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AThe benefits to communities and individuals of screening for active tuberculosis disease: a systematic review

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A systematic literature review of the benefits to communities and individuals of screening for active tuberculosis disease

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Abstract

Background: Screening for tuberculosis (TB) disease aims to improve early TB case detection. The ultimate goal is to improve outcomes for people with TB and to reduce *Mycobacterium tuberculosis* transmission in the community through improved case detection, reduction in diagnostic delays and early treatment. Before screening programmes are recommended evidence is needed of individual and/or community-level benefit.

Methods: We reviewed the literature for evidence that screening for TB disease (i) initially increases the number of TB cases initiated on TB treatment, (ii) identifies cases earlier in the course of disease (iii) reduces mortality and morbidity and (iv) impacts on TB epidemiology.

Results: A total of 846 publications were identified by the search strategy, 785 publications were excluded leaving 61 publications which addressed at least one of the study questions.

Screening increases the number of cases found in the short term. In many settings more than half the prevalent TB cases in the community are undiagnosed. Screening tends to find cases earlier and with less severe disease, but this may be attributed to case-finding studies using more sensitive diagnostic methods than routine programmes. Treatment outcomes among people identified through screening are similar to treatment outcomes among those identified through passive case-finding. Current studies provide insufficient evidence to show that active screening for TB disease impacts on TB epidemiology.

Conclusion: Individual and community-level benefits from active screening for TB disease remain uncertain. So far the benefits of earlier diagnosis on patient outcomes and transmission have not been established.

Introduction

Investments in TB control on a global scale have resulted in reductions in prevalence and deaths from TB. However TB case detection has stagnated in recent years, while estimated TB incidence is declining very slowly. This has resulted in renewed interest in the potential contribution to early case detection from systematic TB screening. TB screening in HIV-infected individuals has been recommended by the World Health Organization (WHO) as part of the 'Three I's' policy initiative[1-2]. Systematic screening of household contacts of infectious TB cases has been recommended[3-5], but population-wide mass-screening has been discouraged due to uncertain impact, high cost, and poor sustainability[6-8]. Recently there has been renewed interest in systematic screening for active TB disease in risk groups, as well as population-wide screening interventions. National TB prevalence surveys have demonstrated that a large pool of undetected prevalent cases exist even in settings with well-functioning TB programmes, and many of the prevalent cases would have been difficult to reach with passive case-finding (PCF) approaches[9-11]. Several screening initiatives have been launched recently, and some have shown promising results[6, 12-13].

The ultimate goals of systematic TB screening are to improve health outcomes among people with TB and to reduce *M.tuberculosis* transmission in the community through improved TB detection, reduction in diagnostic delays and early treatment[7]. Impact evaluation of TB control interventions, however, is technically difficult and expensive and so is rarely included in programmatic or research studies.

Before screening programmes are recommended, evidence is needed of individual or community-level benefit from early diagnosis provided by screening, and that benefits outweigh any harms incurred. We reviewed the evidence of individual and/or community benefit from active TB screening focusing on: additional TB cases detected; reduction in diagnostic delay; improved treatment outcomes; and impact on TB epidemiology.

Methods

Definitions

We define screening for active tuberculosis as the *systematic identification of people with suspected active TB in a predetermined target group by the application of tests, examinations, or other procedures which can be applied rapidly*. Among those with suspected TB, the diagnosis needs to be established through application of one or several diagnostic tests and clinical assessment. Screening can be either done as an outreach activity in the general community, among TB contacts, and in other specific high risk groups, or among people seeking care, including people who seek care for other reasons than symptoms compatible with TB. The latter category includes, for example, people coming for regular check-up of conditions that are risk factors for TB, such as HIV and diabetes. PCF is defined as detecting active TB disease among symptomatic patients who self-present to medical services for diagnosis of symptoms, with a specific focus on people with typical TB symptoms, such as chronic cough. Active case-finding (ACF) implies screening through outreach activities outside health services. Enhanced Case Finding (ECF) primarily aims to make a population aware of TB symptoms (through publicity and education), and encourages self-presentation to medical services, which may be decentralised as part of the intervention. This in effect means ECF is PCF combined with intensified health information[7]. However, ECF can also include a screening element, for example as part of a chest/health camp, in which case the intervention is a combined ACF/ECF intervention. In this paper, we will use "screening" to describe ACF interventions and ECF for interventions that mainly focus on health information.

Specific questions

The review addressed 4 specific questions:

1. Does screening for TB disease increase the number of TB cases detected compared to PCF?
2. Does screening for TB disease identify cases at an earlier stage of TB disease than PCF?
3. Is there a difference in TB treatment outcomes between TB cases found by screening and those found through PCF?
4. Does the addition of screening for TB disease to PCF affect TB incidence or prevalence in the community?

Inclusion criteria

Inclusion criteria for studies addressing the four questions are outlined below.

Does screening for TB disease increase case detection? Studies would ideally be longitudinal with continuous or repeated rounds of screening in addition to PCF, reporting the number of cases detected by screening and PCF over time. This would allow the effects of screening to be assessed beyond the first round, in which a large number of long-term undetected cases may be found. However,

due to the paucity of such studies the inclusion criteria were widened to include cross-sectional studies of one-off screening, reporting the number or proportion of TB cases detected by screening and passively; and prevalence surveys reporting the proportion of undiagnosed TB.

Does screening for TB disease identify cases earlier? All studies comparing at least one of i) the length of time between reported onset of symptoms and start of treatment, ii) sputum positivity rate or iii) chest X-ray abnormalities at time of diagnosis, in TB cases detected through screening and passively were eligible. Contact tracing studies were eligible if the index cases were representative of all TB cases detected passively (so that they could form the comparison group).

Does screening for TB disease affect treatment outcome? Ideally studies should allow direct comparison of outcomes of patients identified actively or passively in the same area. However, as there were few such studies, we included all studies reporting on outcomes of TB cases identified actively, for comparison with WHO target outcomes.

Does screening for TB disease affect TB epidemiology? All studies comparing TB prevalence, incidence or transmission in communities receiving screening and PCF and communities receiving PCF only were eligible. Studies investigating impact in specific groups (such as prisons, mines or risk groups) and did not investigate the impact on the general population were excluded. Study designs could be before-after comparisons, cluster randomised controlled trials or quasi-experimental designs.

Search strategy

The initial search used papers selected on initial screening by an existing systematic review[14] which had already identified TB case-finding studies published up to October 2010. No exclusions were made on the study population, geographical setting, language or year of publication. This review identified a total of 827 publications and abstracts: 759 published in English, 20 in Spanish, 25 in Japanese and 23 in Russian. In addition, data from prevalence surveys provided by the WHO were added, together with further papers identified by experts in the field, and unpublished data from the recently completed Zamstar study. Since treatment outcome data might be published separately from the initial screening results, additional searches were undertaken to identify subsequent publications reporting TB treatment outcomes of all studies with at least 40 TB cases identified through screening and published after 1992 (the time when DOTS became widely available). Searches used Ovid Medline using the first or the last authors' names combined with "treatment outcomes" and "tuberculosis". In addition first and last authors of studies published between 2005 and 2011 were contacted directly.

Selection of publications for inclusion

The full text of all publications identified was screened for relevance for any of the four outcomes. This was done in stages: an initial screen to check for possible eligibility, then a more detailed screen of retained papers, then data extraction of eligible publications. The first 120 publications reviewed in the initial screen were done in duplicate to ensure consistency, and all data extraction of included papers

was done in duplicate using a standardised data extraction tool. Any discrepancies were resolved by discussion.

Data synthesis and analysis

Settings, populations (e.g. homeless, refugees, general population) and screening approach differed considerably. Due to the heterogeneity of studies a narrative approach was adopted for data synthesis. A formal meta-analysis was conducted where appropriate, which was only for the treatment outcome analysis. The relative risk (RR) of successful treatment by case-finding method was calculated, and pooled with the DerSimonian-Laird random-effects method, which treats studies as a sample of all potential studies, and incorporates an additional between-study component to the estimate of variability. The I-squared statistic was calculated as a measure of the proportion of the overall variation that is attributable to between study heterogeneity.

Results

Identification of studies

Of the 828 publications identified in the previous search, 737 were full articles and 91 abstracts. In addition we reviewed unpublished studies and studies identified through expert opinion, prevalence surveys from Cambodia and Myanmar and conference abstracts and unpublished reports from the Zamstar study and identified 19 relevant studies. 712 publications were excluded on the initial screen and 74 subsequently leaving 61 publications which addressed at least one of the study questions.

The studies covered a range of different populations and used a variety of screening algorithms. Details are summarised in table 1. Screening included symptoms, chest X-ray and sputum for smear microscopy and/or culture. A key distinction is whether the methods were used sequentially or together, and in particular, whether only symptomatic cases were screened further, or whether the initial screen included bacteriology or X-ray even on asymptomatic cases (thus increasing the sensitivity of the screen).

1) Does screening for TB disease increase the number of TB cases detected?

a) Studies assessing the contribution of screening over time

One recent study and two historical studies were identified in which the proportion of cases identified through screening could be assessed over time. In Morocco, household contacts were screened for TB[15]. National figures were reported from1993-2004, involving more than one million identified contacts. In this context, with different individuals involved in screening every year, no change in the proportion found due to removal of prevalent cases is expected. The proportion of TB in the population detected through this screening averaged 5.6% and decreased slightly over time; this decrease may be attributed to a fall in the ratio of household contacts screened to index cases over time.

In a district in Czechoslovakia mass miniature radiography (MMR) surveys with >95% coverage were carried out every 3 years since 1960 (together with BCG vaccination of the newborn and revaccination of adolescents), while screening was also done at regular check-up of people with a previously known CXR lesion[16]. The prevalence of smear and/or culture-positive TB was 73/100,000 population at the beginning of the study and declined to 56/100,000 population in 1972. The total number of smear- and/or culture-positive TB cases was 79 in 1966 and 52 in 1972. The proportion detected through screening declined from 0.86 (95%CI 0.76-0.93) in 1966 to 0.56 (95%CI 0.41-0.70) in 1972. Over the whole period, the contribution of MMR was 102/379 cases (27%), which was similar to the contribution of other screening approaches (108/379=28%). In the Netherlands MMR surveys were initiated in 1941[17]. A quarter to a third of the adult population was examined each year. In addition individuals with fibrotic lesions, recent TB contacts and skin test converters were regularly followed. The overall number of smear-positive TB cases declined between 1951-55 (n=2393) and 1962-67

(n=1011).The proportion of bacteriologically positive cases found through mass surveys and active surveillance was 0.35 (95%CI 0.33-0.37) at the beginning of the study and 0.47 (95%CI 0.44-0.50) in the later years

The studies from Czechoslovakia and the Netherlands were conducted before DOTS and standard short-course treatment regimens were available. The screening algorithm applied to individuals with positive chest X-rays were not described, but cases were disaggregated by both smear and culture status, so most likely all patients were investigated with both tests. The Czech study achieved very high coverage at 3-yearly screening intervals. The Dutch study screened continuously with lower coverage. Both studies show a decrease in smear and/or culture-positive TB cases but this may reflect underlying secular trends and/or the combined effect of screening and PCF. The contribution of ACF to the overall number of cases remained high in the Netherlands, but decreased substantially from very high initial levels in Czechoslovakia. Both studies used both MMR surveys and CXR screening in specific high risk groups, notably people with CXR lesions identified in previous screening, and the contribution by the two screening approaches was similar in both countries. Recent community-based screening programs in high prevalence countries have mainly relied on symptom screening, sputum smears and culture partly due to the logistical and operational challenges of mass X-ray screening[6, 18]. It is difficult to assess how the results from these two historic studies compare with the current situation in high TB prevalence countries. Despite these limitations these are the only studies evaluating mass screening activities over prolonged periods of time.

b) Cases identified in trials of screening

Four randomised trials were identified that investigated the effect of screening on TB case-finding, all over a short time period (table 2). They compared TB case notification rates among communities or individuals actively screening or not screened. Different interventions were used, as summarised in the table. In Brazil, door-to-door screening increased the case yield during the intervention, but not overall during the whole period of the study so the effect seemed to be on delay rather than on the total number diagnosed[19]. The Ethiopian studies used community health workers in different ways to increase awareness, case-finding and diagnosis, and were thus ECF interventions with a screening element. One of the Ethiopian studies used pre-advertised outreach clinics[20], whereas the other implemented a combination of increased awareness, facilitation of sputum collection and treatment support[21]. Both found higher case rates in the intervention communities. The South African study followed a cohort of infants randomized to screening or PCF and found that screening increased case-finding by 2.6 times[22].

c) Prevalence surveys

Prevalence surveys provide an estimate of the burden of undiagnosed TB, which could potentially be diagnosed by systematic TB screening. These surveys are summarised in table 3. They vary in scope

from small studies in high prevalence areas, to and national surveys. The prevalence of TB varied considerably between studies, but the proportion of previously undiagnosed TB was high in all: 35-85% of cases. Recent surveys have calculated the "patient diagnostic rate" (reported cases/100,000/year divided by prevalence/100,000). Higher numbers imply a faster rate of diagnosis (less undiagnosed TB), but exactly how this relates to the proportion of cases detected depends on duration of untreated tuberculosis [23]. Many of these studies were large, covered randomly selected representative populations and included a high proportion of eligible individuals (although this was not always stated). Screening algorithms varied (see table 1) and would have had varying sensitivity. Case definitions also varied, and culture was only available in some settings. As shown by the study in Cambodia, the proportion of cases undiagnosed is crucially dependent on the definition used. The case definitions used for those already on treatment were not usually given. The number on treatment sometimes depended on reports by the individuals, sometimes on verification of registers and sometimes on notifications, but as illustrated in the Ethiopian studies[21, 24] the discrepancy between reports and registers could be large. In all studies the number on treatment is an underestimate of the period prevalence of diagnosed TB, as only survivors and non hospitalised patients will be included.

d) Contribution of screening to total number of TB cases diagnosed

In addition to the longitudinal studies cited above, a total of 14 studies provided data on the contribution of screening to the total TB cases diagnosed (table 4). These included studies of home visits to higher risk members of the community, outreach screening combined with information activities in the community, contact screening, or clinic screening. Community-based studies that covered a high proportion of the total community found a substantial proportion of the total cases. In contrast, studies targeting specific groups contributed relatively few cases. Notably none of the studies of contacts, even those from low prevalence areas contributed more than 9% of the total cases identified. Screening algorithms varied widely and the TB case definitions used to estimate the total number of TB cases diagnosed in the region were not clear. Thus it is difficult to draw firm conclusions.

2. Does screening for TB disease identify cases earlier?

Several studies compared delay to treatment or extent of disease at presentation between those identified through screening and PCF (see table 5). All studies found that those who were identified through screening were more likely to be at an earlier stage of disease: they were less likely to be smear-positive, had a lower degree of smear positivity, and were less likely to have severe X-ray changes such as cavitations. There was less direct evidence of a difference in duration of symptoms, but there was a marked shortening of delay in the only large study to measure it[25] In addition, in the case-finding intervention trial in Ethiopia[20] patients from communities with the intervention had shorter delay than did those in comparison communities. In the Brazilian trial, at the community level there was little

difference in the delay with the door-to-door intervention group having a mean delay of 57 days (95%CI 33-82), compared to the pamphlet group with a mean delay 53 days (95%CI 38-68)[19]. However, the short term increase in case-finding during the door-to-door screening, but not subsequently suggests a reduction in delay for those cases (see table 2).

A difficulty in assessing these studies is to know what diagnostic procedures were applied to the passively detected cases. Unfortunately these data were not available for the majority of studies (see table 5). The proportion smear-positive was consistently lower among cases identified through screening and ECF than among passively found cases, but this would be expected if smear is the main method of routine diagnosis in PCF, as was the case in South Africa, where culture was not routinely used for those found passively. The degree of smear positivity (routinely graded from +++ to scanty positive) among smear-positive cases may be a better indicator: in three studies presenting these data (in South Africa, Cambodia and India) the degree of smear positivity was higher in passively diagnosed cases. X-ray grading was restricted to those with X-ray: all three studies reporting this found less extensive disease among screened cases. However, in none of the studies were all cases bacteriologically confirmed, and less severe changes without independent confirmation of TB may have other diagnoses, particularly in actively found patients. Delay is difficult to measure, and some studies were small, but most results were consistent with a reduction in delay.

Overall only three studies, in India, Taiwan and Cambodia, included large numbers of cases identified through screening. Therefore although the evidence was largely consistent that screening reduces delay and leads to diagnosis of cases at an earlier stage of disease, inherent biases – the use of more sensitive and sometimes less specific diagnostic techniques in screening compared to the routine programme - would tend to give the same result. The strongest evidence comes from comparison of the degree of smear positivity which was lower in actively found cases.

3. Does screening for TB disease affect TB treatment outcome?

Unpublished data from two further studies was included. As well as looking at the outcome for those who started treatment, we recorded the proportion who were identified but who did not register for treatment through default, death or loss to follow-up ("initial defaulters").

Table 6 summarises the results from studies reporting on outcomes in TB cases identified through screening (restricted to those that presented results for more than 10 patients). Initial default was not always reported, but was as high as a quarter of cases identified through screening in the South African and Indian studies. Given the range of time periods, settings, treatment regimens, drug resistance and patients, absolute values of treatment outcome are difficult to compare between studies, but many achieved more than 80% successful outcomes, and the Cambodian studies more than 90%.

Five studies (2 in Nepal, 1 in Cambodia, 1 in India and 1 in South Africa) presented comparable data on cases found through screening and passively. In all five the outcomes for cases

found through screening and PCF within each study were very similar (figure 1), and this was seen in the meta-analysis: RR 1.01 (95%CI 0.98, 1.03)), with low heterogeneity (I-squared 0%). In India, subsequent studies reported the initial default rates for actively and passively found cases[26-27]. Initial default was higher in cases identified through screening (29% in 1999-2001 and 24% in 2001-2002) than in passively found cases 14% and 15%. There were no deaths among the 57 actively found initial defaulters and 23 (19%) deaths among passively found initial defaulters[26]. The reasons given by the 57 patients identified through screening for initial default included: unwillingness to start treatment; symptoms too mild to warrant treatment; too sick; and work related problems[26]. For all the other settings initial default rates in passively found cases were not reported, but they can be high, and such patients have poor outcomes[28-33].

There were many differences between the cases found through screening and passively (see tables 5 and 6) including a tendency for cases identified through screening to have less severe disease (which would tend to give lower mortality but possibly higher default rates) and to be older (which would tend to give worse outcomes). There were large differences between the 5 studies in the proportions with successful outcomes, but the internal comparisons were consistent: treatment success was comparable in TB cases found through PCF and screening.

Length time bias (through which slowly progressing and less severe cases with potentially higher chance of treatment success are more likely to be detected through screening than PCF) is likely in all studies comparing outcomes between screened vs. not screened individuals. Controlled trials with comparison of treatment outcomes between the arms are required for firm conclusions. Only two such trial was identified: , In the community randomized trial in Ethiopia[20], the proportion successfully treated was similar in the intervention communities (81%, 128/159) and comparison communities (75%, 165/221), with 3% deaths in each. The South African trial in infants did not find any difference in mortality between infants receiving ACF and PCF despite an increase in case detection, but overall mortality was low (<3%)[22]. These studies are not included in the table or in the meta-analysis as they used a trial design, but findings are consistent with studies for which meta-analysis was performed.

Only one study showed a difference in mortality among TB cases identified through screening (yearly X-ray) compared to TB cases identified through PCF [34]. The study was conducted among South African miners with high HIV prevalence and before the availability of antiretroviral therapy. TB specific mortality was 15.1 (95%CI 2.1-655) times higher in HIV-negative and 2.6 (0.7-14.9) HIV-positive TB cases identified through passive case finding compared to those identified through screening. Length time bias and residual confounding might explain part of the result.

4.Does screening for TB disease affect TB epidemiology in the community?

Five studies provide evidence for the affect of TB screening on the overall epidemiology of TB in the general population over several years (Table 7). The interventions, assessment and settings all vary so they are discussed individually.

The community randomised trial in Zimbabwe used two different case-finding interventions (mobile vans or door-door)[6]. There was no control group without an intervention, so for the purposes of this question the comparison of interest is the TB prevalence in the communities before and after the intervention, as assessed by prevalence surveys. This showed a 41% reduction over 3 years. The reduction was similar in areas covered by the different interventions, although the cumulative yield of cases during the intervention was higher in the mobile van group. The population of the area increased by 10% over the study period. Furthermore HIV prevalence significantly declined during the study period and Zimbabwe experienced a period of severe political unrest. All of these factors may have influenced the TB prevalence

The Zamstar study was conducted in communities in Zambia and South Africa and was a 2x2 factorial trial comparing ECF , a household intervention, both or neither [18]. The ECF sites received community mobilisation and easy access to sputum collection points either at clinics or mobile outreach activities, aiming to return results within 48 hours. In the household intervention sites, households of TB patients were visited three times for education and screening for TB and HIV, and HIV positive household members without active TB were offered isoniazid preventive therapy. The household intervention only directly saw 6% of individuals in the community. Outcomes assessed were TB prevalence from surveys, and *M. tuberculosis* infection incidence, assessed from tuberculin conversion in children. As shown in the table, the household intervention, but not the ECF was associated with a reduction in TB prevalence. From the preliminary results (table 6) it seems that only 13% of patients in the ECF communities were found directly through the ECF.

A follow-up study was conducted in Cambodia two years after a TB prevalence survey, to capture incident TB cases in community clusters screened for TB as part of the National survey[35]. The standardized TB notification ratio was 0.38 (95%CI: 0.27-0.52) in communities included in the National TB prevalence survey, showing a two-thirds reduction in notification in the study areas. Cases identified during the National TB prevalence survey were not included in the calculation of the standardized TB notification ratio. It is thus not clear if screening really decreased the total number of TB notifications or simply diagnosed these cases earlier.

In Brazil four matched pairs of communities were randomized: intervention communities received intensive household screening of contacts including TST testing and isoniazid prophylaxis[19]. The control communities received the standard DOTS package. Although this theoretically includes referral of contacts for investigation, this was thought to be rare in practice and no data on contact tracing were available. Outcomes were assessed from registration data, with the denominator from the national census. Overall TB notifications decreased by 10% in the intervention communities and increased by 5% in the control communities, but long term trends in TB incidence are not presented.

A study in the US evaluated a programme of mandatory screening and mandatory prophylaxis and treatment as indicated for those wanting to use homeless shelters[36]. Trends in tuberculosis in the whole district fell by almost 90% over 10 years. Incidence of TB state-wide, or in other areas shown were much lower, but showed no such fall. The study did not assess the effect of screening alone, and the population of the district was noted to have changed over the period, due to gentrification, which may have accounted for some of the fall.

Discussion

This review assessed four potential beneficial effects of screening for TB disease. The increase in TB cases and earlier diagnosis through screening could be considered intermediate outcomes. Reduction in morbidity, mortality and transmission through earlier detection and detection of cases who would otherwise remain undiagnosed are the ultimate outcomes of interest to assess individual and community-level benefits. Despite extensive implementation of systematic TB screening during the last century, there have been very few studies primarily addressing mortality or transmission and only one (Zamstar) with a cluster-randomised design that directly evaluated impact on TB epidemiology. Thus the available evidence base is weak and shows little evidence of benefit of systematic TB screening for individuals and communities.

There is moderate evidence that screening increases the number of cases found in the short term. The extent depends on the setting and the methods used. In many settings more than half the prevalent TB cases in the community are undiagnosed. Targeting of some high risk groups, or combination of risk groups can contribute a high proportion of cases, but targeting contacts did not contribute more than 9% of cases. It is possible that part of the impact on case detection is due to detection of additional false positive TB diagnosis. The proportion false positive cases out of all cases detected is inversely correlated with TB prevalence, and target groups for screening typically have much lower TB prevalance than people tested through PCF. High proportion false positive is particularly likely when the specificity of the final diagnostic test is suboptimal. Specificity of sputum smear microscopy ranges between 93% and 100%[37-39].

There is moderate evidence that screening tended to find cases earlier and with less severe disease. This may partly be attributed to screening studies using more sensitive diagnostic methods than routine programmes, rather than the screening *per se*. A recent study conducted in miners in South Africa compared 6-monthly versus 12-monthly chest X-ray screening (not included in this review because it did not have a "no screening intervention" arm). TB cases detected in the 6-monthly screening arm had less extensive disease and a lower TB specific mortality compared to TB cases detected in the 12-monthly screening arm [40]. However, South African mines are a special setting, with high prevalence of both HIV and silicosis and a high risk of rapid progression to TB disease, as well as a background of active TB case-finding programs with yearly chest X-ray screening. It is therefore difficult to extrapolate these findings to other settings.

Treatment outcomes for those identified through screening or passively were very similar in all studies. This is surprising, as patient characteristics were different and length time bias is likely in all studies, but the results were consistent in varied settings with different proportions of successful treatment. However, only two studies reported initial default rates in actively and passively found cases[26-27]. It is well documented that a high proportion of passively found cases die before initiating TB treatment[26, 32-33]. Thus "on treatment" mortality in passively found cases might underestimate overall

mortality due to survival bias. The reasons for initial default in cases identified through screening might be different: they are less symptomatic and less likely to use health care[13, 25]. Therefore the overall mortality in cases diagnosed through screening might be lower than in cases diagnosed through PCF, but only one study identified in this review provided data on overall mortality in adults. The South African trial in infants[22] and the community randomized trial in Ethiopia[20] both showed similar outcomes in intervention and control arms

The evidence that screening in addition to PCF impacts on TB epidemiology remains weak, but with an insufficient body of evidence to allow firm conclusions to be drawn about absence of effect. The Zamstar study provides the most thorough assessment, in challenging circumstances of high HIV prevalence. The study evaluated 2 different interventions (TB household and community-wide ECF, respectively) using a factorial design, and reported a significant reduction in undiagnosed TB at community level from the household intervention but not the ECF intervention. The household intervention went beyond the usual remit of TB contact tracing, with multiple visits and a strong focus on HIV as well as TB prevention, but had direct contact with only 6% of the population. Possible explanations include that the household intervention might have had extended benefit beyond the household, through heightened awareness. The ECF intervention detected only a small proportion of cases directly, and did not provide community TB screening as such, instead promoting early diagnosis through facility-based services, and so the negative trial outcomes are not necessarily generalisable to interventions using more intensive TB screening approaches. The study from Cambodia provides some evidence of reduced TB notifications among individuals who underwent intensive screening for TB, but the follow-up time in this study was short (2 years)[35]. The study from Zimbabwe showed a decrease in TB prevalence following 3 years of implementation of community-based TB case-finding, but this was based on before-after comparison with no non-intervention group to control for secular trends[6].

The main limitations of this review include a search strategy starting from a previously conducted review and high heterogeneity in screening algorithms, study setting and population. We supplemented the search strategy by contacting experts in the field and authors and by conducting additional more targeted searches. We adopted a narrative approach to account for the heterogeneity of study designs and settings and only conducted a meta-analysis to calculate pooled risk ratios for treatment outcome.

In conclusion, the evidence of individual and community-level benefit of systematic screening is remarkably limited given the high public health significance, long history, and scale on which this approach has been implemented in the past. Large cluster randomized trials such as the Zamstar study with long term follow-up would be needed to provide more evidence for such a benefit if indeed it exists, ideally including studies that evaluate a range of interventions with different screening intensities in different epidemiological settings. In the meantime more rigorous and consistent reporting of TB notification and mortality rates over prolonged periods of time in settings where large scale screening programs have been implemented should be encouraged, together with capture of mode of detection

and other variables to support TB impact assessment. Furthermore a better understanding of the magnitude of initial defaulting within national TB programs is needed and could be facilitated by including initial defaulters in the routine TB notification registers.

Table 1 Studies included in the review

ID	Year of study	Rural or Urban	Setting	How was screening performed?	Order of screening[1]						
					Symptom screen	Clinical	Smear	Culture	CXR	Anti-biotics	TST
African Region											
Ethiopia 2003a[41]	2003	Rural	Community	Home visits, TB suspects identified by head of household	1 (C2w)		2 (MMS)				
Ethiopia 2003b[20]	2003-2004	Rural	Community	Outreach teams (once per months), advertised by local lay health care worker	1		2 (MSS)				
Ethiopia 2006[21]	2006-2008	Rural	Community	Lay health care workers identified TB suspects in the community and facilitated sample transport	1 (C2w)		2 (MSS)				
Ethiopia 2008[42]	2008	Urban/ rural	Community	Home visits, TB suspects identified by head of household	1 (C2w)		2 (MS)				
Ethiopia 2009[43]	2009	Rural	Community	Home visits	1 (C2w)		2 (MS)	2 (MS)			
Ethiopia 2010[24]	2010	Rural	Community	Home visits	1 (C2w)		2,5 (MS)		4	3	
Botswana 2004[44]	2004-2006	Urban	HIV Clinics	IPT program		2	2	2	1		
Guinea-Bissau 2006[45]	2006-2007	Urban	Community	Home visits	1 (C)		2		2	3	
Ivory Coast 1990[46]	1990-1992	Urban	Prison camp			1	2		2		
Kenya 2006[47]	2006-2007	Rural	Community	Home visits	1		1 (MS)	2	1		
Malawi 1999[48]	1999-2001		Prison	At time of entry into prison	1 (C1w)		2 (UUU)				
South Africa 1993[34]	1993-1997		Mines	Workplaces screening program			2	2	1		
South Africa 2002[49]	2002	Urban	Community (township)	Home visits			1	1	1		

South Africa 2005a[22]	2005-2008	Urban	Community (township), infants	Home visits, TB register checks to identify adult smear positive cases	1 (C2w)	2	2	2	2	2
South Africa 2005b[50]	2005	Urban	Community (township)	Home visits and referral to clinic			1 (MS)	1(MS)		
South Africa 2008[51]	2008	Urban	Community (township)	Home visits and referral to clinic			1 (MS)	1(MS)		
South Africa 2009[13]	2009-2011	Urban	Community (township)	Mobile HIV testing unit	1 (C2w) (if HIV-)		2:HIV- (S) 1: HIV+ (S)	2:HIV- (S) 1: HIV+ (S)		
Uganda 2001[52]	2001-2002	Urban	Community	Home visits and referral to clinic	1 (C2w)		2	2	2	
Uganda 2005[53]	2005	Urban	Slum	Home visits	1 (C)		2 (MS)			
Zambia 2006[18]	2006-2011	Urban/rural	Communities in Zambia and South Africa	Household, clinic, sputum collection points						
Zimbabwe 2005a[54]	2005	Urban	Community	Home visits			1 (MS)	1(MS)		
Zimbabwe 2005b[6]	2005-2008	Urban	Community	Home visits and mobile van	1 (C2w)		2 (MS)			
Eastern Mediterranean Region										
Morocco 1993[15]	1993-2004	Urban/rural	Household contacts of index cases	Active follow-up of contacts at home/by phone and referral to clinic	1	1	2(MS)		1	
Region of the Americas										
Brazil 2005[19]	2005-2006	Urban	Community	Home visits	1 (C3w)		2 (MS)			
Brazil 2000[55]	2000-2004	Urban	Household contacts of index cases	Home visits		1	2	2	1	1

Canada 1960[17]	1960-1969	Rural	Community, 1960-63 > 20 years of age, 1964-1969 >30 years of age	Mass miniature radiography in communities where a case of active TB was discovered in the previous year					1	
Canada 1967[17]	1967-1968	Mixed	Hospital, workplace, community	Chest x-ray survey at admission to hospital, jail, industrial and community surveys					1	
Cuba 2003[56]	2003-2005	Urban/rural	Community	Home visits by family doctors performed for other reasons than TB	1 (C2w)		2	2		
Mexico 1995[57]	1995-1996	Rural	Households, shelters, jails, orphanages, support for alcoholics, diabetics, intravenous drug users (IVDU)	Health promoters identified TB suspects and referred them to clinics	1 (C2w)		2(MSS)			
US 1985[36]	1985-1995	Urban	Homeless, shelters, jails							
US 1999[58]	1999	National								
US 2001[59]	2001-2003	Part of immigration process	Refugees and immigrants	TB suspects identified in the country of departure and screening repeated at entry		1	2	2	1	1
South-East Asia Region										
India 1981[60]	1981-1982	Rural	Community	Lay health care workers identified TB suspects in the community, prepared microscopy slides and facilitated transport	1		1			
India 1999[25, 27]	1999-2000	Rural/urban	Community	Home visits	1		2(UU)	2(UU)	1	
India 1999[26, 61]	2001-2003	Rural/urban	Community	Home visits	1		2(UU)	2(UU)	1	
India 2003[62]	2003-2004	Urban	VCT centres at hospitals		1 (C3w)	2	2			
Myanmar 2009[63]	2009-2010	National	National prevalence survey	Home visits	1 (C3w)		2(MS)	2(MS)	1	

Nepal 1979[64]	1979-1980	Rural	Community	Home visits	1 (C3w)		2 (MMM)		
Nepal 1990[65]	1990-1993	Rural	Community	Temporary microscopy camps with pre-camp publicity	1 (C3w)		2		
Western Pacific Region									
Cambodia 2002a[9]	2002	National	National prevalence survey	Home visits	1 (C3w)		2(MS)	2(MS)	1
Cambodia 2002b[35]	2002-2004	National	Follow-up of National prevalence survey	Home visits	1 (C3w)		2 (MS)	2 (MS)	1
Cambodia 2009[66]	2009-2010	National	Household contacts and neighbours of index cases	Home visits and referral to clinic	1		2 (UUU)		2
China 2000[23]	2000	National	National prevalence survey		1 (C2w)		2 (UUU)	2 (UUU)	1
Hong Kong 2000[67]	2000	Urban	Contact of TB cases						
Japan 2002[68]	2002-2004	Urban	Tertiary hospital				2	2	1
Korea 1995[69]	1995	National	National prevalence survey	Home visits	2		2(SSS)	2(SSS)	1
Papua New Guinea 2010[70]	Unk	Rural	Community	Home visits	1 (C)		2		
Philippines 1985[71]	1985	Urban	Community	Health promoters identified TB suspects in the community and took them to a temporary clinic	1		2		
Philippines 1997[11]	1997	National	National prevalence survey	Home visits			2(UUU)	2(UUU)	1
Taiwan 1993[72]	1993-1996	Urban	Household contacts	Home visits and referral to clinic	1	1	2	2	1
Vietnam 1992[73]	1992-1993	Mixed	Individuals applying for departure	Hospital		1	2 (MMM)		1
Vietnam 2006[10]	2006-2007	National	National prevalence survey	Home visits	1		2(UUU)	2(U)	1

European Region										
Netherlands 1951[17]	1951-1967	National	Community	Mass miniature radiography screening and surveillance of risk groups (contact tracing, recent TST converters, person with fibrotic lesions)				1		
Netherlands 2002[74]	2002-2005	Urban	Methadone centres, night care facilities, street prostitution zones	Mobile X-ray unit				1		
Czechoslovakia 1965[16]	1965-72	Mixed	Community	Mass miniature radiography survey, surveillance of people with fibrotic lesion		2	2	1		
UK 1967[75]	1967-1975	Urban	Hostels	Mobile X-ray unit				1		
UK 1968[76]	1968-1982	Urban	Homeless and hostel dwellers	Mobile X-ray unit	2	3	3	1		
UK 1977[77]	1977-1981	Urban	Contacts of TB cases					1	1	
UK 1982[78]	1982-1990	Urban	Contact of TB cases							
UK 2008[79]	unk	Urban	Hard to reach groups (homeless, drug users, prisoners)	Mobile X-ray unit				1		

Table 2: Community randomized trials , comparing cases registered in the intervention and control communities
See table 1 for screening algorithms used

ID	Setting	Intervention	TB in intervention communities/infants	TB in control communities	Effect of intervention (95% CI)
Ethiopia 2003b[20]	Rural area	Community promoters and outreach sputum collection for symptomatics over 1 year (12 intervention vs 20 control communities)	All: 125/100,000 (159 / 127,607) Adults: 207/100,000 (153 / 74,012)	All: 98/100,000 (221 / 225,284) Adults: 158/100,000 (207/130,665)	Difference 27/100,000 (-19 to 72) Difference 49/100,000 (-27 to 123)
Ethiopia 2006[21]	Rural area	Health extension workers advised symptomatics to attend and collected sputum samples at health posts over 20 months. 30 intervention vs 20 control communities	All: 122/100,000 (230/178,138) Adults: 194/100,000	All: 69/100,000 (88/118,673) Adults: 118/100,000	Difference 52.8/100,000(39.8-65.4) Difference 76/100,000 (56-96)
South Africa 2005a[22]	Urban (township)	4786 infants were randomised to 3 monthly household visits or passive case finding; suspected TB disease was investigated as inpatient	2.2/100 py	0.8/100 py	Rate ratio 2.6 (1.8–4.0)
Brazil 2000[19]	Favela in Rio de Janeiro	Door-to-door screening 7 vs 7 communities (paired)	N=11249	N=12304	Rate ratio
		During intervention (ave 27 days)	934/100,000 py (n=19)	604/100,000 py (n=16)	1.55 (1.10-1.99)
		Intervention + 60 days	516/100,000 py (n=32)	493/100,000 py (n=41)	1.05 (0.56-1.54)
		Whole period (283 days)	818/100,000 py (n=92)	821/100,000 py (n=101)	

py = person years at risk

Table 3: Prevalence surveys in general populations: extent of undiagnosed tuberculosis in house-to-house surveys in the general population.
See table 1 for screening algorithms used

ID	Setting	Population	Proportion included	Type of TB	Number of previously undiagnosed TB cases (diagnosed in the survey)	Number of TB cases on treatment at the time of the survey	Undiagnosed TB as a proportion of the total number of TB cases	Patient diagnostic rate (smear-positive)
Africa								
Ethiopia 2003a[41]	Rural	16,697 adults	not stated	Smear+	13	24	0.35	
Ethiopia 2008[42]	Rural and urban	47,478 adults	not stated	Smear +	38	15[1]	0.72	
Ethiopia 2009[43]	Rural area	29,257 adults	not stated	Smear +	22	4	0.85	
Ethiopia 2010[24]	Rural and urban	23,590 adults	not stated	Smear + All pulmonary	41 58	22[2]	0.65 0.73	
Guinea-Bissau 2006[45]	Urban	3,714 adults	80%	Pulmonary	2	2	0.50	
Kenya 2006[47]	Rural	30,416 adults	68%	Pulmonary	117	86	0.58[3]	0.93
South Africa 2005b[50]	Urban high density	971 adults	78%	Pulmonary	12	11	0.52	
South Africa 2008[80]	Urban high density	1,383 adults	90%	Pulmonary	8	12	0.40	
Uganda 2001[52]	Urban	1,142 all ages	not stated	All	10	9	0.53	
Uganda 2005[53]	Urban	1,000 adults	88%	Pulmonary	33	9	0.79	
Zimbabwe 2005a[54]	Urban	12,426 adults	82%	Pulmonary	82	74	0.53	
Asia								
Cambodia 2002a[9]	National	23,084 age 10+	96%	Smear+ Smear or culture+ All pulmonary	74 260 552	42	0.64[3] 0.86 0.93	0.63
China 2000[23]	National							0.24
Korea 1995[23, 81]	National	~73,000 age 5+	88%	Smear or culture	106			0.43

Myanmar 2009[63]	National	57,607 adults	89%	Pulmonary	280	79	0.78[3]	0.47 (0.36-0.62)
Papua New Guinea 2010[70]	Rural	7211	not stated	Smear+?	19	29[estimated]	0.40	
Philippines 1997[11, 23]	National	15,905 age 10+	81%	Smear or culture+	127			0.51
Vietnam 2006[10]	National	114,389 adults	82%	Pulmonary	263			0.60 (0.49-0.78)

[1] 33 reported being on treatment; 15 found in registers
[2] 150 reported being on treatment; 22 found in registers
[3] Not adjusted for cluster sampling

Table 4: Contribution of screening to total notified cases

ID	Screening program	Total number of TB cases diagnosed by screening	Total number of diagnosed TB cases through PCF in same area	Proportion of TB cases diagnosed by screening of all TB cases
Community-based				
Canada 1960[17]	Mass miniature radiography and tuberculin skin surveys had been carried out since 1941. From 1960-63 individuals with negative TST and aged <20 were not surveyed, and from 1964-1969 individuals with a negative TST and aged <30 were not surveyed. 18% of the total population was examined annually, the screening procedure following an abnormal radiograph was not described	47 (smear + TB) 43 (culture+ TB)	354 (smear+ TB) 202 (culture+ TB)	0.12 (smear + TB) 0.18 (culture+ TB)
Canada 1967[17]	Mass chest X-ray surveys on a community and industrial bases were performed from 1948-1968. From 1968 a hospital admission chest X-ray program was added. In addition contact tracing chest X-ray screening, pre-employment and in jails was conducted. The screening procedure following an abnormal radiograph was not described,	145 (smear+ TB) 136 (culture + TB)	420 (smear+ TB) 183 (culture+ TB)*	0.26 (smear+ TB) 0.43 (culture+ TB)
Cuba 2003[56]	Home visits to risk groups (elderly, heavy alcohol users, ex-prisoners, HIV positive, socio-economically vulnerable)	24	19	0.56
Mexico 1995[57]	Health promoters (each promoter serving 3000 individuals) were trained to identify individuals with cough. They sought out individuals at their houses, jails, shelters, orphanages, alcohol support groups and other risk groups. TB suspects were asked to attend the clinic to submit sputum samples.	92	15	0.86
India 1981[60]	Lay health care workers identified TB suspects in the community, prepared microscopy slides and facilitated transport to microscopy centres.	26	13	0.67
India 1999[25]	Door-door in approx one third of the population	211	508	0.25
Nepal 1990[65]	Temporary microscopy camps were put up in remote villages (at an average walking time from the nearest health post of 4.25h). Pre-camp publicity included theatre shows, house-to-house visits. The camps lasted for 2-4 days	71	1175 [estimate]	0.06
Contact tracing				
Hong Kong 2000[67]	Contacts of TB cases were screened.	31	1635	0.02
Morocco 1993[15]	Contacts of TB cases were screened	?~20,000	?	0.048 (age ≥10) 0.19 (age <10)
UK 1977[77]	Contacts of pulmonary TB cases were	78	816	0.09

	screened.			
UK 1982[78]	Contacts of TB cases were screened.	50	649	0.07
US 1999[58]	Contacts of smear or culture-positive cases were screened.	561	9199	0.06
High risk settings				
India 2003[62]	TB suspects were identified among VCT clients (both HIV+ and HIV-). A total of 5 VCT centres in the district participated: 2 at medical schools, 1 a tertiary hospital, 2 at district hospitals.	83	15835	0.01
Netherlands 2002[74]	Drug users and homeless in Rotterdam	28	562 [estimate]	0.05

See table 1 for screening algorithms used
* 136 additional cases (67 smear-positive TB cases and 69 culture-positive TB cases) were found through routine chest x-rays

Table 5: Symptom duration, smear status and cavitations in screened and passively found cases*
See table 1 for screening algorithms used

ID	Total number of cases		Average/median delay from onset of symptoms to start of treatment.		% of smear-positive cases among pulmonary cases		Smear+ grade (% scanty, 1+,2+,3+)		% of those with CXR which show severe disease		Comments
	Screening	Passive	Screening	Passive	Screening	Passive	Screening	Passive	Screening	Passive	
Africa											
Ethiopia 2003a[41]	13	24	54% had symptoms for more than 90 days	58% had symptoms for more than 90 days							No information on diagnostic algorithm for passively found cases
South Africa 2002[49]	27	473			67%	94%	17,28,22,33	4,26,18,52			Passively found cases from 2-3 years later. Passive cases more symptomatic, eg weight loss in 92% vs 44% in active. Culture not routinely done for passively found cases. Smear grade P trend=0.03 No information on diagnostic algorithm for passively found cases.
Americas											
Brazil 2005[19]	9	64	Median time = 56 days (range 28-336)	Median time = 53 days (range 7-336)							Diagnostic algorithm was probably the same in actively and passively found cases.
Canada 1960[17]	90	425			52%	62%					No information on diagnostic algorithm for passively found cases
Canada 1967[17]	140	403			45%	70%					No information on diagnostic algorithm for passively found cases
US 2001[39]	39	61			26%	59%			3%	21%	Screening in arriving immigrants/refugees compared to passive cases in immigrants arrived in last year. P<0.01. Diagnostic algorithm unclear for both actively and passively found cases.
Asia											
Cambodia 2009[66]	405	602			29%	60%	9,48,26,17	2,40,39,19			P<0.001. smear+ P trend=0.009 smear grade, No information on diagnostic algorithm for passively found cases.
India 1999[25]	211	508	Cough< 3 wks: 37%	Cough < 3 wks: 18%	45%	65%	0,59,38,3	3,28,27,42			P<0.001 for all Diagnostic algorithm did not include routine

								CXR and culture in passively found cases
Taiwan 1993[72]	284	3903				6%	16%	
Europe								
Czechoslovakia 1965[16]	100	119		29%	44%			No information on diagnostic algorithm for passively found cases
Netherlands 1951[17]	1682	2209		38%	58%			No information on diagnostic algorithm for passively found cases
UK 1967[75]	54	71		58%	85%	13%	31%	P<0.01 No information on diagnostic algorithm for passively found cases.
UK 1968[76]	42	26		26%	58%			P<0.01 No information on diagnostic algorithm for passively found cases.
UK 2008[79]	35	240	Passively found cases had 3 times the diagnostic delay of actively found cases.	44%	66%			Adjusted odds ratio for smear positivity comparing active and passive cases was 0.36 (p<0.001) No information on diagnostic algorithm for passively found cases.

*Two studies of mass x-ray screening were not included in this table as all data regarding the screening algorithm following a positive chest-rays were unknown[16-17].

Table 6: Treatment outcomes of cases detected through screening and passively detected cases
See table 1 for screening algorithms used

ID	Type of TB	Actively found (N)	Initial Defaulter	Started Treatment		Treatment Successful		Died		Defaulted, transferred, failed, missing		Comments
			Active	Active	Passive	Active	Passive	Active	Passive	Active	Passive	
Africa Region												
Botswana 2004[44]	Pulmonary	43		43		35 (81%)		5 (12%)		3 (7%)		All HIV positive
Ivory Coast 1990[46]	All	108		108		80 (74%)		28 (26%)				Prisoners, 30% HIV+
Malawi 1999[48]	Smear+	318	22 (7%)	296		181 (61%)		36 (12%)		79 (27%)		Prisoners
South Africa 2002[49]	Smear or culture +	27	7 (26%)	20	473	16 (80%)	380 (80%)					Initial defaulter defined as not starting treatment within 2 month of diagnosis.
South Africa 2009[13]	Smear or culture +	56	14 (25%)	42		34 (81%)		2 (5%)				Mobile HIV testing service, 54% HIV+
Zimbabwe 2005a[54]	Pulmonary	91	4[2]	80		58 (73%)		9 (11%)		13 (16%)		Unpublished results
Zimbabwe 2005b[6]	Smear+	249	15(6%)	234		175 (75%)		26 (11%)				Unpublished results
South East Asia Region												
India 1999[25]	Pulmonary	211	58 (27%)	153	508	107 (70%)	361 (71%)	5 (3%)	36 (7%)	41 (27%)	111(22%)	ACF older, more men, poorer backgrounds
Nepal 1979[64]	Smear+	111	11 (10%)	100	159	62 (62%)[3]	110 (69%)	9 (9%)	17 (11%)	29 (29%)	32 (20%)	Treatment: 2 months streptomycin, 12-18 months of isoniazid and thiacetazone.
Nepal 1990[65]	New smear+	68		68	1306	50 (74%)	997 (76%)	5 (7%)	104 (8%)	13 (19%)	205 (16%)	
Western Pacific Region												
Cambodia 2002b[35]	Smear+ or culture+	271	27 (10%)	244		232 (95%)						
Cambodia 2009[66]	Pulmonary	405	21 (5%)	384	602	370 (96%)	573 (95%)	3 (0.8%)	11 (2%)	8 (2%)	10 (2%)	Screening cases older and higher proportion smear negative

Japan 2002[68]	Pulmonary	17		17	12 (71%)		5 (29%)	From homeless shelters
Philippines 1985[71]	Smear+ or culture +	158	14 (9%)	144	91 (63%)	5 (3%)	48 (33%)	Regimen: 1 month IRPE, 7 months IEP (twice weekly). 82% resistant to at least one drug[4]
Vietnam1992[73]	Smear+	322		322	265 (82%)	3 (1%)	54 (17%)	34% previously treated
European Region								
Netherlands 2002[74]	Pulmonary	28		28	25 (89%)			Homeless and drug users Outcome of other 3 not given

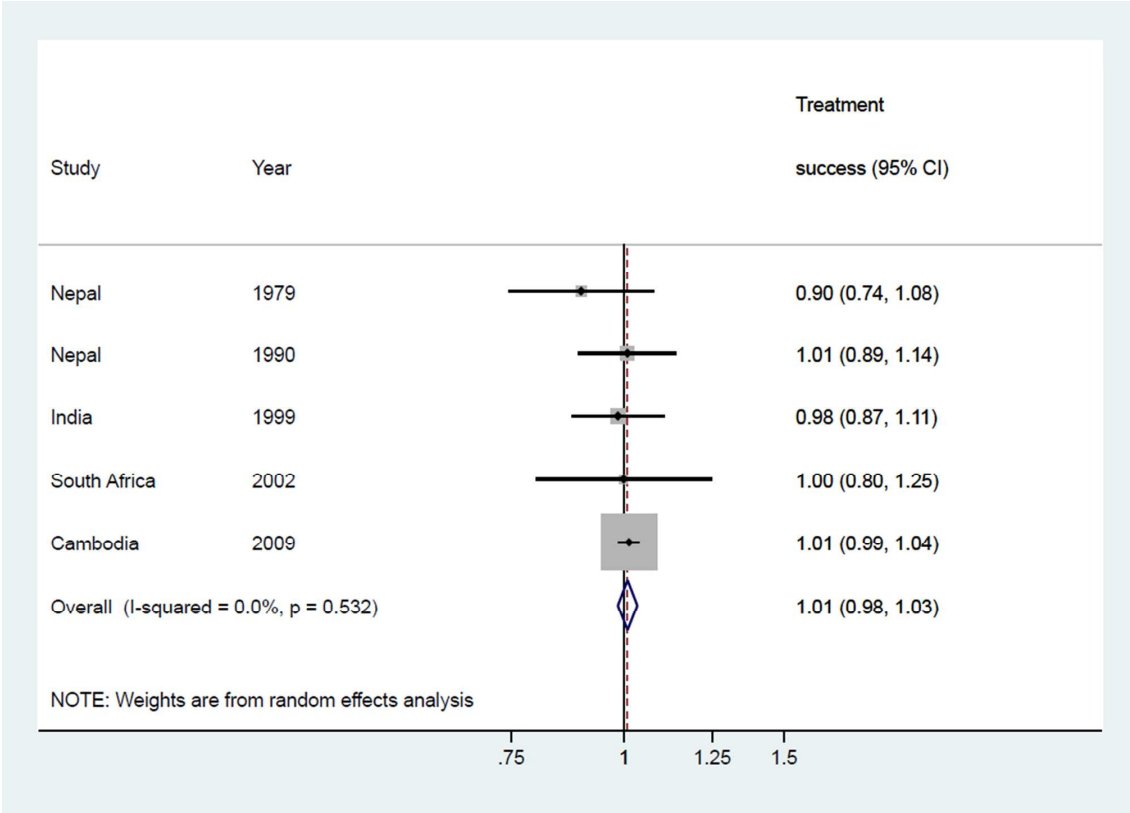
[1] Adjusted for cluster-sampling.
[2] Seven started treatment elsewhere, outcomes unknown
[3] Outcomes were reported including those who did not start treatment. We have assumed they were not among the 62 with "sputum conversion recorded"
[4] IRPE=Isoniazid, Rifampicin, Pyrazinamide, Ethambutol, IEP=Isoniazid, Rifampicin, Pyrazinamide

Table 7: Studies which have measured the general population impact of case-finding interventions
See table 1 for screening algorithms used

ID	Setting	Intervention	Time to assess impact	Outcome in control arm	Outcome in intervention arm	Comparison (values in brackets are 95% CI)
Cambodia 2002b[35]	2 year follow-up of individuals screened in the National prevalence survey	Household screening with chest X-ray and symptom screen followed by sputum investigations in randomly selected clusters	2 years	Expected TB notification	Actual TB notification	Standardised TB notification ratio 0.38 (0.27-0.52)
Brazil 2005[55]	8 urban communities Rio de Janeiro	CRT Intensive screening + IPT in household contacts	5 years	Incidence increased 5% to 358/100,000	Incidence decreased 10% to 305/100,000	P=0.04
Zimbabwe 2005b[6]	High-density suburbs, Harare	CRT Mobile van or door-door vs baseline pre-intervention	3 years	Baseline prevalence 6.5/1000 (5.1-8.3) (66 cases)	3.7/1000 (2.6-5.0) (41 cases)	Adj RR 0.59 (0.40-0.89) p=0.01
Zambia 2006[18]	Communities in South Africa and Zambia	Factorial CRT (i) ECF vs no ECF	3 years	TB prevalence 711/100,000 Infection incidence 1.05%	TB prevalence 927/100,000 Infection incidence 1.41%	Adj RR TB: 1.11 (0.87-1.42) Adj RR infection: 1.36 (0.59-3.14)
		(ii) household intervention vs no household intervention	3 years	TB prevalence 883/100,000 Infection incidence 1.71%	TB prevalence 746/100,000 Infection incidence 0.87%	Adj RR TB: 0.78 (0.61-1.00) Adj RR infection: 0.45 (0.20-1.05)
US 1985[36]	Oregon, Burnside area	Mandatory screening, prophylaxis and treatment for those wanting to use homeless shelters vs baseline	10 years	Annual notifications in area in 1985 227/100,000 (39 cases)	Annual notifications in area in 1995 29/100,000 (5 cases)	Decline over the 10 year period in this district much greater than decline in other districts or state-wide.

CRT= community randomised trial, IPT=isoniazid preventive therapy

Figure 1: Meta-analysis: risk ratio comparing successful treatment in cases found through screening with passively found cases



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