state was divided into North, South Central, and West Zones. To have a representative sample in the state, two districts in each of the four zones were selected using probability proportional to size (PPS) linear systematic sampling. In each district 8000 people were to be selected. This sample was further divided into rural and urban populations, proportionate to the rural/urban ratio of the population in the district. Villages and towns were selected using PPS linear systematic sampling. Within each selected village/town, a fixed number of 100 households was selected using linear systematic sampling. Thus, in order to cover the entire sample 18 villages/towns were selected. The first household in each village/town was randomly selected and subsequent households were obtained following systematic sampling.

Information regarding number of households for each village or enumeration block was obtained. Sampling interval (K) was
computed by dividing the number of households in the village or
enumeration block by 100. A random entrance/exit to the
village or enumeration block was selected. A random number
below K for the household was further selected. Using the
random number identified the first household, from this
household every kth household was selected till 100 households
were attained. Reasons for choosing a household and not the
individual were (1) sampling frames of individuals were not
available and (2) selection and examination of only certain
individuals in a household would be practically difficult.

The survey was conducted from 6 January 2001 to 30 March
2001. Information on age, sex, and residential status of every
member in the household was collected from the head of the
household or any senior member of the family through a
structured questionnaire. It was decided to complete the survey
for the entire sample to generate data on leprosy distribution.
Leprosy inspectors screened all the resident members of the
household that were present at the time of the first and repeated
visits by clinical examination for leprosy. A case of leprosy is
defined as an individual who has manifestations of leprosy and
who needs treatment. Supervisory staff confirmed the diagnosis
of the cases. All the cases were classified by type, i.e. single skin
lesion (SSL), paucibacillary (PB), or multibacillary (MB). A case
was defined as PB if he/she had
 5 skin lesions, with not more
than one nerve lesion, and all the slit skin smears were negative
for acid fast bacilli (AFB). A person was considered as an MB
case if he or she had >5 skin lesions or more than one nerve
lesion or the individual’s skin smear was positive for AFB.
Leprosy patients with a single patch receiving single dose
treatment were not considered for prevalence, but, if put on
6-months PB MDT, they were considered in prevalence. New
cases were those who were diagnosed for the first time through
the present survey. An old case is defined as one who is already
diagnosed and is under treatment. The Directorate of Medical
and Rural Health Services of Tamil Nadu and the National
Institute of Epidemiology, Chennai monitored data quality.

Five to six experienced paramedical staff members were
formed into teams to cover a given district. Each team consisted
of one health educator, three to four leprosy inspectors and one
laboratory technician from the state government. Laboratory
technicians were involved in collecting slit-skin smears. Medical
officers from the Directorate of Public Health, Tamil Nadu and
the National Institute of Epidemiology, Chennai monitored the
quality of clinical examination.

**Statistical analysis**

To investigate whether leprosy cases in the sample survey area
followed Poisson distribution the following procedure was
adopted. Frequency distribution for the number of households
(clusters) with 0, 1, 2, 3, and 4+ cases in the survey was
go (90.8%) were examined. The average household size was 4.3.

During the survey 62 157 people were enumerated and 56 469
(90.8%) were examined. The average household size was 4.3.

Table 1 shows that population coverage for examination was
similar in all eight districts. The coverage for clinical
examination in each district was above 90% and was similar for
both rural and urban areas.

In all, 96 (83 new and 13 old) cases were detected. Of the 96
cases, 31 belonged to the SSL type, 48 were PB, and the remaining

### Table 1 Examination coverages by district of the surveyed area

<table>
<thead>
<tr>
<th>District</th>
<th>No. enumerated</th>
<th>% examined</th>
<th>SSLa</th>
<th>PBb</th>
<th>MBc</th>
<th>PB + MB (rate per 10 000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tanjavur</td>
<td>7806</td>
<td>90.0</td>
<td>7</td>
<td>6</td>
<td>2</td>
<td>8 (11.4)</td>
</tr>
<tr>
<td>Trichy</td>
<td>7553</td>
<td>91.4</td>
<td>5</td>
<td>4</td>
<td>2</td>
<td>6 (8.7)</td>
</tr>
<tr>
<td>Kancheepuram &amp; Tiruvallur</td>
<td>7896</td>
<td>90.4</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>6 (8.4)</td>
</tr>
<tr>
<td>Vellore</td>
<td>8375</td>
<td>90.1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>3 (4.0)</td>
</tr>
<tr>
<td>Tirunelveli</td>
<td>7696</td>
<td>91.4</td>
<td>6</td>
<td>9</td>
<td>2</td>
<td>11 (15.6)</td>
</tr>
<tr>
<td>Virudhunagar</td>
<td>7899</td>
<td>90.3</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>8 (11.2)</td>
</tr>
<tr>
<td>Coimbatore</td>
<td>7363</td>
<td>92.1</td>
<td>4</td>
<td>11</td>
<td>2</td>
<td>13 (19.2)</td>
</tr>
<tr>
<td>Salem</td>
<td>7569</td>
<td>91.2</td>
<td>2</td>
<td>8</td>
<td>2</td>
<td>10 (14.5)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>62 157</strong></td>
<td><strong>90.8</strong></td>
<td><strong>31</strong></td>
<td><strong>48</strong></td>
<td><strong>17</strong></td>
<td><strong>65 (11.5)</strong></td>
</tr>
</tbody>
</table>

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*a* Single skin lesion.

*b* Paucibacillary.

*c* Multibacillary.
17 cases were diagnosed as MB. The number of PB + MB cases varied between 3 and 13 among the districts. There were 46 cases in the rural areas and 50 cases in the urban areas. In all these cases the skin smears were negative for AFB. Two cases with visible disability were observed. Observed prevalence of total leprosy (SSL + PB + MB) in the examined population was 17 per 10,000 and for PB + MB it was 11.5 per 10,000 population.

From Table 2 it is clear that the coverage was about 98% in children. The coverage was more (96%) among adult females and for adult males it was 80%. Twenty-nine cases detected in the survey were re-examined by two medical officers and for 28 of them diagnosis was confirmed (Table 3).

The cases by households for the individual districts followed Poisson distribution. The cases by villages for the individual districts followed Poisson distribution. \( P \) varies from 0.3 to 0.9. The distribution of cases by households for the entire survey area and the distribution of cases by villages (Figure 1) for the entire survey area also followed Poisson \( (P = 0.5) \) (Table 4). The intraclass correlation coefficient for each district was nearer to zero. The design effect for six districts ranged between 0.8 and 1.01 (Table 5). The design effect for the remaining two districts was 0.2 and 1.9. The design effect for the entire state was 1.06.

### Discussion

In the statistical sense, the prevalence of leprosy in different geographical areas can be called very low or rare. The World
Health Organization (WHO) defined elimination of leprosy as a prevalence of less than one case for 10,000 population. To estimate a prevalence of leprosy of one case per 10,000 population with a precision of ±10% using conventional survey methods one needs 3.8 million people in the sample. In contrast, LQAS technique requires a much smaller sample size. This tool offers a distinct practical advantage for health administrators and programme managers. We demonstrated earlier that LQAS would be useful for identifying high prevalence districts in an initially high endemic state such as Tamil Nadu. 1,2 In the present work we are reporting on practical approaches and methodological aspects related to sampling.

LQAS aims to provide information with respect to prevalence levels of the disease in a state or region. It does not provide estimates of the prevalence. LQAS thus needs to be undertaken periodically, rather than as a one-time effort, to help programme managers to understand whether progress is being made over a period of time. WHO, in its review, indicated that there was increasing application of the LQAS technique for assessing a variety of health care parameters including disease incidence. 3 Recently, LQAS was used for identifying ‘high-risk districts’ of neonatal tetanus, to assess and validate whether neonatal tetanus has been eliminated in Rajasthan state in India.4

In this study we tried to examine all the individuals in the sample. However, some people were not available at the time of visits, or they had temporarily migrated, or they were seriously ill, or were not willing to undergo the examination. These non-respondents could be a crucial group. We were successful in keeping the proportion of non-response to less than 10%. We presume non-response is probably not related to any stigma attached to leprosy because generally in an endemic state like Tamil Nadu, it is very low. However, no efforts could be made to find the reasons for non-response.

Trained and experienced leprosy inspectors were deployed for the present survey. The population of Tamil Nadu is generally receptive to routine periodic screening for leprosy as part of leprosy control activities. However, omission of a certain proportion of early leprosy cases cannot be ruled out. This problem might lead to misclassification and underestimation of the actual level of prevalence.

There were 13 known cases of leprosy in the examined population, indicating that the known prevalence of leprosy was only 2.3 per 10,000 in the population examined. This is far below the expected prevalence of 7 per 10,000 in the state. On the other hand even if only PB or MB leprosy cases are considered, the prevalence in the examined population is 11.5 per 10,000.

The number of leprosy cases in the population of each district and the combined selected districts followed Poisson distribution. We made a similar observation earlier in an endemic district of Tamil Nadu.4 The Poisson distribution of leprosy in endemic areas appears to be true in view of the low prevalence of leprosy in the statistical sense. The near-zero intraclass correlation coefficients (variability among the cases) for the households indicated that distribution of leprosy among households was similar. This observation is similar to our previous exercise in a hyper endemic district of Tamil Nadu state.4

While carrying out LQAS we adopted operationally convenient two-stage cluster-sampling design in place of simple random sampling. A recent application of LQAS for neonatal tetanus elimination also used a cluster sampling procedure instead of simple random sampling.7 Since the observed design effect in our study was nearly one, there is no need to increase the sample size in similar situations. Thus pragmatic modifications to the LQAS design using cluster sampling, are a feasible proposition.

Acknowledgement
The study was carried out in collaboration with the Directorate of Medical and Rural Health Services, Tamil Nadu. The authors gratefully acknowledge the financial assistance provided by DANLEP for undertaking the survey. The authors thank the field teams for their meticulous and hard work. Mrs R Janaki provided the secretarial assistance.

KEY MESSAGES

- Lot quality assurance sampling is useful for disease elimination monitoring in endemic areas.
- Leprosy cases in the sample followed near random and Poisson distribution, eliminating the need for enlarging the sample size.
- Cluster sampling design can be adopted in high endemic regions for leprosy.

References