Workshop and training course on TB prevalence surveys with a focus on field operations

Tuberculosis prevalence surveys: a handbook (AKA "the Lime Book")

Overview of key recommendations

Day 1 – Thursday, 28 July 2011
Phnom Penh

Babis Sismanidis
Overview of presentation

- Objectives of the Lime Book
- Outline and authors of the Lime Book
- Key new and updated recommendations
From red to lime book

2007 -- 1\textsuperscript{st} ed.

2011 -- 2\textsuperscript{nd} ed.
Objectives of the Lime Book

• NEW recommendations added

• UPDATE existing recommendations based on recent experience

• Add more practical advice by showcasing recent nationwide prevalence surveys
Overall structure and content

The Lime Book is structured in five parts:

• Part I. Rationale and objectives
• Part II. Design and methods
• Part III. Management, organization, logistics and field work
• Part IV. Analysis and reporting
• Part V. Appendices
• ...and a web appendix

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New recommendations
Co-primary survey objective: collect data on why cases are missed

paragraphs 2.2, 2.3, 16.2.5, 16.2.6, appendix 1.3

- Collect data (typically referred to as "health-care seeking behaviour") from survey participants at the time of screening in order to understand why, if so, TB cases are missed by the NTPs

- A recommended list of minimum questions is presented on this (linked with specific defined indicators)

- Additional data collection or a post survey interview from identified TB cases may also be an option. However, quality of the follow up interview could be a concern, unless survey staff are involved
Repeat surveys

chapter 9

- Guidance is provided on when a repeat survey is appropriate

- Impact of TB control is:
  - (i) slow (allow at least 5 years between surveys) and
  - (ii) its magnitude moderate (therefore potentially large sample sizes are required)

- Both "new" and "old" technologies or algorithms should be used to allow for comparisons between repeat surveys, where possible

- Meta- or pooled-data analysis to estimate the regional or global trend from good quality individual country surveys

- Both frequentist and Bayesian approaches to sample size calculation and inference on prevalence of TB trends are presented
Other than national surveys

paragraphs 1.3, 1.4

- In settings where nationwide prevalence surveys are not appropriate or possible, consider other types of surveys (such as sub-national or among "special" populations)

- "Special" (e.g. prisons, nomads, refugee camps, military barracks) populations are often excluded from national surveys. Such surveys are a programmatic activity and beyond the scope of the Lime Book (despite obvious similarities in the design)
Updated recommendations
Eligibility criteria for participation to survey paragraphs 1.1, 5.4, 14.3, 14.4

- Eligibility of participants is based on:
  - Age, 15+ years (although scarcity of global data on childhood TB!)
  - Household residency status, 2-4 weeks

- Recommend a full census of the household members by the survey team before the cluster operations start

- Prepared enumeration lists (e.g. by village chiefs) are possible in countries with vital registration systems or regularly updated population lists by local authorities
  - Most countries in Asia have local population or household registrations that can be utilized for pre-survey census to define survey sampling area, this may not be applicable in most African settings
Eligibility for sputum examination (screening)  
*paragraph 4.3.2*

- A participant is eligible for sputum examination based on screening from: (i) **chest X-ray** and/or (ii) **symptoms interview**
  
  - Symptom screening
  - Chest X-ray screening

- Eligibility not based on being currently on treatment, having treatment history, or being a TB contact

- **Sputum examination is based on two specimens** (smears for both, ideally culture for both) from everyone identified as eligible from the screening
Screening definitions

*paragraphs 4.3.1, 6.3.2, 6.3.3, 7.9*

- **Chest X-ray (CXR)**
  - *Abnormal CXR* – An abnormal CXR means any lung abnormality detected on interpretation by the medical officer (e.g. opacities, cavitation, fibrosis, pleural effusion, calcification, any unexplained or suspicious shadow, etc.). Bony abnormalities like fractures are excluded by definition as are findings like increased heart size.
  - *Normal CXR* – A normal CXR means clear lung fields and no abnormality detected.
  - Over-reading of CXR as "abnormal" in the field is encouraged.

- **Symptoms interview**
  - *Abnormal interview* – Those with "chronic" cough, or other symptoms (e.g. haemoptysis), according to national policy.
  - *Normal interview* – Those without abnormal symptoms detected.
Chest X-ray: digital or not?

*paragraphs 7.4, 7.5*

- Base your decision according to these parameters:
  - Funding
  - Average workload
  - Manpower availability and cost
  - Accessibility (portable or mountable)
  - Infrastructure in the country (e.g. electricity, water)
  - Long-term use
  - Compatibility with existing imaging infrastructure (what happens to these after the survey?)
  - Availability of maintenance service
Survey objectives & outcomes
paragraphs 2.2, 2.3

• Prevalence of bacteriologically-confirmed TB (either AFB-S+ or CTB+) as the primary outcome
  – Also maintain AFB-S+ as a co-primary outcome, since sample size calculations so far were done based on this
  – Sample size calculations based on AFB-S+ are sufficient for the revised primary outcome because $AFB-S+ < (AFB-S+ \text{ or } CTB+)$

• Leave the decision to countries for using as secondary outcomes
  – Prevalence of healed TB; central (not field) CXR reading
  – Prevalence of X-ray suggestive of TB; central (not field) reading
Survey TB case definition

**Paragraph 4.2**

**Survey TB case definition**¹

**Definite survey TB case (bacteriologically-confirmed survey TB case):**
One CTB positive specimen AND at least one of the following conditions:

- AFB-S positive (smear-positive, culture-positive TB definite case)
- CTB-positive in another specimen
- Chest X-ray abnormal finding in lung at central audited reading
- Evidence from follow-up investigations if planned in the survey protocol

**AFB-S positive survey TB case (smear-positive TB case):**
One AFB-S positive specimen AND at least one of the following conditions:

- CTB-positive (definite survey TB case)
- AFB-S positive in another specimen BUT not CTB positive AND no isolation of MOTT (probable TB case)
- Chest X-ray abnormal finding in lung at central reading BUT not CTB (or NAATB) positive AND no isolation of MOTT (probable TB case)

¹ *CTB +ve could also be read as WHO-endorsed NAATB +ve (e.g. GeneXpert)*
Box 4.3: Types of TB cases

**New case not on treatment:** Patient who has never previously had treatment for TB for more than a month and who is currently not being treated with anti-TB drugs.

**New case on treatment:** Patient who is currently being treated with anti-TB drugs but has not received anti-TB treatment before the current treatment for more than one month.

**Previously treated case not on treatment:** Patient who has previously had treatment for TB for more than a month and who is currently not receiving treatment with anti-TB drugs.

**Previously treated case on treatment:** Patient who has previously had treatment for TB for more than a month and who is currently being treated with anti-TB drugs.
Sampling design

chapter 5

- 9 steps to sampling design for the mathematically faint at heart

- Detailed description of the approach to sample size calculation (no more a "black-box")

- Stratified sampling design (clusters sampled independently from different geographical regions of the country) is recommended to increase precision and representativeness of overall country estimate of TB prevalence

- Cluster size recommended to be between 400-1,000 individuals

- Detailed description of the process for selecting clusters
• Roll-out of prevalence survey to be scheduled according to lab workload and capacity

• 2 sputum specimens per individual, either spot-morning or spot-spot (1 hour apart), depending on survey operations

• Both specimens should be smeared, ideally both cultured (processed at the latest within 5 days from collection when in cold chain)

• Solid or liquid media for culture? Under ideal conditions WHO recommends liquid. However, the method used should be familiar to lab staff and common practice in country

• Concentrated (and not direct) culture method is recommended for prevalence surveys
TB treatment, HIV and DST testing

*chapter 11, appendix 6*

- **TB treatment** should be ensured for all identified definite survey TB cases. At least referral to NTP should be ensured for all probable survey TB cases.

- **HIV testing** should be offered (either as part of the survey or referral to HIV testing and counselling services) to at least all survey TB cases.
  - Preferably offer HIV testing to a wider group (for example those eligible for sputum examination), especially in high HIV settings

- **Drug susceptibility testing** among culture-confirmed cases is encouraged both for: a) patient management (provision of treatment must be ensured) and b) mapping MDR-TB epidemiology purposes

- **Other detected abnormalities** (through CXR and interview findings) should be referred to appropriate health facilities
Data management

*chapter 15, web appendix*

- Data management plan to cover all aspects
- Data manager (100% full-time post, early involvement in planning)
- Real-time data entry; avoid backlog (1.5 million entry points)
- "new" technologies (barcodes, PDAs)
- Software to develop database (local expertise, relational, not Excel!)
- Confidentiality must be ensured
- Personal Identifying Numbers (PINs) to link all forms
- Pilot testing
Statistical analysis

**chapter 16**

- Properly account for the cluster sampling design of the survey in the estimation of TB prevalence

- Start with classical cluster-level approach and continue with individual-level analysis using two types of logistic regression models (allowing for correlation of individuals within cluster):
  - "Robust" standard errors
  - Random-effects (or "hierarchical")

- Always investigate the bias of the estimates due to missing data (using multiple imputation techniques)