Acceptability of Household and Community-based TB Screening in High Burden Communities:

A Systematic Literature Review

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A Systematic Literature Review

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Conducted March 1, 2011-May 22, 2012.

Acknowledgements

This report benefitted from the expertise of a wide range of individuals and institutions. Debby Kramer provided expert librarian services. Technical review was provided by Suzanne Verver. Remaining errors and omissions are attributable to the authors.

ABSTRACT

The acceptability of TB screening in high burden settings is often assumed to be very high. Despite the rapid proliferation of novel TB screening efforts worldwide, queries into the acceptability of these efforts have been limited.

To assess the acceptability of community-based TB screening, two reviewers queried 4 databases and conference abstracts and screened 4507 studies from 2001 to 2011 for potential inclusion. A total of 75 studies met the criteria for inclusion, of which 47 met the analytic threshold of countries with an estimated all-TB prevalence above 100/100,000 in 2009 and contained information on the proportion of 'eligible persons' consenting to be screened for inclusion. Studies were classified by region, screening method, quality, and descriptive results are presented as tables. Due to lack of richer data, the proportion of invited persons who consented to undergo TB screening was used as a proxy for acceptability of TB screening.

Although this inference exercise seems to suggest that screening and active case finding are widely acceptable, it is important to understand that the issue has not been properly studied. For expedience (and out of necessity) a "vote with your feet" proxy for acceptability (% screened among # eligible) has been employed. It is unclear if the recruitment rates of well-executed, well-resourced studies can be extrapolated and deemed legitimate proxies for acceptability in a routine programmatic setting.

"Acceptability" is a composite social construct that denotes complex and inter-related ideas. It is very difficult to quantify and synthesize because it is already a synthesis.[1] There is evidence to suggest it is composed of multiple domains –including structural, personal, and cultural factors.

Community-based screening had high participation rates ranging from 2-99% of eligible individuals. The average participation rate was 82% ± .2 (IQR 80%-95%). Acceptability ranged from 12% to 100%, with a median of 90% and a mode of 80%. We can infer that TB screening conducted using strategies similar to those described in these studies (i.e. voluntary participation, home-based sample collection, small incentives, social mobilization, and free TB treatment) will be widely perceived as beneficial by community members.

The mean participation rate (aka acceptability) of screening does not appear to vary significantly according to the primary screening algorithm and the median acceptability of screening are similar (91-93%) among the three main screening algorithms (symptoms alone, symptoms plus CXR, and CXR alone). It is noteworthy that the mean acceptability of universal sputum collection (i.e. no primary symptom screen:84%± 11%) is comparable to that of other algorithms (85-91%±19%) considered

In keeping with expectations , participation in TB screening did vary significantly by region and by setting (urban/rural), with screening uptake lower among urbanites (82% vs. 91% ($t(26)= -2.2, p=.04$). Screening in South East Asia had higher mean participation than in Africa or the Western Pacific regions (91% vs. 84% ($t(34)=2.1$, $p=.04$). In some contexts, the difference in participation in screening varies by gender, with males less likely to consent, less likely to give samples, and less likely to be retained during repeat screening in longitudinal cohorts.

Contrary to expectation, inclusion of HIV testing in the TB screening exercise did not significantly reduce the acceptability of community-based screening. The mean participation rate in studies with provider initiated counseling and testing (PICT) (μ=86% ± .03) was not significantly different from the rates in studies where HIV screening was not offered(μ=81% ± .04).

Acceptability in large scale TB prevalence surveys is often difficult to calculate and over-reported due to sampling with replacement in some sampling units. For example, few investigators report both the refusal rate at the household level and the refusal rate at the individual level. Investigators were also not routinely candid about the incentives offered, making is challenging to assess this important confounder.

Despite a lack of attention to the issue of acceptability of TB screening and active case finding, it can be inferred from participation rates that mass TB screening (or active case finding) in high burden communities (>100,000/100,000) is widely acceptable in most contexts, including urban slums and more remote rural communities. TB control programs should consider the use of mass screening as a potential tool in hyper-endemic contexts.

Further research is needed to explore specific aspects of mass screening and how it might be tailored to fit the needs of particular communities. Moreover, the potential relationship between the acceptability of mass screening and the acceptability of (and adherence to) TB treatment following diagnosis through mass screening.

INTRODUCTION

TB screening and Active Case finding (ACF) are increasing framed as a potential remedy for stalled TB case detection rates and diminishing returns from the traditional methods of passive detection of M. Tuberculosis (TB) that rely upon health seeking by symptomatic individuals. Indeed ACF has been shown to detect additional TB cases in several controlled trials. Moreover, the effectiveness of TB screening among certain key populations is also suggestive of potential benefit (Kranzer et al 2012). TB screening in the community vs. a health facility presents both opportunities and challenges for the health system. TB screening often identifies a different sort of TB and a different sort of TB patient than the traditional approaches. Moreover, the range of interventions described as "TB screening" can be very broad, the potential target populations are equally diverse, and the diagnostic algorithms applied vary widely making simplistic conclusions about the value of TB screening a challenge.

Mass screening for various health problems has a checkered history. Significant tensions and misunderstandings have been documented when mass screening and household specimen collection efforts for other diseases have been poorly explained or inadequately consultative.[2]

Some studies indicate there may be confusion regarding whether to seek consent for interventions at the household or individual levels and how to know what constitutes true acceptance as opposed to passive resignation or lack of empowerment.[3-6]

Study Rationale

One of the issues that is frequently overlooked in the development of screening policy is the potential acceptability of mass TB screening in endemic settings. It is vital to consider the ethical and affective dimensions of this undertaking due to the large amount of resources that it requires. However, it is first necessary to explore crude participation rates in contemporary mass screening studies in high burden settings to assess whether or not a potential acceptability problem exists. An in-depth appreciation of these issues is difficult due to the limited information available, however through inference and extrapolation, general conclusions on acceptability may be derived. These conclusions can inform the development of global TB screening policies and help to ensure that the principles of autonomy and beneficence are upheld.

Study Objectives

In this systematic literature review, we address one question:

What is the acceptability of <u>community-based</u> or mass TB screening in non-health care settings as compared with passive case finding in settings with an estimated prevalence of all forms of TB above 100/100,000 in the 2000-2011 period?

Review Protocol

Acceptability of Household and Community-based TB screening in High-Burden settings

Introduction

The acceptability of efforts to aggressively detect tuberculosis at the community level can be inferred through the careful scrutiny of recruitment rates of prevalence surveys and large and small community-based studies. There has been a noteworthy increase in such efforts recently, which has offered a window of opportunity to explore acceptability.

Search Strategy PICO Q. 1: What is the acceptability of household and community-based TB symptom screening (2-step) in the settings with an estimated prevalence of all forms of TB above 100/100,000?

To identify potential influences on the acceptability of screening, several secondary questions were posed:

1. Are there differences in Acceptability by Context (urban/rural)?
2. Are there differences in Acceptability by Gender?
3. Are there differences in Acceptability by Incentives and enablers?
4. Is enhanced case finding as acceptable as community-wide screening?
5. Are there differences in Acceptability by Inclusion of HIV testing?
6. Are there differences in Acceptability by region?
7. Are there differences in Acceptability by Screening algorithm?
8. Are there differences in Acceptability by Study type?

To assess the acceptability of community-based screening in settings with an estimated prevalence of all forms of TB above 100/100,000 in the 2000-2011 period, the following approach was adopted:

We searched 4 online databases (Web of Science, PubMed (Medline), LILACS, and EMBASE) for the publication years 2000-2011 to identify studies. In addition, we searched abstracts of the IUATLD/UNION and TSRU conferences by manually screening the abstract books and CD ROMs for the period 2000-2011. Additional papers were identified through searching references and via scrutiny of a power point presentation on a systematic review of active case-finding strategies for TB, which was carried out by Johns Hopkins University and the systematic literature review by Kranzer et al.(2011). Unpublished reports were only included if permission was granted by the investigators.

Study selection process

STEP 1: SCREENING

A database of all articles meeting the search criteria including full reference and abstracts was developed in Endnote and Mendeley (an open source reference manager). These were used to screen titles and abstracts for the following inclusion and exclusion criteria:

Inclusion criteria for titles & abstracts:

1. The paper had to be an original research contribution and not a commentary or modeling exercise;
2. Involved systematic or screening active case-finding
3. Took place in a community or non-health care setting (e.g. school)
4. The diagnosis of TB involved use of clear screening and diagnostic methods and algorithms

Exclusion criteria for titles & abstracts:

1. Study took place in a country with an estimated incidence <100/100,000
2. Referred to only specific risk groups or special populations (e.g. PLHIV, elderly, TB contacts, health care workers, or miners)
3. Took place in a health care facility or congregate setting.

Mass screening studies conducted in countries with a low TB incidence were excluded because the yield (and hence cost effectiveness) of such endeavors is likely to be so low that even if they were highly acceptable, they would not be justifiable on other grounds.

Only studies conducted after 2000 were considered because earlier studies were deemed less likely to meet the higher ethical norms and standards applied in contemporary practice and were deemed more likely to use algorithms and approaches that do not reflect current practice[7].

Titles and abstracts were screened by 1 reviewer (SdB) and a 20% systematic random sample of titles and abstracts were cross-checked by a second reviewer (EMHM). The number of included and excluded studies were recorded; and at the abstract screening stage four reasons for exclusion were noted (see above 3 inclusion criteria, plus "other")

STEP 2: STUDY SELECTION

In the next stage, the full-text of selected papers (or reports, abstracts or posters in the case of grey lit) were scanned by 1 reviewer (SdB) using the same inclusion and exclusion criteria to select the final sample of articles to be included in the review.

Data extraction process

A data-extraction form containing all relevant information for data extraction was developed in MS Word (Appendix 2). One reviewer (SdB) extracted all relevant data-items from the included studies using this data-extraction form, except those in Spanish and Portuguese which were extracted by the author (EMHM). A second reviewer (EMHM) checked the extraction of a 25% subsample of the articles and extracted data from Spanish and Portuguese sources. Inconsistencies were discussed to obtain consensus.

Methods for handling missing information

Missing data are treated as "not reported" (indicated in the tables as "not reported or "—"). Key variables, such as disaggregation by gender, are presented whenever this information was reported.

If detailed information on the components of non-participation were given, we selected the inverse of the refusal rate (1-refusal= acceptance). However, if no breakdown was available, we took the participation rate, as the most conservative estimate. In the five studies(12%) that gave a detailed breakdown of reasons for non-participation, refusal often represented less than 50% of the total non-participation rate. For example, in Bjerregaard-Andersen, M., et al.(2010), the proportion of eligibles screened was 80% but the refusal rate was only 0.8%.[8]

Information to be extracted from included studies

To assess the methodological characteristics of studies we characterized

a. Screening steps
b. Case definitions
c. Study type,
d. region, setting, catchment area
e. Population by age, gender, HIV sero-status and other relevant risk factors

Data were entered into an MS Excel database and imported into SPSS19.0 for analysis.

Methods to appraise the quality of individual studies

Since most of the studies were observational or cohort studies, we applied the STROBE criteria to assess the following dimensions of quality:

1. Identification of potential confounders and effect modifiers
2. Discussion of potential biases
3. Efforts to address potential sources of bias
4. Rationale for the study size / sample size
5. Rationale for how missing data were addressed
6. Sampling strategy accounted for in analysis
7. If applicable, lost to follow-up addressed
8. Reasons for non-participation
9. Confounder adjusted estimates
10. 95% confidence intervals
11. Study limitations
12. Generalizability
13. Funding source given and role of funding source

http://www.strobe-statement.org/

For ease of application the STROBE was applied as an *unweighted summary score* from 0(lowest quality) to 12 (highest quality). This is an unconventional but expedient use of the STROBE checklist to permit the rapid assessment of the quality of the evidence.

Risk of bias in individual studies

This review is likely to be affected by a significant degree of reporting bias and publication bias which may over estimate the acceptability of screening since studies with high refusal rates

face bigger hurdles to publication. To overcome this challenge, where possible, authors have triangulated data from published and unpublished reports of the same study to detect reporting bias and have included studies that were never published to attempt to mitigate the potential publication bias.

Summary measures

The principal summary measure is the proportion of eligible members of the target population who are actually screened. The proportion (screened/eligible) is hypothesized as a proxy for acceptability, due to the limited number of studies of acceptability of screening.

Where possible (n=5) we have broken this down further to tease out how much of non-participation is a function of refusal (lack of acceptability) and how much is a function of other factors. Similarly, where possible, we have indicated where along the diagnostic pathway acceptability may change.

Data analysis

The analysis was descriptive.

Results

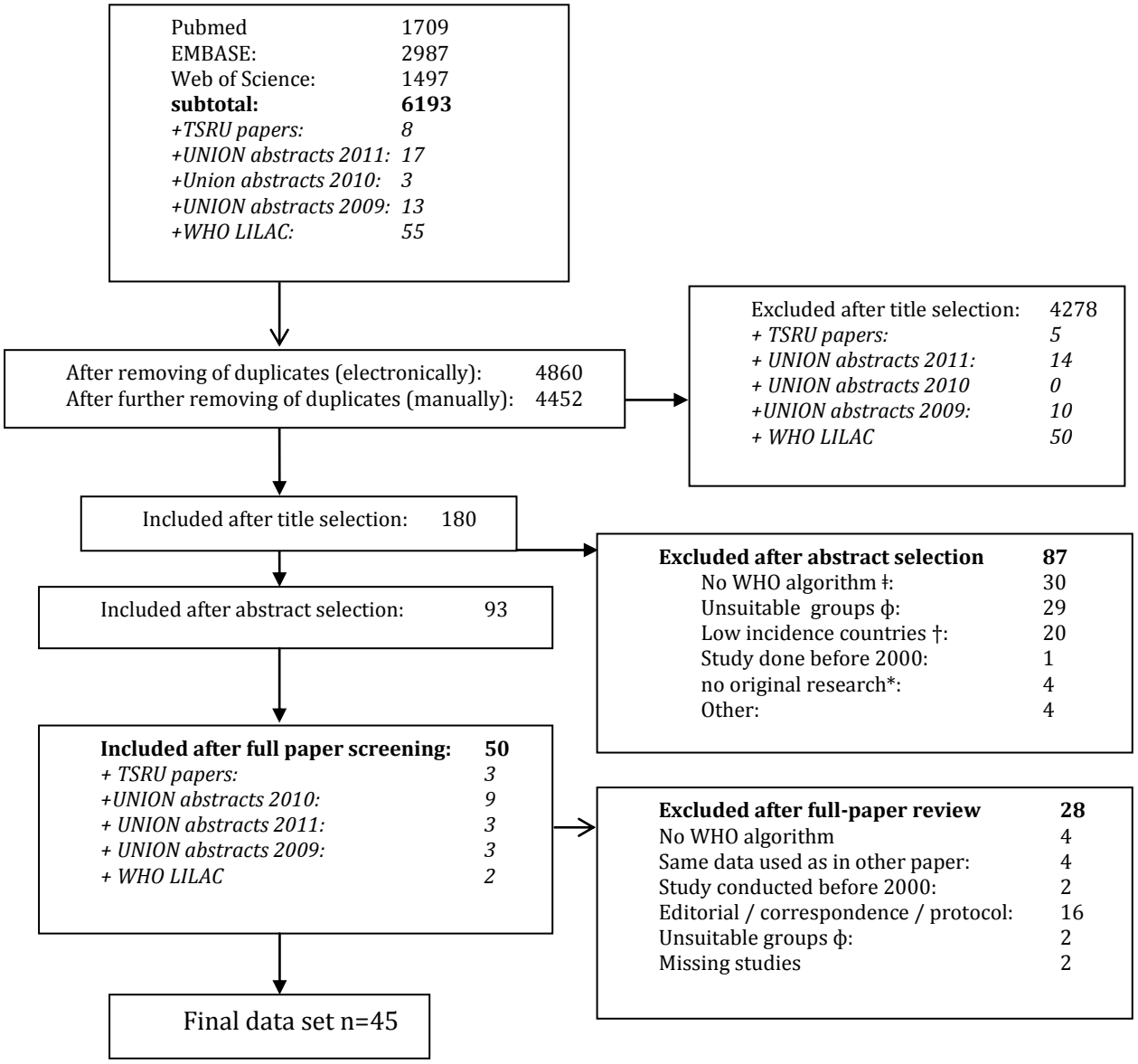
Results section

The final results of this analysis are presented here in tables with explanatory text.

Study selection process

Figure 1 outlines the study selection process and the yield by source as well as reasons for exclusion. Missing studies are indicated.

Figure 1 Selection of studies for Q.1: Acceptability of Community-based Screening [1]



[1] * No original research includes reviews or policy papers. It is possible that these include useful information, or references to original papers: screen references.

ǂ No WHO algorithm also includes studies in which there was no diagnosis for TB disease (for example only cough screening, or TST testing done), or where there was no denominator (for example when only TB cases were included in the study).

Φ The RISK groups include, elderly, people identified through contact screening, health care workers, miners, or only HIV-positive individuals.

† Low incidence countries as defined as <100/100,000.

ᵖ These papers reported further analysis on previously reported prevalence surveys, but without reporting new relevant data: 1) Van de Werf. Emerg Infect Dis 2007; 13(10):1497, 2) Liu. IJTLD 2005;9(4):450, 3) Corbett Bull WHO 2010; 88(1): 13, 4) Vree 2006 (abstract)

Other includes 2 papers in Chinese, and 2 papers that were reporting WHO data for multiple countries.

Results

Forty-seven studies met the eligibility criteria for inclusion. The included studies had an average participation rate of 82% ± .2 (IQR 80%-95%). Acceptability ranged from 12% to 100%, with a median of 90% and a mode of 80%, suggesting high rates of participation.

Table 3 Studies excluded due to on-going Data analysis

Author	Country	Location	Setting	Study design
CENAT	Cambodia	countrywide	urban + rural	nationwide prevalence survey
MOH Pakistan	Pakistan	countrywide-non-conflict	urban + rural	nationwide prevalence survey
MOH Myanmar	Myanmar	countrywide	urban + rural	nationwide prevalence survey

The majority of mass screening studies included in this review came from Africa (13), South East Asia (11), or the Western Pacific (11).

Table 4. Regional Overview of Included Community-based studies

WHO REGION	NUMBER OF COUNTRIES	NUMBER OF STUDIES
Africa	7	20
Americas	2	4
Eastern Mediterranean	1	2
Europe	1	1
South-East Asia	4	11
Western Pacific	6	14
TOTAL	**21**	**47**

Are there differences in Acceptability by TB Screening algorithm?

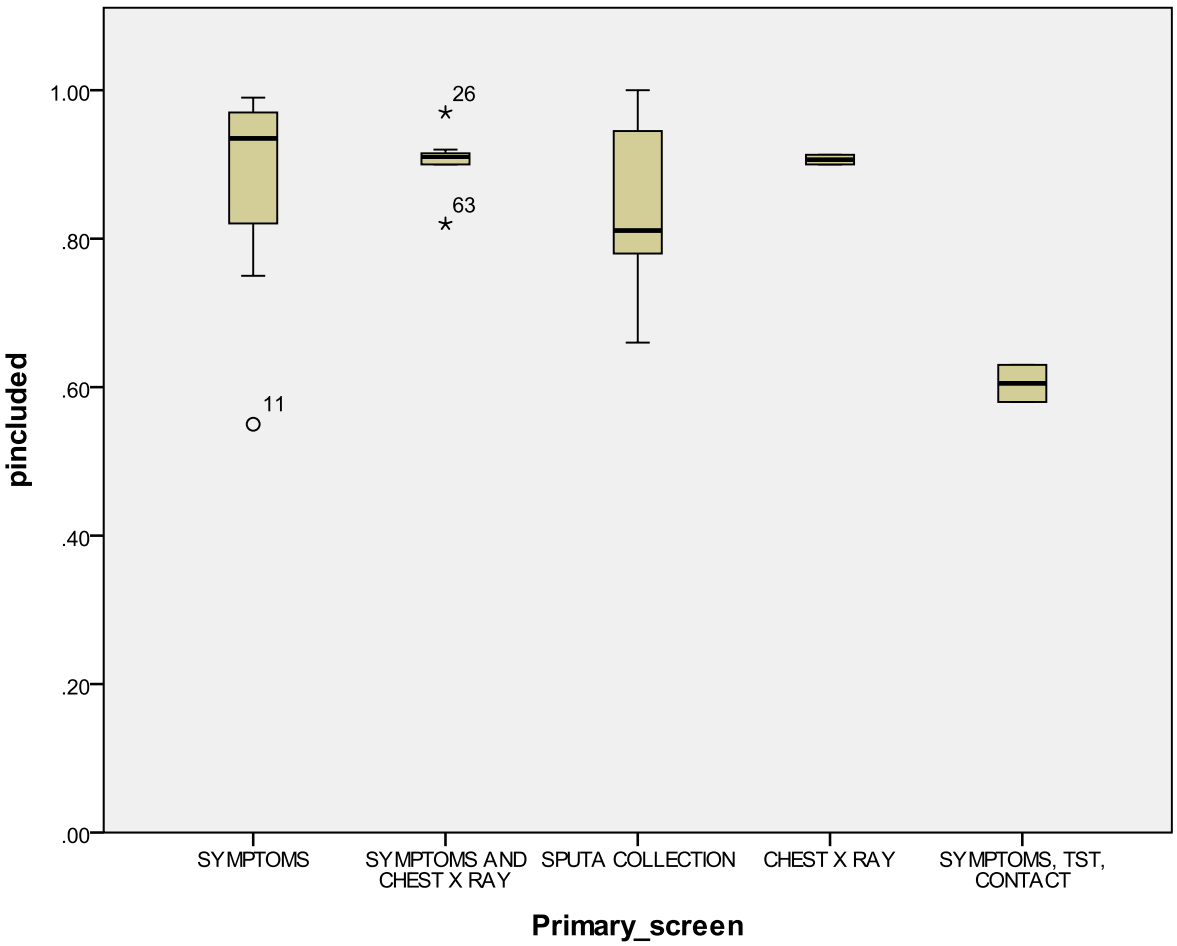
The mean acceptability of screening does not appear to vary significantly according to the primary screening algorithm and the median acceptability of screening are similar (91-93%) among the three main screening algorithms (symptoms along, symptoms plus CXR, and CXR alone). It is noteworthy that the mean acceptability of universal sputum collection (i.e. no primary symptom screen:84%± 11%) is comparable to that of other algorithms (85-91%±19%) considered.

Table 5: Acceptance by Primary Screening Method

Primary_screen	N	Mean	Std. Deviation	Grouped Median	Std. Error of Mean
CHEST X RAY	2	.91	.01	.91	.01

SYMPTOMS AND CHEST X RAY	7	.90	.04	.91	.02
SYMPTOMS	21	.85	.19	.93	.04
SPUTA COLLECTION	14	.84	.11	.81	.03
SYMPTOMS, TST or IGRA, CONTACT- repeat screening	3	.72	.14	.79	.05
TOTAL	**45**	**.85**	**.15**	**.90**	**.02**

Three studies employing periodic screening every 4 to 6 months using a more elaborate combinations of symptoms, history of contact, and annual TST and/or IGRA yielded lower mean acceptability (72%). Qualitative research suggested that this was largely attributable to the more invasive nature of the primary screen, particularly the blood draw, and less a function of the repetitive nature of the screen.[9]



Are there differences in Acceptability by Context (urban/rural)?

Conventional wisdom and anecdotal reports suggest that participation rates in TB screening are lower in urban clusters, and indeed on average participation is lower in urban cohorts ($p<.04$)

Table 6: Participation by Setting

Settings	Mean	N	S.D.	Median	S.E.	Min	Max	Range	Variance
Urban	.82	14	.11	.81	.030	.58	.99	.41	.013
Rural	.91	15	.10	.96	.025	.67	1.00	.33	.009
Combined	.88	16	.11	.91	.027	.55	1.00	.45	.012
Total	**.87**	**45**	**.11**	**.90**	**.016**	**.55**	**1.00**	**.45**	**.012**

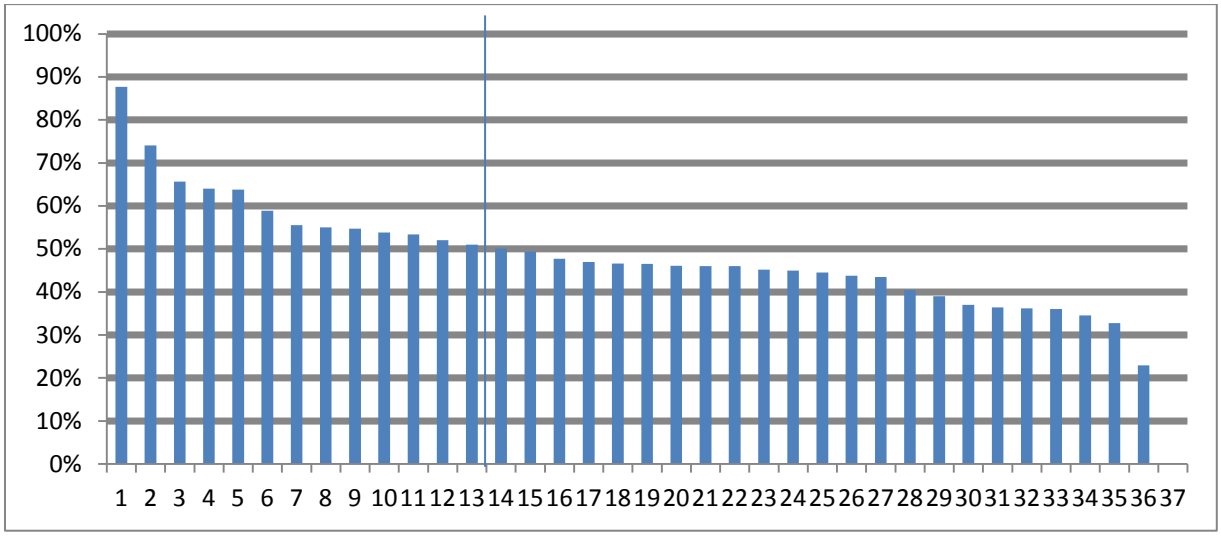
Among 11 urban studies reviewed, the range of consent for TB screening among urban household residents ranged from 58-99% with a weighted average of 91%. Acceptability of conducting screening among residents in urban poor areas has been researched in various regions. Tupasi et al concluded that symptom screening followed by sputum examination was acceptable in urban settlements in the Philippines.[10] Walton et al found that TB case-finding was acceptable in Haitian poor areas particularly when combined with other health services, such as reproductive health care and ART.[11]

Are there differences in Acceptability by Gender?

Active case finding has been shown to improve the detection of TB among women as compared with passive case-finding.[12-13] However the uptake of screening by gender has not been rigorously studied. Preliminary findings from a small number of community –base screening efforts suggest that although males often exhibit more TB than women in many settings, as a proportion of eligible participants, men tended to be less willing to participate in community-based screening efforts, less likely to give samples when screening was positive, and less likely to be retained.[14-15] Quoted in Corbett et al 2010 “In the 12% of ”households randomly selected for survey of tuberculosis” and HIV prevalence, 10,092 adults (81% of 12,426) provided” sputum before intervention and 11,211 (77% of 14 569)”provided sputum after five rounds of intervention, with” lower participation in men (65% [3970/6151] before” intervention, 57% [4061/7185] after intervention) than in” women (98% [6121/6275] before intervention, 97%”[7150/7384] after intervention; web appendix p 5).

It is not clear if this is a function of acceptability or if it simply reflects men’s greater likelihood participation in the labor force and absence from the household in some settings.

Figure 2: Participation of Males in Community wide TB Screening in High burden Settings (n=45 studies)



Conversely, in higher income settings, such as London, women with TB were less likely than men to accept HIV screening.[16]

Are there differences in Acceptability by Incentives?

Although most studies with very vulnerable populations do show an increase in acceptability from incentives and enablers for screening, the acceptability of screening in the general population is not necessarily enhanced.[2] A study of 100 counties in China concluded that other health system factors were more significant drivers of participation in screening than incentives.[17] A 2012 Cochrane systematic literature review concluded that :

> "*There is limited evidence to support the use of material incentives to improve return rates for TB diagnostic test results and adherence to antituberculosis preventive therapy. The data are currently limited to trials among predominantly male drug users, homeless, and prisoner subpopulations in the United States, and therefore the results are not easily generalized to the wider adult population, or to low- and middle-income countries, where the TB burden is highest. Further high-quality studies are needed to assess both the costs and effectiveness of incentives to improve adherence to long-term treatment of TB."[18]*

Is enhanced case finding as acceptable as community-wide screening?

It appears that various forms of enhanced case finding have a wider range of acceptability. This review does not consider all the nuances of using "enhanced case finding" strategies

[2] A Beith, R Eichler, D. Weil *Worldwide: Incentives for Tuberculosis Diagnosis and Treatment,* in Performance Incentives for Global Health: Potential and Pitfalls. Center for Global Development, Washington, DC, 2009;

(mixtures of social mobilization, mass communication, incentives or enablers). However it is noteworthy that combining home-base symptom screening and with traditional "passive" health center based diagnostics appears not to be as acceptable in all settings as household screening and sample collection.

Table 7: Enhanced Case finding

Invention	Mean	N	Std. Deviation	Minimum	Maximum	Median	Range
Enhanced case finding	33%	3	0,49	0%	90%	10%	89%

Are there differences in Acceptability by Inclusion of HIV testing?

There were 11 studies that included HIV testing in the TB screening process. In qualitative studies this was mentioned as a possible driver of acceptability of TB screening. However, the mean participation rate in studies with HIV testing (μ=86% ± .03) was not significantly different from the rates in studies without HIV screening (μ=81% ± .04). In some screening studies, the HIV testing decision was independent of the TB screening decision, and where distinct refusal rates were HIV testing acceptance tended to be lower (e.g. 81% TB vs. 73%VCT, Corbett 2010).

Are there differences in Acceptability by region?

There were few regional differences in uptake of TB screening. Screening in South East Asia had higher mean participation than in Africa and the Western Pacific regions (91% vs. 84% ($t(34)=2.1$, $p=.04$)..

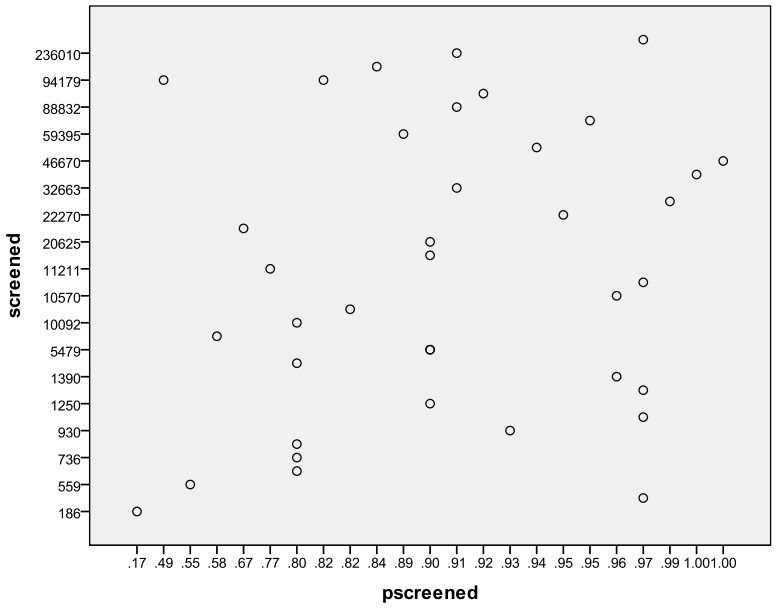
Table 8: Variation in TB Screening Participation Rates by Region

region	Mean	N	Std. Deviation	Grouped Median	Std. Error of Mean	Min	Max	Range	Variance
AFRO	.84	20	.13	.83	.03	.58	1.00	.42	.017
WPRO	.84	8	.16	.86	.07	.55	1.00	.45	.026
SEAC	.91	14	.05	.91	.01	.80	.97	.17	.003
LAC	.85	3	.13	.80	.07	.75	.99	.24	.016
EMRO	.90	1	.	.90	.	.90	.90	.00	.
Total	**.87**	**46**	**.11**	**.90**	**.02**	**.55**	**1.00**	**.45**	**.013**

Are there differences in Acceptability by Study size?

As shown in Figure X, participation rates were not related to the overall size of the TB screening exercise.

Figure 4: Scatter Plot of the number of Persons Screened and proportion of eligibles screened



Is there a difference in acceptability of mass screening by Age?

With regard to younger age groups, three studies in adolescents found rates of participation to be slightly lower than adults, but may have been a function of the use of TST/IGRA in younger populations. Most mass screening exercises have excluded children, so it is difficult to discern what participation rates among children would be. However, qualitative work on the role of children in active case finding in Zambia suggests that children are generally supportive of the activity.[19]

Multiple experts have suggested that the elderly find household TB screening more than acceptable passive case finding or self referral due to access barriers but the evidence for this assertion is still emerging. Two case-control studies in Kenya and Cambodia comparing TB cases first identified during household TB prevalence surveys with those detected through the passive self-referral system suggest that the elderly are more likely to be detected through household TB screening programs. [13]

Synthesis of results

Data have been combined for regional, gender, age, algorithmic, size and setting comparisons. Since there were no predictors at the bivariate level, no multivariate analysis was performed.

Risk of bias across studies

The most serious limitation of these analyses is the absence of studies focused upon

acceptability and the lack of qualitative ethnographic work on reasons for refusal (with certain exceptions)[20-21]. Another limitation is that only 5 (12%) of studies listed reasons for non-participation.

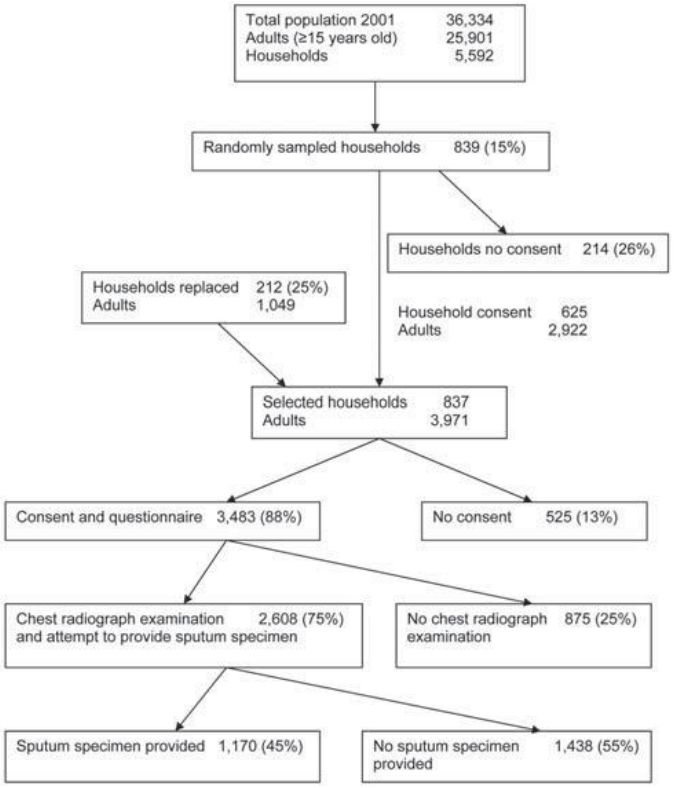
Due to a dearth of studies, this review does not consider enough of the interesting studies using "enhanced case finding" strategies or explore the nuances of incentives and enablers to case finding. Combining home-base symptom screening and health center based diagnostics is a cheaper alternative to mobile sample collection that may have different level of acceptability and sustainability. Another limitation of the review of Q. 1 is that is includes only cross sectional studies, but a proper answer to the acceptability question might also consider the inclusion of longitudinal cohort studies with periodic screening[15].[3] There is preliminary evidence that a population that is subject to too frequent TB screening may under-report symptoms to avoid invasive testing.

This review is likely to be affected by significant degree of reporting bias and publication bias which may over estimate the acceptability of screening since studies with high refusal rates face bigger hurdles to publication. To overcome this challenge, authors have triangulated data from published and unpublished reports of the same study to detect reporting bias and have included studies that were never published to attempt to mitigate the potential publication bias.

Acceptability in large scale TB prevalence surveys is often difficult to calculate and over-reported due to sampling with replacement. Few investigators report both the refusal rate at the household level and the refusal rate at the individual level. An example of full reporting is den Boon 2007: Twenty-five percent of households declined to participate and were replaced with willing households. Among those households who agreed, 13% of individual members who declined. So the acceptability is said to be 87% but it would be much lower if the refusal at the first sampling unit (household) were taken into account.

[3] Quoted in Corbett et al 2010 "In the 12% of "households randomly selected for survey of tuberculosis" and HIV prevalence, 10,092 adults (81% of 12,426) provided" sputum before intervention and 11,211 (77% of 14 569)"provided sputum after five rounds of intervention, with" lower participation in men (65% [3970/6151] before" intervention, 57% [4061/7185] after intervention) than in" women (98% [6121/6275] before intervention, 97%"[7150/7384] after intervention; webappendix p 5).

Figure 5: Sample selection of 3,483 adults, Cape Town, South Africa, den Boon et al 2007



A similar bias is the lack of information on the acceptability of the secondary screen. For example, in Bjerregaard-Andersen, M., et al.(2010), the initial refusal of symptom screening is only 0.8% (n=26), however the refusal of the diagnostic test (submission of sputa) was 13%.

Figure 6: Example of Multiple Refusal Points in a TB Screening Algorithm

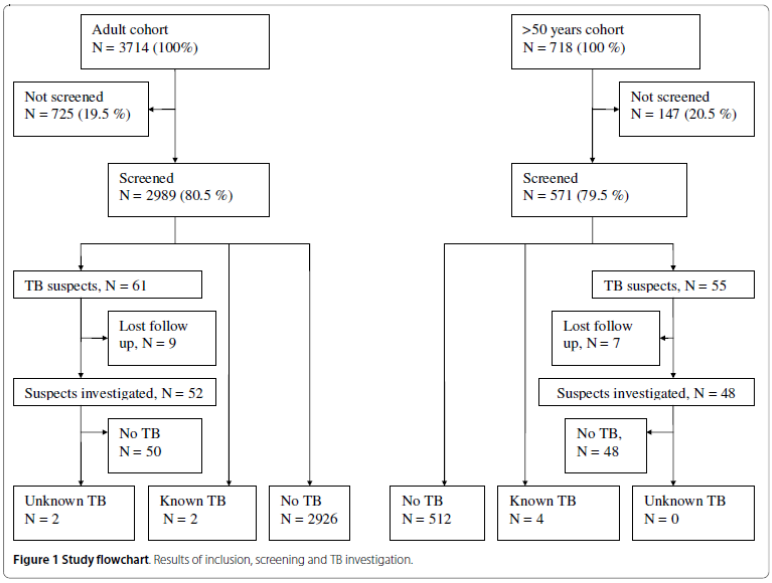


Figure 1 Study flowchart. Results of inclusion, screening and TB investigation.

A countervailing risk of bias to the two mentioned above is the potential for under estimating acceptability by using the proportion of eligible individual screened as a proxy for acceptability. Often eligible people are not screened for reasons unrelated to acceptability. In

the five studies(12%) that gave a detailed breakdown of reasons for non-participation, refusal often represented less than 50% of the total non-participation rate. For example, in Bjerregaard-Andersen, M., et al.(2010), the proportion of eligibles screened was 80% but the refusal rate was only 0.8%.[8]

Such a high level synthesis in the face of significant methodological diversity is a perennial challenge of the systematic review technique and it was not always possible to report key nuances and make concise summary tables[22-23]. Statistical methods for combination of qualitative and quantitative data, where there are many missing values, such as Bayesian augmentation methods might have been more appropriate for this analysis.[24-25]

DISCUSSION

The proportion of eligible persons who ultimately participate in screening is an imperfect though highly convenient proxy of the acceptability of screening in a population. Consent has been shown to be influenced by the demeanor of the research staff, incentives offered, and other intangibles.

Although the results rest on an inference, it is logical that screening and active case finding would be acceptable because it removes the many barriers to care that regularly hamper health seeking for symptoms. A systematic review of delay in TB diagnosis identifies cost and distance as significant contributors to refusal, and mass TB screening at the community level addresses these[26-27].

Marked differences in acceptance of screening by gender and ethnicity reported in some settings suggest that TB screening has cultural, social dimensions that preclude broad generalizations about acceptability[28]. These differences were not apparent at the regional level[14-15, 29]

Conclusions

Despite a lack of attention to the issue of acceptability of TB screening and active case finding, it can be inferred from participation rates that mass TB screening or active case finding is widely acceptable in most contexts, including urban slums and more remote rural communities. The results of this inquiry suggest that TB screening participation rates do not vary significantly by region, by setting, by diagnostic algorithm. It was not possible to review the issue of incentives in detail due to under-reporting.

This synthesis used a comprehensive strategy and creative approach to identify potential studies on acceptability within a large and diverse literature on TB screening. The main strengths of the analysis are the diverse sources from which the results were drawn and the harmonization of disparate study results into coherent, digestible information. There are multiple limitations identified in the design and interpretation of the data included in this review. Better documenting and reporting efforts to facilitate the study of acceptability and reasons for refusal and limited uptake where it occurs. Qualitative studies embedded in prevalence surveys are recommended to shed light on the reasons why certain approaches are unacceptable.

FUNDING

This study was funded by the United States Agency for International Development under the USAID Tuberculosis CARE I, Cooperative Agreement No. AID-OAA-A-10-000020. The funder had no role in the study.

Appendix 1

Table 9.Western Pacific Regional table of community studies reporting prevalence >100/100,000

country	location	study design	author	pub year
Cambodia	countrywide	follow-up (after 2 yrs) of people with CXR abnormalities identified in prevalence survey (26)	Okada	2006
Cambodia	countrywide	nationwide prevalence survey	Williams	2008
Cambodia	countrywide	nationwide prevalence survey	CENAT	In progress
China	countrywide	nationwide prevalence survey	China TB Control Collaboration	2004
China	countrywide	prevalence survey	Jiang	2011
Papua New Guinea	SumKar district of Madang Province	community-based prevalence survey	Phuarukoonnon	2010
Philippines	countrywide	nationwide prevalence survey	Tupasi	2009
Vietnam	countrywide	prevalence survey	Hoa	2010
Vietnam	countrywide	prevalence survey	Hoa	2011

Table 10. African regional table of community studies reporting prevalence >100/100,000

country	location	study design	author	pub year
Guinea Bissau	6 suburban districts, capital Bissau	community-based prevalence survey	Bjerregaard-Andersen	2010
Kenya	Nyanza province, Western Kenya	prevalence survey	van 't Hoog	2011
South Africa	Worcester	survey at high schools	Mohamed	2011
South-Africa	Ravensmead and Uitsig communities, Cape Town	community-based prevalence survey	Den Boon	2007
South-Africa	2 communities, Cape Town	community-based prevalence survey	Den Boon	2006
South-Africa	township	community-based prevalence survey	Middelkoop	2010
South-Africa	township	community-based prevalence survey	Wood	2007
South-Africa	township	notified TB incidence	Wood	2007
Uganda	Kawempe division, Kampala	community-based prevalence survey	Guwatudde	2003
Uganda	Kisenyi slum, Kampala	community-based prevalence survey	Sekandi	2009
Uganda	Rubaga division of Kampala	Community-based prevalence survey	Sekandi-Nabbuye	2010
Zambia	sub-districts of Lusaka province	community-based prevalence survey	Ayles	2009
Zimbabwe	suburbs of Harare	community-based prevalence survey	Corbett	2009
Zimbabwe	Harare	2 year follow-up of business workers	Corbett	2007
Zimbabwe	suburbs of Harare	capture-recapture of routinely diagnosed patients and electronic TB case register	Corbett	2009
Zimbabwe	Harare	prevalence survey among business workers included in incidence study	Corbett	2010
Zimbabwe	Harare	prevalence survey among business workers included in incidence study	Corbett	2007

Table 11. Latin America regional table of community studies reporting prevalence >100/100,000

country	location	study design	author	pub year
Brazil	Surui tribe, Randonia State, Amazon	community-based prevalence survey	Basta	2006
Brazil	Rio de Janeiro, favela (squatter settlement)	community-based prevalence survey	Miller	2010
Ecuador	Chine / Cotopaxi	community-based prevalence survey	Romero Sandoval	2007

Table 12. South East Asian Regional Table of community studies reporting prevalence >100/100,000

country	location	study design	author	pub year
India	tribes, Madhya Pradesh, Central India	community-based prevalence survey	Bhat	2009
India	Tiruvallur district, Tamil Nadu, South India	prevalence survey	Gopi	2003
India	Jumma district	community-based prevalence survey	Gupta	2002
India	tribe, Island Car Nicobar	community-based prevalence survey	Murhekar	2004
India	Saharia tribe, Madhya Pradesh, Central India	community-based prevalence survey	Rao	2010 (1)
India	Bharia tribe, Patal Kot valley, Chhindwara District, Madhya Pradesh, Central India	community-based prevalence survey	Rao	2010 (2)
India	Tiruvallur district, South India	community-based prevalence survey	Santha	2003
India	Tiruvallur district, Tamilnadu, South India	prevalence survey	Subramani	2007
India	Tiruvallur district, South India	community-based prevalence survey	Balasubramanian	2004
India	Tiruvallur district, Tamilnadu, South India	prevalence survey	Subramani	2008
Myanmar	Yangon division	prevalence survey	Lwin	2007
Myanmar	National-prevalence survey	prevalence survey	MOH	2010
Thailand	hill tribe, Chiang Rai	community survey through junior school students (who find coughers and collect sputum)	Luangjina	2009

Table 13 Eastern Mediterranean regional table of Community studies reporting prevalence >100/100,000

country	location	study design	author	pub year
Pakistan	two neighborhoods, Karachi	community-based prevalence survey	Akhtar	2007

Table 14 European regional table of Community studies reporting prevalence >100/100,000

country	location	study design	author	pub year
Kosovo	Not reported	community survey	Kurhasani	2009

Table 15: Selected Characteristics of Community-Based Studies

author	pubyear	country	location	setting	study design
Akhtar	2007	Pakistan	karachi	two neighbourhoods, Karachi	community-based prevalence survey
Alebachew	2011	Ethiopia	country-wide	urban+rural	nationwideprevalence
Ayles	2009	Zambia	sub-districts of Lusaka province	urban + rural	community-based prevalence survey
Basta	2006	Brazil	Surui tribe, Randonia State, Amazon	rural	community-based prevalence survey
CENAT	2012	Cambodia	countrywide	urban + rural	nationwide prevalence survey
China TB Control Collaboration	2004	China	countrywide	urban + rural	nationwide prevalence survey
Corbett	2009	Zimbabwe	suburbs of Harare	urban	community-based prevalence survey
Corbett	2010	Zimbabwe	suburbs of Harare	urban	community-based prevalence survey
Demissie	2002	Ethiopia	Addis ababa	urban	prevalence survey
Den Boon	2006	South-Africa	2 communities, Cape Town	urban	community-based prevalence survey
Den Boon	2007	South-Africa	Ravensmead and Uitsig communities, Cape Town	urban	community-based prevalence survey
Gopi	2003	India	Tiruvallur district, Tamilnadu, South India	urban + rural	prevalence survey
Guwatudde	2003	Uganda	Kawempe division, Kampala	peri-urban	community-based prevalence survey
Lwin	2007	Myanmar	Yangon division	urban + rural	prevalence survey
Middelkoop	2010	South-Africa	township	peri-urban	community-based prevalence survey
Miller	2010	Brazil	Rio de Janeiro, favela (squatter settlement)	urban	community-based prevalence survey
MOH Myanmar	2011	Myanmar	countrywide	urban + rural	nationwide prevalence survey
MOH Pakistan	2012	Pakistan	countrywide-non-conflict	urban + rural	nationwide prevalence survey
Romero-Sandoval	2007	Ecuador	Chine / Cotopaxi	mountainous / rural	community-based prevalence survey
Salim	2004	Bangladesh	Damien Foundation covered areas	not indicated	prevalence survey
Satyanarayana	2011	India	countrywide	urban + rural	nationwide prevalence survey (self-reported prevalence)
Sebhatu	2007	Eritrea	countrywide	not indicated	nationwide prevalence survey
Sekandi	2009	Uganda	Kisenyi slum, Kampala	peri-urban	community-based prevalence survey
Shargie	2006	Ethiopia	Lemo district, Southern Ethiopia	rural	community-based prevalence survey

Subramani	2007	India	Tiruvallur district, Tamilnadu, South India	urban + rural	prevalence survey
Subramani	2008	India	Tiruvallur district, Tamilnadu, South India	rural	prevalence survey
Thorson	2004	Vietnam	Bavi district, Ha Tay Province	not indicated	population-based survey
Tupasi	2009	Philippines	countrywide	urban + rural	nationwide prevalence survey
van 't Hoog	2011	Kenya	Nyanza province, Western Kenya	rural	prevalence survey
Williams	2008	Cambodia	countrywide	urban + rural	nationwide prevalence survey
Wood	2007	South-Africa	township	peri-urban	community-based prevalence survey
Yimer	2009	Ethiopia	Mecha district, Amhara region	rural	community-based prevalence survey
Zaman	2011	Bangladesh	countrywide	urban + rural	nationwide pervalence survey
Bhat	2009	India	tribes, Madhya Pradesh, Central India	rural	community-based prevalence survey
Gupta	2002	India	Jumma district	rural	community-based prevalence survey
Luangjina	2009	Thailand	hill tribe, Chiang Rai	rural	community survey through junior school students (who find coughers and collect sputum)
Murhekar	2004	India	tribe, Island Car Nicobar	not indicated	community-based prevalence survey
Rao	2010 (1)	India	Saharia tribe, Madhya Pradesh, Central India	rural	community-based prevalence survey
Rao	2010 (2)	India	Bharia tribe, Patal Kot valley, Chhindwara District, Madhya Pradesh, Central India	rural	community-based prevalence survey
Santha	2003	India	Tiruvallur district, South India	rural + urban	community-based prevalence survey

Table 16: Studies in which Sputum Samples were requested from All Community Members *Regardless Of Symptoms*

author	**pubyear**	**country**	**location**	**setting**	**study design**	inclusion	**exclusion**	**study population**
Ayles	2009	Zambia	sub-districts of Lusaka province	urban + rural	community-based prevalence survey	>=15 years	no consent, not contactable after 3 visits	general population
Corbett	2009	Zimbabwe	suburbs of Harare	urban	community-based prevalence survey	>=16 years	no consent; not contactable after 3 visits (incl weekend)	general population
Corbett	2010	Zimbabwe	suburbs of Harare	urban	community-based prevalence survey	>=16 years	no consent; not contactable after 3	general population

							visits (incl weekend)	
Den Boon	2006	South-Africa	2 communities, Cape Town	urban	community-based prevalence survey	>=15 years	none	general population
Den Boon	2007	South-Africa	Ravensmead and Uitsig communities, Cape Town	urban	community-based prevalence survey	>=15 years, consent	none	general population
Middelkoop	2010	South-Africa	township	peri-urban	community-based prevalence survey	>=15 years, resident in area	no consent; not contactable after 5 home visits	general population
Satyanarayana	2011	India	countrywide	urban + rural	nationwide prevalence survey (self-reported prevalence)	stayed in the household at least 6 months prior to survey	none	general population
Sebhatu	2007	Eritrea	countrywide	not indicated	nationwide prevalence survey	slept in the household the night before the survey	none	general population
van 't Hoog	2011	Kenya	Nyanza province, Western Kenya	rural	prevalence survey	>=15 years, residing in cluster for at least 1 month	none	general population
Wood	2007	South-Africa	township	peri-urban	community-based prevalence survey	>=15 years	no consent; not contactable after 5 home visits	general population

Appraisal of individual studies' quality

There was a great deal of variability in the quality of the 45 studies reviewed. No study met all the quality criteria. Low scores were due to both poor design and omission of methodological information. Southern and East African studies tended to provide more details and employ more rigorous assessment of limitations, potential bias, role of funding, analysis, etc. Twenty-four studies scored in the 6-11 range (Table 17)

Table 17: Studies with a strobe score of 6 or more out of 12

author	pubyear	country	STROBE score
Ayles	2009	Zambia	11
Corbett	2009	Zimbabwe	11
Corbett	2009	Zimbabwe	11
Corbett	2010	Zimbabwe	10
van 't Hoog	2011	Kenya	10
Subramani	2008	India	9
Akhtar	2007	Pakistan	8
Corbett	2007	Zimbabwe	8
Corbett	2007	Zimbabwe	8
Den Boon	2007	South-Africa	8
Hoa	2010	Vietnam	8
Bjerregaard-Andersen	2010	Guinea Bissau	7
China TB Control Collaboration	2004	China	7
Wood	2007	South-Africa	7
Balasubramanian	2004	India	6
Hoa	2011	Vietnam	6
Miller	2010	Brazil	6
Williams	2008	Cambodia	6

A sizable fraction (n=209 or 19%) of the studies selected in the first screen had a STROBE score of zero, indicating inadequate disclosure of the methodologies to permit the assessment of the study quality (Table B). Most importantly to the main question of this review, only 5 (12%) of included studies gave detailed attention to reasons for non-participation (aka lack of acceptability of TB screening).[4]

In many cases the information on studies with a score of 0 came from abstracts, posters, or draft papers and thus were not indicative of the quality of study.

Table 18 studies with a STROBE score of zero

Author	Year	country	STROBE SCORE	Illustrative comments
Fadzilah	2006	Malaysia	0	It is not clear how many participants underwent which stages of the screening and how many ultimately produced a sputum. In discussion the low sputum uptake is mentioned as a limitation

[4] Ayles, Bai, Zaman, and Bjerregaard-Andersen (2x) were the five authors who indicated reasons for refusal.

Gopi	2006	India	0	This study does secondary data analysis of (16) and (17). Aim of this study was to look at sensitivity and specificity of different screening methods
Gopi	2008	India	0	
Gupta	2002	India	0	This study has very limited description of the methodology; difficult to judge whether study is of good quality and how it was exactly carried out
Jiang	2011	China	0	This is an abstract and therefore very limited information on the methodology is reported.
Kurhasani	2009	Kosovo	0	This is an abstract and therefore very limited information on the methodology is reported.
Luangjina	2009	Thailand	0	This is an abstract and therefore very limited information on the methodology is reported.
Mahomed	2011	South Africa	0	Consult full Aeras EB for details
Nabbuye-Sekandi	2010	Uganda	0	This is an abstract and therefore very limited information on the methodology is reported to date.
Odermatt	2007	Laos	0	This survey was not conducted in a systematic way to obtain a reliable prevalence estimate (not aim of study).
Okada	2006	Cambodia	0	This is a TSRU report containing less information on the methodology compared to a research paper.
Phuarukoonnon	2010	Papua New Guinea	0	Only the abstract was reported to date, but publication is forthcoming, author contacted for manuscript
Radhakrishna	2006	India	0	
Shahea-Hossain	2010	Bangladesh	0	Consult full WHO prevalence survey report
Soemantri	2007	Indonesia	0	

Appendices

Appendix 1 Search Strategy PICO Q. 1:

What is the acceptability of community-based TB symptom screening (2-step) in the settings with an estimated prevalence of All forms of TB above 100/100,000?

Inclusion criteria:

1. Time span = 2000 - November 2011
2. Languages = English, Spanish, Portuguese, French, Dutch, German, and Japanese
3. Peer-Review literature: EMBASE, Web of Science, LILACS and PubMed (Medline)
4. Conference abstracts from 2000-2011 & unpublished literature: WHO website or KNCV Tuberculosis Foundation Archive, IUATLD / UNION Conferences

The **Title** will contain one or more of the following terms:

- tubercul*
- lung tuberculosis
- pulmonary consumption
- consumption, pulmonary
- TB
- TB/HIV

AND the article will also have one or more of these terms as a MeSH heading or subject:

1. case find*
2. mass + radiograph*
3. screen*
4. contact examin*
5. screening survey*
6. cross-sectional
7. case-detect*
8. detect*
9. prevalen*
10. contact investigat*
11. algorithm
12. household + survey
13. employ*+ testing
14. undiagnos*
15. contact trac*
16. inciden*
17. checking
18. pre-entry
19. intensified + case
20. active + case
21. passive
22. TB suspect*
23. notificat*

SEARCH STRATEGY EXCLUSION CRITERIA

1. The search strategy **excluded** TB studies that mention special populations unsuitable for vaccine trials in HIV-neg adults in their **TITLES**

1. prison*
2. intravenous drug user
3. homeless
4. migrant*
5. diabet*
6. alcohol*
7. substance abus*
8. mental ill*
9. hepatit*
10. child*
11. infant
12. refuge

2. The search strategy **excluded** TB articles with **TITLES** containing the following words:

1. zoonotic
2. deer
3. cattle
4. possum
5. macaque*
6. guinea pig*
7. animal
8. mice
9. regimen
10. fixed-dose
11. side-effect*
12. biopsy
13. interferon-gamma
14. pathophysiology
15. clinical + outcome*
16. meningitis
17. treatment+ outcome*
18. genotyp*
19. missing+data
20. drug resistance survey*
21. re-vaccination
22. candidate
23. bovi*
24. non-tubercul*
25. strain
26. diabet*
27. case+ report
28. dose-response
29. adverse
30. phenotyp
31. immune correlate*
32. modelling

3. The search strategy **excluded** TB studies from **journals** on these subject areas:

1. Agriculture,
2. Allergy
3. Anatomy & Morphology
4. Anesthesiology
5. Applied Radiology,
6. Biochemistry & Molecular Biology
7. Biology
8. Biophysics

9. Cardiac & Cardiovascular Systems
10. Cell Biology
11. Chemistry,
12. Chemistry, Medicinal
13. Chemistry, Organic
14. Dentistry,
15. Dermatology
16. Ecology
17. Endocrinology & Metabolism
18. Engineering, Biomedical
19. Environmental Sciences
20. Evolutionary Biology
21. Food Science & Technology
22. Gastroenterology & Hepatology
23. Genetics & Heredity
24. Geriatrics & Gerontology
25. Gerontology
26. Hematology
27. History & Philosophy Of Science
28. Immunology
29. Legal Mathematical & Computational Biology
30. Nephrology/Neuroimaging
31. Nuclear Medicine
32. Nutrition & Dietetics
33. Oncology
34. Ophthalmology
35. Oral Surgery & Medicine
36. Orthopedics
37. Otorhinolaryngology
38. Parasitology
39. Pathology
40. Pharmacology & Pharmacy
41. Physical
42. Rehabilitation
43. Rheumatology
44. Surgery
45. Toxicology
46. Urology
47. Veterinary Sciences
48. Virology
49. Zoology

Table 18 Search Strategies for Review 1

DATABASE	SEARCH TERMS	AND	LIMITS
PubMed/Medline	(“case finding” OR ("Mass Screening"[MeSH Terms] OR "Mass Chest X-Ray"[MeSH Terms]) OR “screen*” OR “contact examination” OR “screening survey*” OR “cross-sectional” OR “case-detection” OR “detect*” OR “prevalen*” OR “contact investigation” OR “contact tracing” OR “algorithm” OR “household survey” OR “employment testing” OR “undiagnosed” OR “contact tracing” OR “inciden*” OR “checking” OR “pre-entry” OR “intensified case finding” OR “active case” OR “passive” OR “TB suspect*” OR “notification” OR “notified”)	**AND**((“tuberculosis”[MeSH Terms] OR "tuberculosis" OR "Pulmonary Consumption" OR "Consumption, Pulmonary" OR "Pulmonary Phthisis" OR "Tuberculoses") OR ("Mycobacterium tuberculosis"[MeSH terms]))	**NOT** ((“prison*” OR “intravenous drug user” OR “homeless” OR “migrant*” OR “diabet*” OR “alcohol*” OR “substance abuse” OR “mental ill*” OR “hepatit*” OR “child*” OR “infant” OR “refuge”) OR (“zoonotic” OR “deer” OR “cattle” OR “possum” OR “macaque*” OR “guinea pig*” OR “animal” OR “mice” OR “regimen” OR “fixed-dose” OR “side-effect*” OR “biopsy” OR “interferon-gamma” OR “pathophysiology” OR “clinical outcome*” OR “meningitis” OR “treatment outcome*” OR “genotyp*” OR “missing data” OR “drug resistance survey*” OR “re-vaccination” OR “candidate” OR “bovi*” OR “non-tuberculosis” OR “strain” OR “diabet*” OR “case report” OR “dose-response” OR “adverse” OR “phenotyp” OR “immune correlates” OR “modeling”)) *Language=English, German, French, Spanish, Portuguese, Japanese* *Publication date: 01-01-2000 until 01-11-2011* **# titles: 2541**
WEB OF SCIENCE	TS=(case find* OR mass SAME radiograph* OR screen* OR contact examin* OR screening survey* OR cross-sectional OR case-detect* OR detect* OR prevalen* OR contact investigat* OR contact trac* OR algorithm OR household SAME survey OR employment SAME testing OR undiagnos* OR inciden* OR checking OR pre-entry OR intensified SAME case OR active SAME case OR	**AND** TI = (tubercul* OR lung tuberculosis OR pulmonary consumption OR consumption, pulmonary OR TB) *DocType=All*	**NOT** TI = (prison* OR intravenous drug user OR homeless OR migrant* OR diabet* OR alcohol* OR substance abus* OR mental ill* OR hepatit* OR child* OR infant OR refuge OR zoonotic OR deer OR cattle OR possum OR macaque* OR guinea pig* OR animal OR vaccin* OR mice OR regimen OR fixed-dose OR side-effect* OR survival OR biopsy OR interferon-gamma OR pathophysiology OR mortality OR

	passive OR TB suspect* OR notificat*)	*document types; Language=English, German, French, Spanish, Portuguese, Japanese*	clinical SAME outcome* OR meningitis OR treatment SAME outcome* OR genotyp* OR missing SAME data OR drug resistance survey* OR re-vaccination OR candidate OR bovi* OR non-tubercul* OR strain OR diabet* OR case+ report OR dose-response OR adverse OR phenotyp OR immune correlate*) **AND** Refined by: [excluding] Subject Areas= **# titles: 4582** AND [excluding] Countries/Territories=(ARGENTINA OR AUSTRALIA OR HUNGARY OR AUSTRIA OR BELGIUM OR IRAN OR IRELAND OR ISRAEL OR ITALY OR JAPAN OR SINGAPORE OR KUWAIT OR SPAIN OR CANADA OR SWEDEN OR CHILE OR SWITZERLAND OR COLOMBIA OR CUBA OR CZECH REPUBLIC OR MEXICO OR DENMARK OR TUNISIA OR EGYPT OR NETHERLANDS OR TURKEY OR NEW ZEALAND OR FINLAND OR NORWAY OR USA OR FRANCE OR GERMANY OR GREECE OR POLAND OR PORTUGAL) **# titles: 1545**
EMBASE	(case find* or mass radiograph* or screen* or contact examin* or screening survey* or cross-sectional or case-detect* or detection or detecting or prevalen* or prevalent or contact investigation or algorithm or household survey or employment testing or undiagnosed or contact tracing or inciden* or incident or checking or pre-entry or intensified case or active case or passive or TB suspect or notifi*).mp.	**AND** (tuberculosis or lung tuberculosis or pulmonary consumption or consumption, pulmonary or pulmonary phthisis or TB).m_titl.	**NOT** (prison OR intravenous drug user OR homeless OR migrant OR diabet* OR alcohol OR substance abus* OR mental ill OR hepatit* OR child* OR infant OR refuge OR zoonotic OR deer OR cattle OR possum OR macaque OR guinea pig OR animal OR vaccin OR mice OR regimen OR fixed-dose OR side-effect* OR survival OR biopsy OR interferon-gamma OR pathophysiology OR mortality OR clinical outcome* OR meningitis OR treatment outcome OR genotyp* OR missing data OR drug resistance survey OR re-vaccination OR candidate OR bovi* OR non-tuberculosis

			OR strain OR diabet* OR case report OR dose response OR adverse OR phenotype OR immune correlate).m_titl. **# titles: 7668**
WHO Global Health Library (Regional Indexes)	tuberculosis OR TB OR "pulmonary consumption" OR "pulmonary phthisis" OR "consumption, pulmonary" (Title) # titles: 9161	**AND** Refined by: MAIN SUBJECT Tuberculosis # titles: 3257 Further refined by: TYPE OF STUDIES **Prevalence studies #79** **Incidence studies #73** **Cohort studies # 18** (thus excluding case reports, case control, systematic reviews)	**OR** Refined by: MAIN SUBJECT Tuberculosis, Pulmonary # titles: 1574 Further refined by: TYPE OF STUDIES **Prevalence studies #78** **Incidence studies #54** **Cohort studies # 20** **OR** Refined by: DISEASE Tuberculosis # titles: 2868 Further refined by: DISEASE **Epidemiology #572**

Web of Science search: "Refined by" as specified in the proposal.

Refined by: [excluding] Subject Areas=(Agriculture OR Allergy OR Anatomy & Morphology OR Anesthesiology OR Applied Radiology OR Biochemistry & Molecular Biology OR Biology OR Biophysics OR Cardiac & Cardiovascular Systems OR Cell Biology OR Chemistry OR Chemistry, Medicinal OR Chemistry, Organic OR Dentistry OR Dermatology OR Ecology OR Endocrinology & Metabolism OR Engineering OR Biomedical OR Environmental Sciences OR Evolutionary Biology OR

Food Science & Technology OR Gastroenterology & Hepatology OR Genetics & Heredity OR Geriatrics & Gerontology OR Gerontology OR Hematology OR History & Philosophy Of Science OR Immunology OR Legal Mathematical & Computational Biology OR Nephrology/Neuroimaging OR Nuclear Medicine OR Nutrition & Dietetics OR Oncology OR Ophthalmology OR Oral Surgery & Medicine OR Orthopedics OR Otorhinolaryngology OR Parasitology OR Pathology OR Pharmacology & Pharmacy OR Physical OR Rehabilitation OR Rheumatology OR Surgery OR Toxicology OR Urology OR Veterinary Sciences OR Virology OR Zoology)

Appendix 3 data extraction form Q.1

GENERAL INFORMATION	
ID	
IDsub	
Author	
Title	
Journal	
Year	
Language	☐ English ☐ Spanish ☐ Portuguese ☐ French ☐ Dutch ☐ German ☐Japanese
Reviewer	☐ article ☐ abstract ☐ report ☐ website ☐ other, specify……
Type	☐ article ☐ abstract ☐ report ☐ website ☐ other, specify……
Report	☐ manuscript ☐ annual report ☐ unknown ☐ other, specify……
Study period	
Country	
Location	
Setting	☐ urban ☐ peri-urban ☐ rural ☐ mountainous ☐ other, specify……
METHODOLOGY	
Study design	☐ prevalence survey ☐ community survey ☐ risk group screening ☐ notification data ☐ other, specify……
Sampling	☐ random ☐ systematic ☐ stratified ☐ clustered ☐ multistage
Sampling_step1	☐ districts ☐ villages ☐ enumeration areas ☐ households ☐ individuals ☐ other, specify……
Sampling_step2	☐ districts ☐ villages ☐ enumeration areas ☐ households ☐ individuals ☐ other, specify……
Sampling_step3	☐ districts ☐ villages ☐ enumeration areas ☐ households ☐ individuals ☐ other, specify……
Sampling_step4	☐ districts ☐ villages ☐ enumeration areas ☐ households ☐ individuals ☐ other, specify……
Inclusion criteria	
Exclusion criteria	
Study-population	☐ general populations ☐ contacts ☐ other, specify……
Screening	☐ yes ☐ no ☐ maybe
Screening_step1	☐ symptoms ☐ CXR ☐ TST ☐ other, specify……
Screening_step2	☐ symptoms ☐ CXR ☐ TST ☐ other, specify……
Screening_step3	☐ symptoms ☐ CXR ☐ TST ☐ other, specify……
Symptoms	☐ cough ☐ cough≥2 weeks ☐ fever ☐ weight loss ☐ night sweats ☐ other, specify……

Sputum strategy	☐ spot-morning-spot ☐ spot-morning ☐ morning-spot ☐ spot-spot ☐ unknown ☐ other, specify……
LABORATORY TESTING & DIAGNOSIS	
Bacteriological case definition	
Clinical case definition	
Diagnosis ZN	☐ yes ☐ no ☐ maybe
Diagnosis FM	☐ yes ☐ no ☐ maybe
Diagnosis LJ	☐ yes ☐ no ☐ maybe
Diagnosis MGIT	☐ yes ☐ no ☐ maybe
Identification MTB	☐ yes ☐ no ☐ maybe
Diagnosis Xpert	☐ yes ☐ no ☐ maybe
Laboratory QA	
STUDY OUTCOMES	
Outcome	☐ prevalence ☐ incidence ☐ notification ☐ other, specify……
Outcome subgroups age, sex, HIV-status	☐ yes ☐ no
Other subgroups	☐ yes ☐ no
Sub_other1	
Sub_other2	
Sub_other3	
Follow-up	☐ yes ☐ no ☐ unknown
HIV INFORMATION	
Previous HIV test	☐ yes ☐ no ☐ unknown
Known HIV status	☐ yes ☐ no ☐ unknown
HIV test results	☐ yes ☐ no ☐ unknown
HIV subgroups	☐ yes ☐ no
HIV indirect	☐ yes ☐ no
HIV indirect group	
HIV indirect source	
HIV antenatal	☐ yes ☐ no
HIV antenatal source	
STUDY POPULATION	
Sampling number 1	
Sampling number 2	
Sampling number 3	
Sampling number	

4			
Total population size			
Eligible		Percentage eligible	%
Screened		Percentage screened	%
Included		Percentage included	%
Males		Percentage males	%
Age		☐ mean ☐ median	
Age range		☐ min - max ☐ interquartile	
RESULTS / OUTCOMES			
Denominator			
TB patients detected		TB patients on treatment	
Prevalence		95% CI	
Incidence		95% CI	
Outcome age			
Outcome sex	Males:	Females:	
Outcome HIV	HIV neg:	HIV pos:	
Outcome other 1			
Outcome other 2			
Outcome other 3			
STROBE – STUDY QUALITY			
Potential confounders and effect modifiers discussed?			
Potential biases discussed?			
Efforts to address potential sources of bias?			
Study size / sample size explained?			
Explained how missing data were addressed?			
Sampling strategy accounted for in analysis?			
If applicable, lost to follow-up addressed?			
Reasons for non-participation given?			
Confounder adjusted estimates provided?			
95% confidence intervals provided?			
Study limitations discussed?			
Generalizability?			
Funding source given and role of funding source?			

Appendix 4: Q1 Screening methods code book

Variable	Explanation	Answer categories
ref_id	reference number in EndNote Data Base File TOM	
author	first author	
pub year	year of publication	
ref_idsub	subcategories if data on multiple subgroups are presented	
type	type of reference	article, report, website
report	how are results reported?	manuscript, annual report, others, unknown
study_period	period of data collection	
country	country study is performed	
location	detailed information about study location	province, district, city, hospital
setting	study setting	urban, peri-urban, rural, mountainous, …
study design	study design	prevalence survey, community survey, risk group screening, notification data, …
sampling	sampling frame	random, systematic, stratified, clustered, multistage
sampling_step1		districts, villages, enumeration areas, households, individuals
sampling_step2		districts, villages, enumeration areas, households, individuals
sampling_step3		districts, villages, enumeration areas, households, individuals
sampling_step4		districts, villages, enumeration areas, households, individuals
inclusion	inclusion criteria	
exclusion	exclusion criteria	
study population	target population of the study	general population, mine-workers, prisoners, contacts, …
screening	was a form of screening done	yes, no, maybe
screening_step1	what was used for screening step 1?	symptoms, CXR, TST, …
screening_step2	what was used for screening step 2?	symptoms, CXR, TST, …
screening_step3	what was used for screening step 3?	symptoms, CXR, TST, …
symptoms	if symptom screening was used, list symptoms	cough, cough > 2 weeks, fever, weight loss, night sweats, …
sputums	what was the sputum collection strategy	spot-morning-morning, spot-spot, …
tbcase_def_bact	What is the TB case definition for bacteriologic confirmed TB?	
tbcase_def_clin	What is the clinical TB case definition?	
diagnosis_ZN	ZN smear used for diagnosis	yes, no
diagnosis_FM	FM smear used for diagnosis	yes, no
diagnosis_LJ	LJ used for diagnosis	yes, no
diagnosis_MGIT	MGIT used for diagnosis	yes, no
identification	culture identification done to differentiate NTM and MTB	yes, no, maybe
diagnosis_Xpert	Xpert used for diagnosis	yes, no
lab_QA	list laboratory quality assurance measures	
outcome	calculated study outcome	prevalence, incidence, notification

		rate, …
outcome_subgroups	is outcome reported for subgroups age, seks or HIV?	yes, no
sub_other	is outcome reported for other subgroups?	yes, no
sub_oth1	specifiation of which other subgroup outcome is reported	
sub_oth2	specifiation of which other subgroup outcome is reported	
sub_oth3	specifiation of which other subgroup outcome is reported	
follow-up	were patients followed-up?	yes, no
hiv_previoustest	is info on previous HIV-testing reported?	yes, no
hiv_self-reported	is info on previous HIV-testing results reported?	yes,no
hiv_test	was HIV-testing done?	yes, no

Appendix 5 Q. 1 TB burden codebook

Variable	Explanation
ref_id	
author	first author
pub year	year of publication
sampling_n1	number of sampling units in sampling step 1
sampling_n2	number of sampling units in sampling step 2
sampling_n3	number of sampling units in sampling step 3
sampling_n4	number of sampling units in sampling step 4
pop_total	total population size in study area (sampling frame)
eligble	number eligible for the study
peligible	percentage of eligible (eligible / total population)
screened	number screened for the study
pscreened	percentage screened for the study (screened / eligible)
included	number included in the study
pincluded	percentage included in the study
males	number of males
pmales	percentage of males (males/sample size)
age	median or mean age
age_c	specify is age is median or mean
age_r	age range
age_rc	specify what range (min-max, interquartile)
denominator	denominator used for prevalence / incidence calculation
tb	number detected with tb
tb_rx	number detected with tb already on treatment
prevalence	prevalence estimate
prevlow	lower 95% CI prevalence estimate
prevup	higher 95% CI prevalence estimate
incidence	incidence estimate
inclow	lower 95% CI incidence estimate
incup	higher 95% CI incidence estimate
TB_age_rslts	outcome for age categories
TB_sex_rslts	outcome by seks
TB_hiv_rslts	outcome by HIV-status
TB_oth1_rslts	outcome for subgroup 1
TB_oth2_rslts	outcome for subgroup 2
TB_oth3_rslts	outcome for subgroup 3

Appendix 3: Acronyms

ACSM Advocacy, Communication & social Mobilization
AFB Acid-fast baccili
AFRO WHO Regional Office for Africa
AIDS Acquired Immunodeficiency Syndrome
ARTI Annual risk of tuberculosis infection
ARV Antiretroviral
AZT Zidovudine
BCG Bacille Calmette Guérin
CB Coordinating Board
CDC Centers for Disease Control and Prevention
CMS Central medical stores
DEWG DOTS Expansion Working Group
DFID Department for International Development
DOT Directly Observed Treatment
DOTS branded name of the WHO recommended tuberculosis control strategy
DOTS Internationally recommended strategy for TBc ontrol
DOTS Plus TB control strategy for multi drug resistant Tuberculosis based on the DOTS scheme
DST Drug susceptibility testing
E Ethambutol
ECHO Humanitarian Aid Office of the European Union
FDC Fixed-dose combination
FIND Foundation for Innovative New Diagnostics
GATB Global Alliance for TB Drug Development (TB Alliance)
GAVI Global Alliance for Vaccines and Immunization
GDEP Global DOTS Expansion Plan
GDF Global Drug Facility
GDP Gross Domestic Product
GFATM Global Fund to Fight AIDS, TBand Malaria
GLC Green Light Committee
GMP Good Manufacturing Practice
GNP Gross National Product
GPSTB Global Plan to Stop TB
GTRI Global TB Research Initiative
H FA Health For All
H Isoniazid
HAART Highly Active Antiretroviral Therapy
HBC High-burden countries
HIV Human immunodeficiency virus
IDU Injection Drug Users
IEC Information, education and communication
ILO International Labour Organization
INRUD International Network for the Rational Use of Drugs
IPT Isoniazid Preventive Therapy
IUATLD International Union Against Tuberculosis and Lung Disease
IVR Initiative for Vaccine Research
KNCV Royal Netherlands Tuberculosis Association
MDR TB Multi drug resistant Tuberculosis, TB bacillus resistant to at least Isoniazid and Rifampicin
MDR-TB Multidrug-resistant tuberculosis
MOH Ministry of Health
MSH Management Sciences for Health
NGO Nongovernmental organization
NIAID National Institute of Allergy and Infectious Disease
NICC National Interagency Coordination Committees
NIH National Institutes of Health
NRL National Reference Laboratory
NTP National Tuberculosis Control Programme
OECD Organization for Economic Cooperation and Development
PIA Phased implementation of activities
PIH Partners In Health
PLWHA People living with HIV/AIDS
PLWHA, PLWH People living with HIV/AIDS,
PPM Public-Private Mix
PPM-DOTS Public private mix DOTS, a strategy to involve private health care providers in DOTS strategy
QA Quality assurance
R Rifampicin
R&D Research and Development
R&D Research and development
RBM Roll Back Malaria
RICC Regional Interagency Coordination Committee
RMB Resource Mobilization
S Streptomycin
SBIR Small Business Innovative Research
SCC Short Course Chemotherapy
SEARO WHO Regional Office for South-East Asia
SRL Supranational Reference Laboratory
STB WHO Stop Tuberculosis Department
STI Sexually Transmitted Infection
SW Sex Workers
SWAP Sector Wide Approach
TASO The AIDS Support Organization
TB Tuberculosis
TB/HIV TB and HIV co-infection
TBCTA TB Coalition for Technical Assistance
TBDI TB Diagnos tics Initiative
TBVIAC Tuberculosis Vaccine Initiative Advisory Committee
TDR Special Programme on Research and Training in Tropical Diseases
UNAIDS Joint United Nations Programme on HIV/AIDS
UNICEF United Nations Children's Fund
USAID United States Agency for International Development
VCT Voluntary counselling and testing
WG Working group
WHO World Health Organization
Z Pyrazinamide

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