Meeting report

Repeat prevalence surveys in Asia: design and analysis

8 - 11 February 2012, Phonm Penh, Cambodia

A. Meeting overview

Four Asian countries are planning repeat TB prevalence surveys around 2015: Bangladesh, Myanmar, the Philippines and Viet Nam. These surveys are of strategic importance, since findings will provide evidence about changes in TB disease burden, will inform assessment of whether the MDG/Stop TB targets are met, and will provide a baseline for targets and measurement of progress post-2015. The design of repeat surveys is more challenging than the design of first surveys, since sample sizes need to allow for the measurement of changes since the last survey. Lessons are also available from Cambodia and China, where repeat surveys were recently conducted in 2011 and 2010 respectively.

The objectives of the workshop were: 1) to learn from the recent experience of designing repeat surveys in Cambodia and China and 2) to discuss the design of the repeat surveys planned in Bangladesh, Myanmar, the Philippines and Viet Nam. Participants included people who will have a lead role in the design of the surveys in each of the four countries, experts in survey design and analysis from Cambodia and China, WHO staff and (as facilitators) experts in the design of repeat surveys from collaborating technical agencies.

During the workshop, the latest status of progress in repeat prevalence surveys worldwide was presented, followed by presentations on a) WHO recommendations on how to design repeat surveys and b) the design and eventual results from repeat surveys concluded in Cambodia in 2011 and China in 2010. The remainder of the workshop was used for group work in which country teams explored different plausible scenarios for the sample sizes required for their surveys, using alternative assumptions about improvements in TB control since the previous survey, alternative statistical assumptions and methods, and alternative years in which surveys could be conducted.

The provisional conclusions were that:
1) Given problematic methods used in the 2008 survey in Bangladesh (sputum smear for all participants, with no X-ray or sputum culture examinations), discussions focused on how to design a first survey according to the internationally-recommended screening strategy around 2013/2014.
2) The optimal time for the implementation of the survey in Myanmar should be around 2016/17.
3) The optimal time for the implementation of the survey in the Philippines should be around 2017.
4) The optimal time for the implementation of the survey in Viet Nam should be around 2015/2016.

Funding for these surveys is provided mainly by Global Fund (with the exception of Viet Nam which is mostly supported by government funding).

B. Bangladesh

1. Background

A nationwide prevalence survey was completed in 2008 in Bangladesh including 52,098 survey participants (equal to or more than 15 years of age) and a participation rate of 80%. At the time when the survey was conducted no international guidelines for prevalence surveys were available hence the choice for the design of the survey was based on what was considered feasible and affordable in the context of the country. Two sputum specimens for smear microscopy (no culture examination performed) were taken from all survey participants. A chest X-ray was only done for participants with at least one smear positive result. The chosen strategy for the survey is not recommended in the current international guidelines (Tuberculosis prevalence surveys: a handbook, AKA the Lime Book), due to associated problems with under-estimation of prevalence. 33 survey smear positive cases were identified. The associated estimate for smear-positive prevalence was 63 per 100,000, 95% confidence interval (44-89).

2. Conclusions

- Key aspects of the Bangladesh survey protocol were developed according to international recommendations.
- The survey is designed as a first survey, and not as a repeat to the 2008 one.
- The survey implementation will be in 2013/2014.

C. Myanmar

1. Background

The first nationwide prevalence survey was completed in 2010 in Myanmar including 51,367 survey participants (equal to or more than 15 years of age) and a participation rate of 89%. The correlations of between-cluster variability (k) were quite high, expressing large heterogeneity of the level of TB prevalence between clusters.

Rates per 100,000 (95% CI)	**2010**
Bacteriologically-confirmed	613 (502-748) k=0.62
Smear positive	242 (186-315) k=0.81

The repeat survey is planned and budgeted for 2014 (4 years later).

2. Factors driving prevalence in the country

Notifications for the period between 2002 to 2010 show similar levels of increase both among smear positive and smear negative TB. The annual decrease in bacteriologically confirmed TB in Cambodia (measured by nationwide prevalence surveys in 2002 and 2011) was 5.7%. Smear positive annual reduction was even higher. The situation in Myanmar over the next 5 years is

considered to be similar to that of Cambodia between the period 2002 to 2011 and hence a similar decrease in TB prevalence is hypothesized.

2010 – 2014 (planned survey)

a. DOTS expansion, low coverage of MDR
b. Low level HIV
c. PPM expansion
d. Faster economic expansion expected
e. Limited health insurance

3. Sample size calculation

a. Assumptions

Outcome	*Prevalence of TB in 2010*	*Annual decrease*	*Prevalence of TB in 2014 (20% reduction)*	*Coefficient of between-cluster variation*	*Cluster size*
Smear +ve	p_1=242	5%	p_2=242*0.8=194	k=0.81	m=730
Bact. confirmed	p_1=613	5%	p_2=613*0.8=490	k=0.62	m=730

b. Sample size calculation examples

20% precision, 20% reduction compared to 2010 prevalence levels, same cluster size and k as with the 2010 survey		
Method of calculation	**Smear positive outcome**	**Bacteriologically-confirmed outcome**
Single survey[1]	110,844	54,750
Repeat surveys (equation 9.1)[2]	145,270	71,540
Repeat surveys (equation 9.2)[3]	*Undefined*	*Undefined*
Bayesian[4]	90,520	*Not yet calculated*

[1]Perform sample size calculation as a stand-alone survey, based on precision.
[2]Perform sample size calculation assuming 2010 prevalence estimate is the true level of prevalence (see Chapter 9, the Lime Book).
[3]Perform sample size calculation assuming 2010 prevalence level and allowing for uncertainty around this level (see Chapter 9, the Lime Book).
[4]Perform sample size calculation using prior information from 2010 survey to inform anticipated values of prevalence in 2014 (see Chapter 9, the Lime Book).

4. Conclusions

- For the smear positive outcome, prohibitively large sample sizes are required, either because the level of prevalence is not very large, or the duration between the two surveys not long enough to allow for a large reduction in prevalence.
- For the bacteriologically-confirmed outcome, the single survey approach is considered feasible.
- Consider delaying the survey to 2016/2017 in order to allow for large reductions in prevalence levels to be reached.

D. The Philippines

1. *Background*

There have been two nationwide TB prevalence surveys conducted in the country in 1997 and 2007 among individuals aged equal to or more than 10 years of age. Key results are shown in the table below.

Rates per 100,000 (95% CI)	1997	2007	Annual decrease (%)
Bacteriologically-confirmed	960 (750-1160)	660 (510-810) k=0.55	-3.7%
Smear positive	360 (280-450)	260 (170-360) k=0.79	-3.3%

A repeat survey is currently planned for 2014 (7 years later).

2. *Factors driving prevalence in the country*

1997 – 2007:

a. DOTS expansion, low coverage of MDR
b. Low level HIV
c. PPM expansion
d. Slow economic expansion
e. Limited health insurance

2007 – 2014 (sustained levels of decrease in TB are expected)

a. Some more PPM (PPM coverage currently stable)
b. Universal health insurance?
c. Faster economic growth?
d. MDR control (target 30% DST in retreatment)
e. Negative factors: diabetes rising fast, aging population

3. *Sample size calculation*

a. Assumptions

Outcome	*Prevalence of TB in 2007*	*Annual decrease*	*Prevalence of TB in 2014*	*Coefficient of between-cluster variation*	*Cluster size*
Smear +ve	p_1=260	-3.3%	p_2=260*0.77=200	k=0.79	m=450
Bact. confirmed	p_1=660	-3.7%	p_2=660*0.74=488	k=0.55	m=450

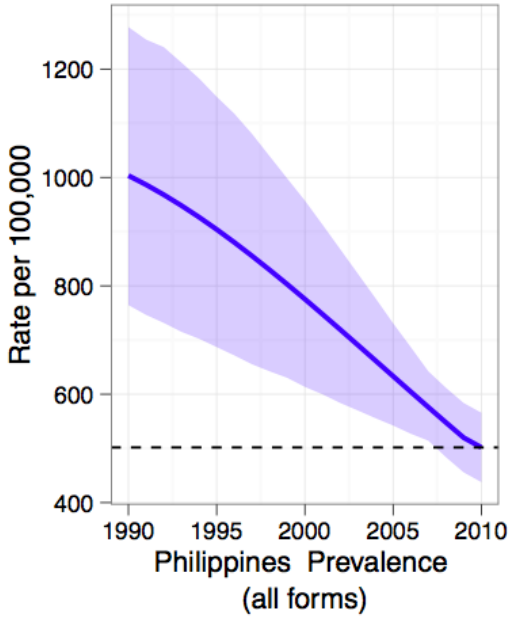
b. Sample size calculation examples

20% precision, 23% and 26% reduction respectively for smear positive and bacteriologically confirmed compared to 2007, same cluster size and k as with the 2007 survey		
Method of calculation	**Smear positive outcome**	**Bacteriologically-confirmed outcome**
Repeat surveys (equation 9.1)[1]	88,557	38,054
Repeat surveys (equation 9.2)[2]	*Undefined*	*Undefined*
Bayesian[3]	47,517	18,855

[1]Perform sample size calculation assuming 2007 prevalence estimate is the true level of prevalence (see Chapter 9, the Lime Book).
[2]Perform sample size calculation assuming 2007 prevalence level and allowing for uncertainty around this level (see Chapter 9, the Lime Book).
[3]Perform sample size calculation using prior information from 2007 survey to inform anticipated values of prevalence in 2014 (see Chapter 9, the Lime Book).

4. *Conclusions*

- Decline 2007–2014 should not be assumed faster than decline 1997–2007 (-3.3%/year).
- If sample size based on smear positive:
  - use Bayesian approach, but still almost 50,000 (too expensive),
  - do the survey in 2017 or later instead of 2014.
- If sample size is based on bacteriologically-confirmed, the survey will not be powered to detect a 2007–2014 trend in smear positive TB, but may show an overall decline since 1997.
- Consider delaying the survey to 2017. This would be too late for an MDG assessment but there is already evidence from 3 surveys indicating the country is on track.



E. Viet Nam

1. *Background*

The first nationwide prevalence survey was completed in 2007 in Viet Nam including 94,179 survey participants (equal to or more than 15 years of age) and a participation rate of 91%. The correlations of between-cluster variability (k) were high, expressing large heterogeneity of the level of TB prevalence between clusters.

Rates per 100,000 (95% CI)	**2007**
Bacteriologically-confirmed	307 (249-366) k=0.59
Smear positive	197 (150-244) k=0.75

The repeat survey is planned for 2014 (7 years later).

2. *Factors driving prevalence in the country*
    a. DOTS expansion, low coverage of MDR
    b. Low level of HIV: Antenatal clinic surveillance 0.37% in 2005, 0.25% in 2010, an annual decrease of -9.3%.
    c. PPM expansion: currently only covers about 5% of private health providers.
    d. Fast economic expansion. Total increase between 2007 and 2010 in GDP per capita is about 10%.
    e. Aging of the population.
    f. Suspect:Notified smear positive ratio increased from 10.4 in 2007 to 11.4 in 2010.

3. *Sample size calculation*

a. Assumptions

Outcome	*Prevalence of TB in 2007*	*Annual decrease*	*Prevalence of TB in 2014*	*Coefficient of between-cluster variation*	*Cluster size*
Smear +ve	p_1=197	-4.3%	p_2=197*0.7=138	k=0.7	m=1500
Bact. confirmed	p_1=307	-4.3%	p_2=307*0.7=215	k=0.7	m=1500

b. Sample size calculation examples

4. 20% precision, 30% reduction for both smear positive and bacteriologically confirmed compared to 2007, same cluster size as with the 2007 survey and k=0.7		
Method of calculation	**Smear positive outcome**	**Bacteriologically-confirmed outcome**
Repeat surveys (equation 9.1)[1]	95, 524	81,517
Repeat surveys (equation 9.2)[2]	*Undefined*	*Undefined*
Bayesian[3]	*Not yet calculated*	133,592

[1]Perform sample size calculation assuming 2007 prevalence estimate is the true level of prevalence (see Chapter 9, the Lime Book).
[2]Perform sample size calculation assuming 2007 prevalence level and allowing for uncertainty around this level (see Chapter 9, the Lime Book).
[3]Perform sample size calculation using prior information from 2007 survey to inform anticipated values of prevalence in 2014 (see Chapter 9, the Lime Book).

5. Conclusions

- There is political commitment in the country to measure the level of prevalence in 2015, in order to assess if the West Pacific Region target of 50 % reduction in prevalence, compared with 2000 levels, has been reached.
- The 2007 survey cultured only one specimen per survey participant. The repeat survey should instead culture two specimens per participant.
- To end up with a manageable sample size of less than 100,000 the repeat survey must be:
    - conducted when the reduction in prevalence is more than 30% compared with the 2007 survey, which could be around 2015/2016,
    - consider using bacteriologically-confirmed as the primary outcome,
    - reduce the cluster size (reduced design effect),
    - consider using the Bayesian approach to sample size calculation.