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Active case finding of tuberculosis: historical perspective and future prospects

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SUMMARY

Despite a history of remarkable scientific achievements in microbiology and therapeutics, tuberculosis (TB) continues to pose an extraordinary threat to human health. Case finding and treatment of TB disease are the principal means of controlling transmission and reducing incidence. This review presents a historical perspective of active case finding (ACF) of TB, detailing case detection strategies that have been used over the last century. This review is divided into the following sections: mass radiography, house-to-house surveys, out-patient case detection, enhanced case finding, high-risk populations and cost-effectiveness. The report concludes with a discussion and recommendations for future case finding strategies. Understanding the strengths and weaknesses of these methods will help inform and shape ACF as a TB control policy in the twenty-first century.

Keywords

tuberculosis; active case finding

Despite a history of remarkable scientific achievements in microbiology and therapeutics, tuberculosis (TB) continues to pose an extraordinary threat to human health. *Mycobacterium tuberculosis* infection is prevalent throughout the world, case rates are escalating and TB continues to claim almost 2 million lives annually.[1–3] Control of TB is currently based on three strategies: case finding and treatment of active disease; treatment of latent TB infection; and vaccination with bacille Calmette-Guérin (BCG). The latter two approaches have minimal impact on TB incidence, as treatment of latent TB is not widely practiced and BCG vaccine has little effect in the prevention of adult TB cases. Hence, case finding and treatment of TB disease are currently the principal means of controlling transmission and reducing incidence.

Passive case finding (PCF) is defined as detecting active TB disease among symptomatic patients who present to medical services for diagnosis of symptoms, and it is now widely

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promoted in developing countries as part of the World Health Organization (WHO) recommended DOTS strategy.[4]

Active and enhanced case finding (ACF and ECF) require a special effort by the health care system to increase the detection of TB in a given population. These strategies identify and bring into treatment people with TB who have not sought diagnostic services on their own initiative. By detecting and treating TB in patients earlier than would occur otherwise, ACF and ECF can reduce the number of subsequent TB infections and prevent secondary cases. The primary difference between ACF and ECF is the level of direct interaction with the target population. ACF is often more labor intensive, involving face-to-face contact and immediate onsite evaluation. ECF makes a population aware of TB symptoms (through publicity and education), and encourages self-presentation to medical services. ACF and ECF are of considerable interest for TB control because of the failure of current control strategies to reduce TB incidence, particularly in areas with a severe human immunodeficiency virus (HIV) problem.[5]

The impact of ACF on TB incidence is unknown, but several mathematical models suggest that it could have a marked effect on TB case rates.[6,7] Murray and Salomon modeled three ACF approaches.[8] After considering costs and prevalence in different regions of the world, the authors concluded that ACF strategies combined with DOTS would yield enormous benefits in areas with high TB prevalence, and millions of cases and deaths could be averted. Currie et al. proposed another model estimating the effectiveness of various interventions on the incidence of TB in regions with high HIV prevalence.[7] Their model suggested that the most effective way to reduce TB incidence and mortality was to increase TB case detection and cure rates. Another model evaluating the short-term impact of ACF suggests that little benefit is offered if cure rates are below 70%.[6,9] Interestingly, various models with different underlying assumptions have reached similar conclusions. In the current context of high TB prevalence, more aggressive efforts are required to detect and cure TB.

This review presents a historical perspective detailing case detection strategies that have been used over the last century. Understanding the strengths and weaknesses of these methods will help inform and shape ACF as a TB control policy in the 21st century. Several factors are considered in determining the value of a case detection method, including effectiveness (measured by number of cases detected and/or treatment outcome of the cases), population impact (measured by decreases in TB incidence or transmission), required resources (personnel, facility, equipment) and the associated financial burden. Based on our review findings, we will offer insight for development of future ACF and ECF interventions.

METHODS

A search of the Medline database (includes journals from 1966–present) was conducted using the following phrases in conjunction with ‘tuberculosis’: ‘case detection’, ‘case finding’, ‘active case finding’ and ‘screening’. Papers identified were classified both chronologically and according to case detection method. The reference lists of these articles were reviewed for additional studies, and TB experts were asked to suggest additional important papers for inclusion, especially those predating 1966. This review focuses primarily on publications reporting findings of case finding strategies. Large scale countrywide prevalence surveys that utilized probability sampling of the population to estimate TB prevalence (China, Korea, India, Cambodia and Uganda) were excluded from this review. While prevalence surveys may incorporate some ACF methodology, the objectives of prevalence surveys and ACF studies are different. Likewise, contact investigations were excluded, given that their methodology differs from ACF and reviews have already been published on them.[10–17] The review was limited to publications written in English.[*]

This review is divided into the following sections: mass radiography, house-to-house surveys, out-patient case detection, ECF, high-risk populations and cost-effectiveness. An accompanying table summarizes each study, including author, publication year, country, sample surveyed, case finding method, and brief results. Studies that provide background, review and/or model case detection strategies are not included in the Table. The report concludes with a discussion and recommendations for future case finding strategies.

RESULTS

Mass radiography

Soon after the advent of streptomycin, isoniazid and para-aminosalicylic acid (PAS), it was shown that TB could be effectively treated in the home, and the sanatorium era gradually came to an end.[18] This marked a significant change in case finding of TB, from detection and isolation to detection and treatment. Mass radiography was the primary ACF strategy in the industrialised world prior to the 1960s. Later, a transition in case detection methodology began and ACF through mass radiography was no longer endorsed by the WHO for developing countries. Papers discussing early mass radiography strategies, large scale studies and the most influential papers leading to the shift away from mass radiography will be discussed.

Mass radiography: pre-1960

Early active case detection strategies were frequently large scale mass radiography campaigns conducted in industrialized countries between the 1930s and 1960s. Mass radiography in the pre-chemotherapy era had three objectives: 1) to detect patients earlier in disease progression in an effort to reduce TB mortality; 2) to isolate active TB patients from society to reduce TB transmission; and 3) to identify high-risk TB suspects who could be followed due to suspicion of later developing active TB.

In the early 1930s, a series of mass case finding surveys in New York City (NYC) included chest radiographs (CXRs) of over 150 000 residents.[19–21] They concluded that chest radiography targeting populations most at risk of TB, including the poor, prisoners, and transient groups, would be the most effective case detection strategy.

Mass radiography campaigns came to rely on manpower and innovation. A series of studies conducted in Minnesota in the late 1930s and early 1940s made use of wide-scale publicity

[*]A more detailed and comprehensive description of these publications can be found at www.tbhiv-create.org/

campaigns and a mobile X-ray unit.[22–24] The entire St Louis County population was surveyed, and follow-up surveys in two communities several years later revealed no new cases of TB.[23,24]

Mobile X-ray units were used from New York to Wales.[25,26] In 1946, a mobile X-ray unit was used to examine 50 population groups in Baltimore, Maryland.[27] Among 48 000 people, 292 cases were diagnosed (608/100 000). It was suggested to limit examinations with recommendations to target close family, social, and occupational contacts.

Active case detection in Alaska relied primarily on radiography through unique service delivery methods. In 1945, a floating TB unit consisting of an X-ray unit and clinic debuted on a motor ship. In 1954, two additional ships, a railroad car, a truck and airplane, all equipped with X-ray and clinic facilities, were employed. From 1950 to 1957 the TB death rate among Alaskan Eskimos and Indians made an astonishing drop, from 655 to 116/100 000.[28,29] It has even been reported that dog sleds were used to transport X-ray equipment.[30]

Between 1945 and 1948, the United States Public Health Service (USPHS) surveyed over 6 million people with mass radiography in 21 communities.[31] A greater proportion of cases were diagnosed at an earlier stage of disease than cases reported outside of the scope of mass radiography. At least two of the areas with between 2 and 3 years of follow-up were able to show significant decreases in TB mortality. Furthermore, on average 90% of the active cases and 85% of the inactive cases identified through these surveys were previously unknown to local health departments. Nevertheless, targeted radiography was advocated once again.

In 1946 and 1950, Comstock and Sartwell assessed TB morbidity in Georgia, surveying over 38 000 residents.[32,33] The authors concluded that a complete radiographic survey of populations with a low incidence of TB, followed by adequate isolation and treatment, could effectively reduce TB burden.[34,35] However, they noted that in pockets of the population where TB incidence is high, repeat radiographic screening may be necessary.

European countries also conducted mass radiography activities. Between 1950 and 1952, the Danish government conducted an extensive mass TB case finding campaign.[36] Overall, between 1946 and 1958, more than 2 million individuals were screened and over 2000 cases were diagnosed.[37] In all, 503 (63/100 000) previously unknown active TB cases were diagnosed. An extremely thorough mass radiography campaign in Reykjavik, Iceland, in 1945 discovered 19% of the TB cases detected during the period.[38] Prior to a mass radiography screening of a mining community in the early 1950s in Wales, lectures were conducted and propaganda leaflets were widely distributed.[39] The survey covered 89% of the population. When the population was surveyed again in 1953, total prevalence had decreased significantly (from 602 to 307/100 000).[40] During 1956, a community X-ray survey examined 95% of the population in Scotland.[41] The authors stressed that the success of mass radiography in approaching 100% coverage depended on personal contact, active cooperation of physicians, and prompt notification of results.

One of the first published mass radiography surveys in the developing world was conducted in 1945 by Aspin among army recruits in India.[42] Although this population was considered to be healthier than the general population, the prevalence among army recruits was found to be 800/100 000. A mass radiography survey conducted from 1950 to 1951 in 200 rural villages in South India surveyed 20 975 people, of which 89 (424/100 000) probably had active TB.[43] An ambitious study among civil servants in Delhi X-rayed an estimated 90% of workers.[44] The study was conducted first in 1953–1954 among 44 371 employees, and again in 1960–1962 among 76 951. Prevalence rates of active disease in the first and second survey were 620 and 1090/100 000, respectively.

In 1958, given the evidence, a USPHS statement promoted the selective use of mass radiography.[45] It declared that mass radiography 1) was a fundamental technique in the detection of TB; 2) should be applied selectively in high risk groups; 3) should have the approval of relevant government services; 4) should consider the use of the tuberculin skin test (TST) as an initial screening device in low prevalence groups; 5) should be evaluated continually; and 6) should utilize appropriate safeguards to protect from unnecessary radiation. The risk of excessive radiation exposure was considered to be relatively small when compared to the expected benefits of a mass radiography program. Despite the relative success of mass radiography as a case detection strategy in industrialized countries, by the late 1950s it had become evident that these campaigns were not practical in the developing world, primarily due to the prohibitive cost and less developed public health infrastructure.[46]

Overall, mass radiography has been successful in detecting previously unknown TB cases and diagnosing TB cases earlier. While the benefits were substantial, the financial expense and logistics that accompanied these studies made them difficult to implement at a population level, particularly in developing countries.[46] Recent experiences in HIV populations suggest a possible role for routine radiographic screening of this high-risk group.[*]

Paradigm shift

Beginning in the early 1960s, researchers in developing countries began investigating new case finding strategies, relying more on the detection of symptomatic patients. A seminal publication from India in 1963 concluded that a strong health system infrastructure could detect most symptomatic TB cases.[47] Sixty-two villages in South India were surveyed over a 6-month period. The authors found that 70% of sputum-positive and 80% of radiologically active cases were aware of their TB symptoms, and that more than 50% of these patients had sought care for these symptoms. Another Indian study found that 95% of all cases detected were among 80% of patients who were aware of TB symptoms.[48] Thus, weaknesses in the health system were a more important problem than lack of awareness among patients.

Another Indian program surveyed out-patients attending dispensaries and health units for respiratory symptoms.[49] This study confirmed that limiting sputum collection to patients complaining of cough of at least 2 weeks would greatly reduce the cost of testing without compromising yield. If bacteriological examinations had been limited to patients

[*]Roux S, Fielding K, Grant A D, et al. Annual vs. 6 monthly radiological screening for the active case-finding of TB: a randomized controlled trial. Presentation at the 34th IUATLD World Conference on Lung Health. Paris, France: 2003.

spontaneously reporting a cough of >2 weeks, only one case would have been missed and 381 examinations would have been conducted rather than 724.

In a house-to-house prevalence survey in Burma, including patients with cough of at least 2 weeks increased the number of sputum specimens examined by the laboratory by 19%, but with a proportionate (18%) increase in diagnosed cases compared to examining only patients with cough for 4 weeks.[50] Similar to the 1963 study, 88% of symptomatic cases were aware of their symptoms, and 50% of these were motivated to seek care. More recently, Santha et al. reported a 46% increase in smear-positive case detection when cough duration was reduced from 3 to 2 weeks among out-patients in six districts of India, with very little extra burden on the laboratories.[51]

Two major findings from this era have influenced subsequent ACF policies. First, extensive questioning was not necessary to identify those most likely to have active TB. Rather, focusing on cough as a determining symptom was sufficient. Second, over half of the sputum-positive patients had previously sought care for their symptoms but had not been diagnosed with TB. PCF could be successful if augmented with diagnostic services and improved training of health care personnel. Moreover, the authors of these studies believed that strengthening health care services would promote a higher level of health consciousness in the society, which would ultimately lead to an increased number of symptomatic patients visiting health facilities.

These findings were instrumental in leading to the dismantling of remaining mobile X-ray units. The Eighth Report of the WHO Expert Committee on Tuberculosis in 1964 concluded that mass radiography was indicated only if financial resources permitted.[52] The committee emphasized that the development or enhancement of the PCF infrastructure was a greater priority. Later, in its Ninth Report in 1974, the Committee supported PCF and strongly discouraged mass radiography.[53]

Large scale countrywide surveys in Czechoslovakia, the Netherlands, Canada, and Japan during the time period of the Eighth and Ninth WHO reports (1960–1974) supported the decision to discourage mass radiography as a case finding tool.[54–57] All studies found the majority of cases to be detected through PCF and not through periodic radiographic screenings. Moreover, despite the finding that annual incidence rates were decreasing, the proportion of smear-positive TB cases among newly detected patients remained unchanged. Targeted radiographic screening of high-risk populations was again recommended.

From the late 1960s to the early 1980s, case finding and treatment activities became part of general out-patient facilities, and mobile radiography units began to disappear.[46] This shift, in combination with the economic crisis that plagued TB control programs worldwide in the late 1970s and 1980s, meant that TB control often came under the aegis of other public health programs. As a result, case finding and treatment were not monitored closely, and TB control programs were unprepared to cope with the devastating effects of the future acquired immune-deficiency syndrome (AIDS) pandemic.[46]

House-to-house surveys

The prevailing recommendations in the 1970s and 1980s stated that PCF was adequate for TB control and the conventional wisdom was that TB was on its way to becoming a minor global problem.[46,53] Despite these beliefs, several studies during this era investigated the utility of house-to-house case detection through symptom survey, TST, mass radiography, or combinations of these techniques, in a variety of population settings.

In 1968, the Korean National Tuberculosis Programme replaced their long-standing mass radiography program with a sputum examination strategy.[58] A health aide was sent to collect sputum samples from symptomatic cases at their homes and refer them to the local health center. Sputum was also collected from all symptomatics who sought care at health centers. Over a 5-year period, the yield for health center screening was 5.4% (5000/92 000 examined) compared with 2.1% (14000/659000) through home visits. Although health care screening was more efficient, household visits detected almost three times more cases.

In New Mexico, a health team visited each Navajo Native American home, treating all health problems and screening for TB.[59] The impetus behind the project was the belief that the traditional Navajo is reluctant to seek care at available medical clinics, thus potentially creating a significant reservoir of unknown disease in the population. Over 97% of the population participated, and 29% were TST-positive, but only five pulmonary TB (PTB) cases were diagnosed. The authors concluded that this procedure, coupled with a health education program, can be an effective case finding tool in pockets of the population with suspected high TB incidence.

A more recent study in rural India tried to reduce the proportion of patients receiving further testing by initially screening with TSTs.[60] They determined that 78% of the registered population was required to undergo sputum examination based on the TST results; therefore, the work burden was not significantly reduced. Researchers in Bangalore, India, surveyed 96% of their population.[61] Overall, similar rates for active TB (320/100 000) were found when those only receiving CXR were compared with those receiving both CXR and symptom screening. Although symptom screening did not add significantly to radiographic screening, preliminary symptom screening reduced the number of radiographs required.

In a prevalence survey of KwaZulu, South Africa, the survey team went to randomly selected communities to publicize the survey and gain consent of the local chiefs.[62] All adults were asked to provide a sputum specimen and a CXR was taken. Over 60% of the population reported TB symptoms, but only 15 of 1136 (1320/100 000) were sputum smear-positive. The official notification figure for KwaZulu in 1974 was 177/100 000, compared to a prevalence of 804/100 000 estimated from this survey. The authors concluded that ACF would be necessary if TB incidence was to be reduced. Reliance on symptom surveys or mass radiography, however, would be impractical and too costly.

In a series of studies in the late 1970s and 1980s, Kenyan investigators tested several different case detection strategies.[63–66] An interesting finding was that each method resulted in similar outcomes whether conducted in different districts or different tribal and social conditions.[63] House-to-house surveys yielded the highest proportion of the estimated annual incidence of smear-positive cases, but this procedure required full population coverage, and was cumbersome, costly and time-consuming.[64,67,68] It was therefore considered an impractical strategy for many developing countries with limited resources. Although interview of tribal elders was more practical, this yielded only half the cases produced by house-to-house surveys, and only half were new cases.

Several studies have compared patients detected through ACF with those diagnosed through passive methods. In Eastern Nepal, patients identified through ACF were more likely to be older, female and to refuse or default from treatment.[69] More recently, a similar study in South India also found that patients detected through ACF were more likely to refuse or default from treatment, and were more likely to be smear-negative and less symptomatic than patients identified through PCF.[70]

A house-to-house symptom survey was conducted in a region of Central India with hilly forest terrain and small, isolated, sparsely populated villages consisting of tribal and non-tribal populations.[71] Over a 1-year period, over 114 000 (94% of total population) were surveyed, of whom 1987 (1.7%) were symptomatic. There were 148 (129/100 000) sputum smear-positive patients among the symptomatic cases. The authors concluded that control practices should not be limited to the more populated regions, but should also include more difficult to reach tribal groups. Likewise, TB prevalence can vary greatly from urban to rural areas, particularly given the crowding found in urban areas that facilitate TB transmission. A house-to-house survey in the Philippines using mobile CXR units was equally successful in both urban and rural populations.[72]

A house-to-house symptom survey in Addis Ababa, Ethiopia, surveyed over 12 000 residents in four kebeles, or urban neighborhoods, and revealed 173 (1.4%) symptomatic cases, of whom 23 (189/100 000) were sputum smear-positive for acid-fast bacilli (AFB).[73] Over 90% of the cases had been previously undetected, and the entire survey cost less than US$1000.

Out-patient symptom screening

The current recommended TB control policy advocated by the WHO is dependent on the evaluation of symptomatic patients who voluntarily seek care at health facilities for their symptoms. Patients attending a hospital are willing to seek care, but may not recognize that their respiratory symptoms are indicative of TB. A commonly used ACF strategy is surveying out-patients at a hospital for TB symptoms. This strategy is not as laborious as actively searching for patients in the community, and it is only slightly more intensive than a PCF system.

It was found that by using cough as a primary symptom among out-patients at health centers in a district of South India, the workload of the personnel at each center could be minimized, while 65% of all prevalent smear-positive TB cases could be detected.[49] In total, 10 792 patients were surveyed and 724 (6.7%) were symptomatic. Of these, 45 (417/100 000) were diagnosed with smear-positive TB. In Chiapas, Mexico, three strategies of ACF were compared: surveying for chronic coughers in a regional hospital, seven primary care centers and 32 communities.[74] High rates were obtained with each method, although case detection was highest in the hospital.

Surveying out-patients in Kenya was an effective way to detect previously unknown TB cases while not putting a strain on the hospital staff or laboratory.[65,75] Over 80% of patients detected through house-to-house surveys or interview of tribal elders stated that they had attended a health unit while symptomatic and had not been diagnosed.[66] The proportion of suspects detected at four district hospitals decreased with increasing distance from hospital; however, the proportion of bacteriologically-positive cases increased with increasing distance from the hospital. This finding suggests that patients living far from the hospital were less likely to present until their symptoms had progressed significantly.[65] Screening hospital out-patients for TB symptoms was successful in yielding 41% of the estimated annual incidence in this population.[75] Case detection was limited, however, to patients living in relatively close proximity to the hospital. Patients living far from the hospital were more likely to attend peripheral health units where diagnostic resources were limited.

Enhanced case finding

The Framingham Demonstration emphasized the importance of community awareness and involvement in case detection.[76] Patients came for screening due to the aggressive community promotion of the value of physical examinations. In 1917, mass screening for TB was conducted among the 16 000 residents of Framingham, Massachusetts. Following the implementation of a series of medical examination campaigns consisting of physical and sputum examinations, 83% of patients were detected at an early stage of disease compared to 45% before the survey began.

Another ECF effort, however, was not as successful. Prior to a case finding campaign in Vancouver, British Columbia, advertising appeared in local newspapers and television asking residents to attend clinics voluntarily to receive TB screening.[77] Only 1271 individuals participated in the survey, representing a small minority of the population, of which only eight were ultimately diagnosed with active TB (673/100 000).

In Kenya, a study explored the strategy of asking mothers attending maternity and child welfare clinics to identify TB suspects living in their households.[78] Mothers were asked to give letters to the suspects asking them to come to the clinic and undergo screening for TB. Of the 342 suspects who came to be screened, 261 were identified by the mothers, and 81 others said they came on their own initiative. In all, only 4% of the estimated annual incidence of smear-positive cases was detected, although very few resources were expended for this modest yield. The authors note that such an approach may reduce the problems associated with stigmatization because the suspects were approached by a family member.

An innovative approach towards case finding was the utilization of temporary camps. The allure of camps is that they do not require substantial financial or human resources investment. Rather, they can be conducted periodically, depending on TB incidence and public health resources. However, it is important to guarantee follow-up and treatment at a local health center for those diagnosed at such camps. The first camps for detecting TB were held in Maharashtra, India, in the 1970s, where a team screened a rural population and left treatment cards at the local health center with the names of patients who should receive treatment. The findings of these camps were not recorded and are therefore unknown.[79]

In a study in a remote mountainous area of Nepal, microscopy camps were set up for 2 to 4 days in areas of high TB prevalence.[80] Significant publicity, including house-to-house visits, pamphlets, posters, street theater shows and talks at schools, preceded the opening of the camp. Anyone attending the camp with a cough of more than 3 weeks was asked to provide a sputum specimen. Less than 6% of all TB over the 3-year study period was diagnosed through the camps. Costs associated with the campaign were increased because many non-symptomatic cases attended the camps for a free medical check-up. The microscopy camps might have been more cost-effective if house-to-house surveys had limited the invitations to symptomatics.

Investigators in Khon Kaen Province, Thailand, found that a case finding tool referred to as a rapid village survey was as effective as a total village survey in detecting TB.[81] For the rapid village survey, advertising was done via a vehicle with a loudspeaker inviting those with chest symptoms to come to the examination area. Symptomatic patients had a spot sputum taken and were asked to bring another the following day. One week later, a house-to-house survey asked all residents to attend for screening. During the rapid village survey, 1117 people were contacted and 7 (627/100 000) smear-positive cases were detected. An additional 19 613 were seen in the total village survey, and only one additional TB case was detected.

A rapid village survey was used again in the Shimshai Valley of Pakistan.[82] The procedure differed slightly in that the investigators went house to house asking any residents with a cough >3 weeks, hemoptysis, past history of TB or close contact with a TB patient to report to a central site for a CXR and spot sputum. Of 1077 residents, 231 (21%) were studied. Six (5.5%) of those who provided a sputum specimen were smear-positive, for a prevalence of 5505/100 000 among symptomatic cases.

In an attempt to increase case detection and treatment completion rates in central Sulawesi, Indonesia, a study was conducted to investigate the effectiveness of community education.[83] Communities that introduced a community-based TB program tripled their case detection rates, and treatment completion also increased considerably. Over the same period, detection in the control communities increased by only 13%.

A mass media health education campaign was launched in Cali, Colombia, in an attempt to increase case finding while reducing stigma associated with TB.[84] The campaign consisted of television and radio broadcasts focusing on public service announcements, talk shows involving TB patients and doctors, and leaflets inside daily newspapers. The importance of seeking care for a cough >15 days, the availability of a free diagnostic test and treatment, and promotion of a favorable attitude towards TB patients were highlighted. The media campaign resulted in a 64% increase in processed smears and a 52% increase in new PTB cases compared to the previous 3-month period. This increase did not continue, with case notification returning to the pre-intervention norm within 6 months. A control community showed no increase during the same period.

We therefore see throughout the world, and over time, that ECF efforts focusing on publicity and education tend to increase community awareness and the likelihood of self-presentation to health services. It is important to choose locally appropriate ECF methods, as not all methods in all settings are guaranteed to be successful, as shown in the Canadian study.[77]

High risk populations

Restricting ACF to populations known to be at increased risk for TB is an effective way to reduce costs while increasing yield. In this section, we examine ACF efforts among HIV-infected populations, the homeless and prisoners.

HIV

The HIV epidemic presents new challenges for case detection. Patients with both HIV and active TB present with different respiratory symptoms or atypical CXR results. Moreover, the literature suggests that HIV patients with TB are more likely to be sputum smear-negative or have extra-pulmonary abnormalities, and potentially be less likely to contribute to TB transmission.[85–87] These findings may result in reduced sensitivity of symptom surveys, leading to less effective case detection. Case detection strategies in this arena must be tailored to account for the many obstacles that the pandemic has wrought.[5]

Screening patients attending HIV voluntary counseling and testing (VCT) centers is a recent ACF strategy used in several countries. Research in Haiti combined community-wide education with HIV and TB testing at study clinics, and found 242 (2281/100 000) TB cases among 10 611 adults.[88] Among 1629 HIV-positive patients, 94 (5770/100 000) had TB. A similar study in Santo Domingo, the Dominican Republic, detected active TB in 39 of 400 (9750/100 000) people seeking HIV testing.[89] Of these, 29 (14 500/100 000) were HIV-positive and 10 (5000/100 000) were HIV-negative. Further research in Haiti found that 20% of patients reported cough when presenting for VCT, 32% of whom were diagnosed with PTB.[90] After the study, the center began screening all clients for TB symptoms as part of their standard protocol. A Ugandan study investigated the effect of TB prophylaxis to reduce TB in HIV-infected patients screened via symptom and CXR surveys for active TB among potential study participants to exclude them from their study.[91] Overall, active TB was discovered in 85 of 1524 (5577/100 000) evaluated participants.

A prospective, multicenter study in the US offered routine CXRs to a cohort of asymptomatic HIV-infected individuals.[92] Of 5361 annual screening CXRs among 1065 patients, only 11/114 (10%) patients with abnormal CXRs received a new pulmonary diagnosis, of which one was diagnosed with TB, for a prevalence of 94/100 000. This poor yield was replicated in a study in Hong Kong where only one of 22 abnormal CXRs among 191 HIV-infected patients (524/100 000) led to a diagnosis of PTB.[93] Limiting surveys to HIV-infected patients with symptoms is likely to be most effective, as case detection among over 1100 asymptomatic HIV-infected patients from six HIV centers in the US found only one (91/100 000) infectious case of TB.[94]

In 1998, an initiative supported by the WHO, the United States Agency for International Development (USAID) and the Centers for Disease Control and Prevention (CDC) Global AIDS Program, aimed at promoting collaboration between HIV and TB programs in detecting, treating and providing preventive medicine for people co-infected with HIV and TB. Six ProTEST (Promotion of Voluntary TESTing and Counseling) projects began in 1998 in South Africa, Malawi and Zambia.[95] Data were available from only three sites where HIV-infected persons were screened for TB. In two sites in South Africa, among 3463 screened patients, a TB prevalence of 8403/100 000 was detected. Among 1453 patients screened in Zambia, the prevalence was 9704/100 000. In Malawi, however, a significantly lower prevalence (677/100 000) was seen.

In a rural area of South Africa with a reasonably well-established health care infrastructure, ACF was not found to be a cost-effective method for reducing TB burden.[96] It is possible that a high prevalence of HIV altered the sensitivity and yield of a symptom survey that relied on prolonged cough to identify suspects.

ACF among HIV patients receiving home care in Cambodia detected 40 new TB patients compared to only 14 detected when passive case detection was used.[97] The ACF strategy offered a high yield (9297/100 000) among a group of patients who were not likely to seek care on their own. A study targeting HIV-infected women and their male partners in South Africa found a TB prevalence rate of 1083/100 000 in subjects with a positive TST.[98]

Routine mass radiography has been useful among South African gold miners, a population at unusually high risk of TB. This population undergoes annual chest radiography as a programmatic requirement. Men who self-reported were twice as likely to present with smear-positive disease compared to those detected through routine radiography.[99] Moreover, self-presenting patients were also more likely to be HIV-positive. A recent trial compared semi-annual radiographic screenings with annual screenings in this population.[*] Among over 22 000 randomized miners, the proportion of TB was similar in both screened groups (28–29%). Mortality within 2 months of TB treatment was significantly lower in the semi-annual group (10/100 person-years [py]) compared to the annually screened group (23/100 py). While this randomized trial found that reducing the interval of routine chest radiographic surveys was effective in diagnosing TB in earlier stages of disease, it was not successful at detecting more active cases.

The only other published randomized trial of ACF also looked at the effectiveness of periodic CXRs among a high-risk group.[100] Over 15 000 patients with inactive TB were followed. There were 69 confirmed reactivations, 42 in the ‘check-up’ group and 27 in the ‘discharge group’, an increase of over 50%. The authors concluded that annual check-ups for this population were not necessary and should be stopped, despite the fact that almost half of the patients were detected through this strategy.

The WHO has recognized the need for creating and validating protocols for TB screening in HIV-infected patients prior to initiating preventive therapy.[101] Two research groups have compared symptom-based screening with chest radiography in HIV-infected patients. Among 129 patients being screened for TB in three HIV clinics in Cape Town, South Africa, 11 (8.5%) cases were diagnosed.[102] Cough >2 weeks had a sensitivity of 82%

[*] Roux S, Fielding K, Grant A D, et al. See note above on p. 1185.

compared to a suggestive CXR of 27%, sputum smear of 55% and sputum culture (91%). A similar study in Botswana attempted to use radiography to rule out TB in 560 asymptomatic HIV-infected patients.[103] Only 24 (4.2%) patients had abnormal CXRs, and one was diagnosed with TB based solely on the CXR result.

Homelessness, poverty and prisons

Homeless shelters present a high-risk population for TB in the US,[104–106] and have been found to offer a low yield due to high levels of participant refusal and loss to follow-up in the US.[107,108] An evaluation in Los Angeles, California, suggests that screening for TB in homeless shelters may miss many cases among the homeless population that does not live in shelters.[109] Most of the homeless people evaluated were likely to visit emergency departments when sick, suggesting that a potential cost-effective screening method may be CXR screening of homeless patients presenting to emergency rooms for treatment.

Homeless shelters have been the focus of ACF efforts in many countries.[110–113] Public advertisements encouraged homeless people to receive screening from mobile X-ray units in South Wales,[110] while a study in Barcelona found that the majority of TB among the homeless (70%) was diagnosed in hospitals.[112] Although both studies detected unknown TB, the expense of the surveys precluded further implementation.

Organized ACF can be conducted on a large scale in a short period of time when high-risk targeted populations are identified. In just 11 days, the Tuberculosis Coordination Program in Sao Paulo, Brazil, surveyed 2.4 million people at over 9000 health services, prisons and shelters covering 7% of the population, and detected an overall prevalence of 25/100 000.[113] In another campaign in Sao Paulo, ACF among residents of 17 homeless shelters discovered an overall prevalence of 138/100 000.[111]

Alcoholism[114,115] and drug abuse[116] have been implicated as risk factors for the development of TB. To ascertain the effectiveness of screening for TB among the alcoholic and drug abusing welfare population in NYC, 2641 welfare clients were interviewed, of which 970 were characterized as alcoholics or drug abusers.[117] Only nine (928/100 000) active TB cases were diagnosed; however, this was 28 times the rate found in the age-matched general population of NYC.

In the Philippines, a church used 28 ‘promoters’ as volunteer outreach workers ministering to the ill and needy to bring people with chronic coughs to the church where they were evaluated for TB.[118] In the district of 55 000, 1990 (4%) coughers had sputum specimens collected, of which 207 (376/100 000) were smear-positive. These patients were then hospitalized for treatment initiation and followed in the community by the promoters.

Case detection strategies have combined house-to-house surveys with targeted intervention among high-risk populations, such as those in jails, shelters and orphanages.[119] A recent study in Mexico detected 86% of all reported cases over an 18-month period, suggesting that a complete house-to-house survey in addition to targeted screening of high-risk populations is an effective method for detecting the majority of prevalent TB in an area where such high-risk facilities are likely to contribute significantly to TB dynamics in a community.

It has long been known that prisons and jails are particularly high-risk locations for transmission of *M. tuberculosis*, given the high density living conditions.[120] While inmates and jailers are at increased risk, so too are the communities to which they return. Failure to prevent and control TB in jails and prisons increases the risk of transmission once inmates and prison workers return home. Surveys discovered a TB prevalence of 72/100 000 in a San Francisco, California jail[121] and 568/100 000 in four provincial prisons in southern Thailand.[122] Studies in Connecticut, Illinois and California in the US, as well as in Spain and Malawi, noted that prevalence of active disease was higher in jails and prisons than in the surrounding communities.[120,123–126] A study in Thailand found prevalence to be eight times higher than in the general population,[122] and in Barcelona it was 50 times higher.[123]

Cost-effectiveness

The financial and economic costs of conducting an ACF intervention should be carefully assessed. When cost-effectiveness is not measured appropriately, the results of ACF initiatives may be missing a vital component that may hinder future replication.

None of the ACF studies in this review conducted a cost-effectiveness study with established guidelines, although they may have concluded that a particular intervention was ‘cost-effective.’ Cost-effectiveness studies provide results in terms of incremental cost-effectiveness ratio (ICER). The ICER measures the change in cost per change in effect, such as $100 per case of TB found with a particular case finding method compared to another method. As the studies under review did not directly compare an alternative method of case finding, incremental cost-effectiveness ratios could not be calculated.

The studies suffered from various deficiencies with regard to cost-effectiveness measures, including not stating what costs were included or excluded for calculations, and estimated costs were not provided. Sometimes important costs such as laboratory costs were not included in the calculation.

Future ACF efforts should consider including cost-effectiveness analysis. Important considerations such as savings incurred from preventing future TB cases, reduction of treatment and rehabilitation costs through early detection and loss of income for patients should be included in these studies. This will provide decision-makers with much needed information on which to base their policies and programs.

DISCUSSION

Studies of ACF and ECF carried out over more than 80 years have had various levels of success. The majority have shown some yield from ACF and ECF in selected populations, but whether this was deemed worthwhile depended on the setting and assessment strategies employed. Too often the impact of ACF on TB incidence was not assessed, however.

At present, there is a recognized global urgency to improve case detection.[127,128] Heightened interest regarding the utility of ACF and ECF as measures to increase case detection has recently sparked a resurgence in research into this issue. It has become evident that case finding will only succeed if an effective treatment program is concurrently in place.

Likewise, the success of DOTS depends on substantial increases in case detection.[129,130] However, few studies have investigated case finding strategies in areas with high cure rates. This gap in the literature calls for innovative approaches towards case finding that, when coupled with comprehensive treatment, will significantly reduce TB incidence.

This need is especially evident in areas with high TB and HIV co-infection. The Second Ad Hoc Committee on the Tuberculosis Epidemic acknowledged that DOTS alone was incapable of reducing morbidity and mortality in this context. It called for additional interventions to supplement DOTS, including 'intensified' case finding.[2,127] The WHO Expanded DOTS Framework for Effective Tuberculosis Control also advocated more than DOTS in high HIV settings. Specifically, it recommended earlier interventions.[128] A new initiative funded by the Bill and Melinda Gates Foundation is addressing the effectiveness of large scale ECF and ACF strategies in such areas. The ZAMSTAR study of the Consortium to Respond Effectively to the AIDS/TB Epidemic (CREATE) will investigate the value of ECF in reducing TB incidence in Zambia and South Africa, areas with extraordinarily high HIV-TB co-infection rates.[*]

Anatomy of a case detection strategy

The choice of a case detection strategy is a locally motivated decision. ACF campaigns are more costly from a financial and human resource perspective, but have the potential to capture a large yield of TB cases. ECF may produce fewer cases, but it is an effective strategy that many resource-poor countries may be able to afford more readily than a large scale campaign.

The utility of ACF can be influenced by four conditions: 1) prevalence, 2) epidemiological importance, 3) chance of being detected otherwise, and 4) cost.[131] *Prevalence* refers to the proportion of the population with undiagnosed TB and any individual's risk of having TB at screening. The greater the risk, the higher the priority for screening that individual, or population of such individuals. The *epidemiological importance* refers to the effect that an individual or population of individuals with TB will have on the community. Those most likely to infect others (such as those in small congregate settings or exposed to HIV-infected populations) should be targeted for detection and treatment. If symptomatic patients have an increased *chance of being detected* because they are likely to present to health services within a short time, then a community-wide program may not be worthwhile. Surveys of remote areas with patients unable to access medical care can greatly reduce the TB burden. The *cost* of ACF must be assessed in the context of the incremental yield of the strategy in finding cases and preventing future cases as well as competing uses of limited funds. Additional factors that influence the impact of a case detection strategy are the method (e.g., house-to-house, flyers, mass media) and location (e.g., community, hospital, HIV clinic). Resources needed per case finding strategy differ substantially according to these components.

When ACF is planned, the most appropriate screening and detection tools need to be chosen. Cough of 2–3 weeks' duration is the primary symptom used to survey populations for TB.

[*]Available at www.tbhiv-create.org/

Studies have shown that cough duration of >3 weeks provides a reasonable balance between sensitivity and specificity.[49–51,63]

In countries encumbered with severe TB epidemics and limited resources, smear-positive PTB is often under-diagnosed.[132] As the number of suspects increases, the burden on the health system and the need for trained personnel also rise. Training of more laboratory technicians, clinicians and field staff is vital to the success of any strategy.

Proper and accurate bacteriological examination is integral to any case detection program, but specifically to ACF, which often relies on rapid reporting of results. A strong bacteriological laboratory network is essential to any large-scale case finding program.[133] Two surveys in the Transkei in South Africa investigated the most effective tools to aid ACF.[134,135] Sputum collection followed by AFB smear microscopy was most often the tool of choice for its practicality, relative ease of collection and interpretation and cost-effectiveness. Culture was most efficient in detecting less infectious cases.

Evaluating case finding programs

The most important measure of success for any case detection strategy is the reduction of TB incidence over time. Most studies have not measured changes in TB incidence, but rather have assessed the efficiency of health services in detecting cases. The impact of ACF on the TB infection rate and TB incidence must be measured to determine its long-term impact.

With any ACF program, an initial increase in reported incidence is expected, as case detection methods identify many TB patients who were undetected under the current health care system. Measuring the impact on incidence requires a sufficiently long period of follow-up. Repetition of an ACF strategy at established intervals should yield declining trends in incidence, but may not be necessary. The impact of a single round of ACF may substantially reduce new TB infections and subsequent incidences, particularly if TB services are strengthened simultaneously. Repeating ACF adds significantly to the cost of any ACF strategy and needs to be carefully studied to determine if multiple rounds of ACF add appreciably to the desired outcomes, or if a ‘one shot’ ACF strategy followed by strong PCF is adequate. Adding other interventions, such as treatment of latent TB and HIV counseling and testing, will also improve the benefits of an ACF strategy.

Programmatic considerations

ACF can have several important roles in both disease control and program evaluation and performance. An ACF campaign can provide more accurate estimates of TB prevalence in a region, which will permit assessment of program performance and may help garner the required resources. Borgdorff has recently proposed using population prevalence surveys as a means of determining the patient detection rate, replacing the estimated case detection rate based on modeled incidence data, for example.[136] In addition to these roles, for ACF, the attendant publicity and community mobilization for ACF may also increase the number of patients self-referring to health care facilities by increasing awareness of available health services.

In several studies reviewed, many cases detected through ACF had previously sought health care, but were not tested for or diagnosed with TB. This stresses the need for augmenting the current PCF capabilities in many high incidence areas and for increased training of all health care workers. In areas where PCF is doing a fair job, new case finding strategies should incorporate PCF, rather than displacing these necessary components of disease control. If a substantial proportion of a population is symptomatic and willing to seek care for their symptoms, a passive TB control program based on accurate detection of TB among these patients may prove to be economical, practical and effective. Moreover, when an ACF program is started, there will be an inherent heightened awareness of TB in the community, thus causing more people to seek care. In areas where patients do not routinely seek care voluntarily for TB, targeted ACF of symptomatic patients should be considered. Focusing these strategies on symptom surveys and then further screening symptomatic patients is the most cost-effective method available.

CONCLUSIONS

Many ACF strategies have been successful in the context in which they were assessed. Unknown active cases were detected; prevalence estimates were made, leading to appropriate allocation of resources; TB prevalence decreased in the short term; TB patients were found earlier in their disease; and programs were able to evaluate the success of their current systems at detecting TB in their communities. ACF is prohibitively expensive in some settings, however, such as in low-prevalence populations. In other settings, patients identified through ACF may refuse care. When applied to epidemiologically appropriate settings and coupled with strong and effective DOTS programs, ACF has the potential to substantially reduce TB incidence in high burden areas.

RECOMMENDATIONS

Choosing a case detection strategy

Passive case finding

1. When local health care facilities are functioning efficiently, additional case finding strategies may not be required. Moreover, in areas with very low TB prevalence, PCF accompanied by contact tracing is often sufficient.
2. Prior to initiating a case finding program, local health care facilities should diagnose and treat TB effectively, preferably with DOTS. Moreover, the effects of a successful ACF program will be sustainable if PCF is strengthened.

Enhanced case finding

1. ECF through media campaigns, pamphlets, and outreach at schools and workplaces may help to destigmatize TB and increase voluntary presentation at a minimal cost.
2. ECF should only be used in conjunction with a strong PCF system.
3. ECF can also be conducted in conjunction with an ACF program.

Active case finding

1. Targeted ACF is often the most cost-effective ACF strategy. Use local epidemiologic data to identify appropriate populations and geographical locations. Successful programs have been implemented in HIV voluntary counseling and testing centers, and this practice is currently recommended by the WHO. Other settings where ACF has been effective are homeless shelters, prisons, nursing homes and impoverished areas. At a minimum, ACF among TB contacts provides significant yield with minimal resources and should be considered in areas with and without high HIV prevalence.
2. Symptom screening in clinical and community settings has been shown to be an efficient, high yield ACF strategy and should be used when available resources are limited.
3. House-to-house screening is a more comprehensive ACF strategy and may detect more TB cases. The high costs associated with these programs are often prohibitive. However, when resources are available, this method can be highly effective, particularly in high-incidence populations.

Choosing a case detection tool

1. Symptom screening is the primary tool for any case detection program. Varying the threshold of cough duration (e.g., 2 weeks, 3 weeks) affects the sensitivity and specificity of screening. Three weeks of cough has better specificity, but 2 weeks has somewhat higher sensitivity.
2. Sputum smear microscopy is the least expensive and most rapid diagnostic tool, and is appropriate for use in most developing countries. Culture will increase yield in areas with high rates of smear-negative disease (i.e., HIV populations), but at substantial cost.
3. Mass chest radiography is an effective case detection method when limited to targeted groups, and is best utilized as a programmatic routine screening activity conducted at regular intervals. Measures to ensure accurate readings of radiographic films are essential.
4. New tools to better diagnose smear-negative TB are desperately needed, especially for HIV-infected individuals.

Outcomes of a case detection program

1. Reduction in incidence is the ultimate goal of case detection. Studies should be conducted allowing for appropriate follow-up to measure changes in incidence.
2. Prevalence surveys before and after a case detection program can be an effective method of measuring impact.
3. Measuring delays in diagnosis before and after a case detection program can be an effective method of measuring impact.

4. **4.** Treatment completion should be monitored to ensure high completion rates among newly detected patients.
5. **5.** If more than one intervention aimed at reducing TB incidence is implemented, which is highly recommended, the monitoring and assessment should allow for separation of the intervention effects.

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Table

Active case finding literature: case detection methods and results*

				Case detection method†									Case detection tool‡					
Ref #	Author	Year and country	Sample surveyed	Mass CXR	H-H (home)	H-H (refer)	Temp site	Hosp/ clinic§	Publ/ educ	CI	Reg/ FU	PCF	Sym sur	TST	Sm	Cx	CXR	Results
19 21	Edwards	1940 USA	162 446 individuals representing 15 population groups in NYC	x													x	Studies include radiograph surveys of over 160 000 individuals in NYC representing 15 population groups. In 1934, of 25 170 screened, 824 TB cases were diagnosed, of which 90% were previously unknown.
20	Plunkett	1939 USA	5713 TB suspects and 6215 contacts of TB cases in 4 NYC TB hospitals							x							x	11 928 received X-rays; 319 (2674/100 000) cases were detected among new patients; 127 (3369/100 000) among contacts; 192 (3603/100 000) among suspects.
22	Davies	1946 USA	34 000 residents of St Louis County, MN	x					x				x		x	x	x	38 (112/100 000) had active TB, 6.6% with TB lesions. Median completeness of community examination was 87%.
23	Davies	1946 USA	367 residents of a small, rural township in St Louis County, MN	x					x				x		x	x	x	Compared to the 19 cases that occurred previous to 1937, the authors stated that 10 cases should have occurred post 1937, but none were identified.
24	Davies	1948 USA	Village of 6000 in Ely, MN	x					x				x		x	x	x	Examination of the community in 1943 identified 14 active TB cases. Only 1 new case was diagnosed between 1943 and 1946 compared to the expected 11.
25	Ames	1953 USA	330 585 persons in Buffalo, NY (1946–1950)	x												x		656 (198/100 000) previously unknown TB cases were detected
26	Cochrane	1956 South Wales	5691 in a rural, agricultural population	x											x	x	x	95% of the population screened; TB prevalence for females: 70/100 000; males: 150/100 000. Yield of previously unknown infectious cases was 90/100 000.
27	Silverman	1949 USA	48 175 residents of Baltimore, MD (50 population groups)	x													x	80% participation; 292 TB cases (606/100 000); 64% had minimal lesions; 14% of total TB burden for the year
28	Arctic Health Research Center	1960 USA	Mostly 'native' members of the 3 aboriginal groups in Alaska, 1950–1957	x										x	x	x	x	In addition to many forms of mobile radiograph units (marine units, railroad cars, trucks and airborne units), additional beds were made available at hospitals and sanatoriums. TB mortality decreased from 1950 (239/100 000) to 1957 (116/100 000).
31	Anderson	1952 USA	Over 5 800 000 residing in 17 areas throughout the US	x		x									x		x	Of 5 840 897 initial X-rays, 126 881 (2.2%) were considered TB suspects. When followed with 14 × 17 inch, 53 686 of 166 226 (32%) were TB suspects. In Seattle, WA, TB mortality dropped

Ref #	Author	Year and country	Sample surveyed	Case detection method[†]										Case detection tool[‡]				Results
				Mass CXR	H-H (home)	H-H (refer)	Temp site	Hosp/ clinic[§]	Publ/ educ	CI	Reg/ FU	PCF	Sym sur	TST	Sm	Cx	CXR	
																		from 40/100 000 in 1948 to 19 in 1950; Minneapolis, MN reported a decr from 40/100 000 in 1948 to 19 in 1950; Minneapolis, MN reported a decr from 40/100 000 in 1948 to 19 in 1950; Minneapolis, MN reported a decr from 40/100 000 in 1948 to 19 in 1950; Minneapolis, MN reported a decr from 40/100 000 in 1948 to 19 in 1950; Minneapolis, MN reported a decr
32 33 34 35	Comstock	1949 USA 1955 1951 1956	38 190 residents of Muscogee County, GA	x							x		x		x	x	x	712 (1.9%) had positive initial CXR; 568 were retained for follow-up. Of the 37 478 with negative initial CXR, 227 became cases (138 'new', 89 'positive' previously in 1946). Over a 5-year period, incidence among the negative population increased from year 1 to year 3 (9 to 25/100 000), then decreased to 15/100 000 and then to 5/100 000 in the final year.
36	Groth-Petersen	1959 Denmark	1 400 000 population in Denmark				x		x					x			x	Of 795 125 adults examined, 20 420 (2.6%) were diagnosed with possible pulmonary disease, of whom 503 (63/100 000) were diagnosed with active TB.
37	Horwitz	1976 Denmark	Surveys from Denmark, 1946–1972; main emphasis on 836 800 adults examined in 1972	x													x	599 (72/100 000) TB cases detected; 168 (28%) from mass screening of 677 808 persons; 305 (51%) among 100 416 symptomatic patients; 30 (5%) among contacts of TB cases; 18 (3%) among previous TB cases; 78 (13%) for other reasons.
38	Sigurdsson	1947 Iceland	43 595 children and adults in Reykjavik			x								x	x	x	x	98% of population initially examined by either TST or CXR. In all, 71 (160/100 000) new cases of active TB diagnosed.
39 40	Cochrane	1952 South Wales 1955	19 000 rural population in the Vale of Glamorgan	x		x									x		x	89% of the population screened. Among 8492 men, 47 (553/100 000) TB cases detected; rates similar among miners and non-miners; rate among women was 709/100 000. In second survey, prevalence decreased among women (602/100 000), but remained similar in men.
41	Cochrane	1957 Scotland	8236 persons >5 years of age; (95%) in rural south Scotland	x		x									x		x	98% of population was X-rayed; 12 (145/100 000) new TB cases detected.
42	Aspin	1945 India	3511 civilian personnel and 3097 army recruits	x													x	Two groups were X-rayed: 3511 civilian personnel, of whom 108 (3.1%) had PTB; and 3097 army recruits, of whom 24 (0.8%) had TB.
43	Frimodt-Moller	1960 India	37 000 in 189 small rural villages in South India	x											x	x	x	Over a 1-year period, 20 975 people were X-rayed and 618 (2946/100 000) had abnormal findings, of whom 89 (424/100 000) were probably active TB.
44	Pamra	1968 India	44 371 (1953–1954) and 76 951 (1960–1962) in Delhi	x											x	x	x	1st survey: 274 TB cases detected (618/100 000); 2nd survey: 842 TB cases detected (1094/100 000)
	Roux**	2003 South Africa	22 634 gold miners at 1 particular company	x											x	x	x	TB cases in intervention arm had less extensive disease than the control arm. Mortality rate was

Ref #	Author	Year and country	Sample surveyed	Case detection method†									Case detection tool‡					Results
				Mass CXR	H-H (home)	H-H (refer)	Temp site	Hosp/ clinic§	Publ/ educ	CI	Reg/ FU	PCF	Sym sur	TST	Sm	Cx	CXR	
																		significantly lower in intervention (10 100/100 000 py) compared to contr significantly lower in intervention (10 100/100 000 py) compared to contr
47	Banerji	1963 India	2000 in 39 villages and towns in South India	x		x							x	x	x	x	x	2.5% had active or probably active TB on CXR, and 0.4% of the X-rayed population had AFB in their sputum; 50% of symptomatic patients sought care for their symptoms
48	Nagpaul	1970 India	2425 randomly selected patients attending a TB clinic in India					x							x	x	x	Of 2308 (95%) sputum samples collected, 179 (7755/100 000) were Sm+, Cx+ or both; 163 (7062/ 100 000) were Cx+.
49	Baily	1967 India	10 792 out-patients at a health facility in the Tumkur district in South India					x					x		x		x	724 (6.8%) were symptomatic; 622 reported cough spontaneously, 102 upon further questioning; 39% reported cough of ≤13 days. Of 45 (6.2% of all symptomatic patients) new Sm+ cases detected, 44 reported cough and 43 had cough ≥2 weeks' duration.
50	Nyunt	1974 Burma	35 026 persons in rural and urban areas		x								x	x	x		x	2339 (6.6%) had chest symptoms (86% cough); 51 (145/100 000) were sputum Sm+.
51	Santha	2005 India	55 561 out-patients in 3 states					x					x		x			2210 had cough ≥2 weeks, including 1370 with cough ≥3 weeks; 50% sought care for symptoms
54 55	Styblo Krivinka	1967 Czechoslovakia 1974	100 000 general population	x							x			x	x	x	x	Mass radiography surveys every 3 years revealed 30 Sm+ cases from 200 000 exams (15/100 000). Incidence of bacillary TB decreased from 142/100 000 in 1961 to 52 in 1972, a mean annual reduction of 9.4%.
58	Sung	1976 Korea	92 000 reporting to health centers and 659 000 community residents in Korea		x			x					x		x		x	In 1973, 1 491 000 X-ray examinations discovered 87 000 suspects, of whom 12 000 (805/100 000) were bacteriologically confirmed. Sputum-based case finding contributed 19 000 cases among 751 000 (2530/100 000). Among sputum-based ACF, 5000 were discovered at health centers compared to 14 000 at home visits.
59	Tempest	1974 USA	760 residents on a Navajo Indian reservation in New Mexico		x									x	x		x	97% of community screened; 29% had a positive TST; 5 (679/100 000) had active TB, only 1 was symptomatic.
60	Chakraborty	1995 India	29 400 residents of Bangalore			x								x	x			Only a 21% reduction in screening burden was observed with TST; 96 cases were detected (438/100 000); 15 Sm+ (68/100 000).
61	Gothi	1976 India	22 957 rural residents of 55 villages in Bangalore		x								x	x	x		x	Symptoms and CXR detected 60 cases (318/100 000); CXR alone detected 49 cases (321/100 000); symptoms alone detected 38 (208/100 000).
62	Arabin	1979 South Africa	3789 people from 10 locations; total population 1.2 million		x				x				x		x			893 CXRs revealed 25 active TB cases (2800/100 000); 1149 sputum samples detected 15 Sm+

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				Mass CXR	H-H (home)	H-H (refer)	Temp site	Hosp/ clinic§	Publ/ educ	CI	Reg/ FU	PCF	Sym sur	TST	Sm	Cx	CXR	
																		(1305/100 000), 9 Cx+ (783/100 000); 60% of the adult population sympt
63	Aluoch	1983 Kenya	320 TB patients in 17 district hospitals					x					x				x	62% of study participants were diagnosed within 6 months and 13% were diagnosed after 6 months.
64	Nsanzumuhire	1977 Kenya	6090 households in Machakos district, Kenya		x						x		x		x	x		Elders identified 363 (19%) of 1907 TB suspects, 6 (40%) of the 15 Sm+ and 8 (31%) of the 26 Cx+. Household survey identified 1716 (90%) of all suspects, 14 (93%) of Sm+ and 25 (96%) of Cx+.
65	Aluoch	1984 Kenya	20 756 new out-patients attending a district hospital					x					x		x	x	x	601 (2.9%) were considered suspects; 13 Sm+ (1997/100 000), 7 Sm−/Cx+ (1165/100 000). In all, 33 patients (5491/100 000) considered to have active TB.
66	Aluoch	1982 Kenya	27 515 in Kirinyaga, Kenya			x		x		x	x		x		x	x		Of all cases detected through ACF: H-H survey detected 70% of Sm+ and 60% of Sm− cases; elders detected 33% of Sm+ and 16% Sm−. Only 35% of patients reporting with cough to health care services were examined radiographically (12%) or bacteriologically (8%); 15% had both exams.
67	Aluoch	1978 Kenya	38 669 in 2 locations in Machakos district, Kenya			x				x	x				x	x		Elders named 421 suspects, of whom 2 were Sm+/Cx+, 1 more Sm−/Cx+. Previously registered TB patients yielded a high proportion of Cx+ cases (9.3%); 651 contacts of 124 TB registered TB cases yielded 3 (0.5%) Sm−/Cx+ cases.
68	Nsanzumuhire	1981 Kenya	35 264 in Mukaa location of Machakos district, Kenya			x		x		x	x				x	x		Of 1293 suspects identified by household elders (8%), household survey (75%); 10% by both, 7% through health units. 25 Cx+ (1933/100 000), 12 Sm+ (928/100 000) (5 of 12 old cases).
69	Cassels	1982 Nepal	67 068 (58% of total population) in Sankhuwa Sabha			x						x	x		x	x		2843 (4.2%) symptomatic; 111 (3.9%) Sm+ (165/100 000). Over same time period, 159 new Sm+ patients self-referred to health care facilities. Estimated overall prevalence was 403/100 000.
70	Santha	2003 South India	32 683 in 209 villages in Tiruvallur district, southern India		x							x	x		x	x	x	91% of population screened; 211 (646/100 000) TB cases detected through ACF; 508 cases detected through PCF at health care facilities. Treatment cure rates were similar between the 2 groups (72%).
71	Narang	1999 India	Tribal population of 20 596 and non-tribal population of 93 670 >5 years of age		x								x		x	x		1987 (1.7%) symptomatic patients; 55 were Sm+/Cx+ (2768/100 000), 65 Sm−/Cx+ (3271/100 000), 18 Sm+/Cx− (906/100 000). TB prevalence 133/100 000 in tribal and 144/100 000 in non-tribal populations.
72	Tupasi	1999 Philippines	15 905 of Metro Manila and urban/ rural areas in Philippines		x									x	x	x	x	Of 15 905 eligible patients, 12 850 (81%) received a CXR; 537 (4.2%) suggestive of TB; of 1390

(1305/100 000), 9 Cx+ (783/100 000); 60% of the adult population sympt

Ref #	Author	Year and country	Sample surveyed	Case detection method† Mass CXR	H-H (home)	H-H (refer)	Temp site	Hosp/ clinic§	Publ/ educ	CI	Reg/ FU	PCF	Sym sur	Case detection tool‡ TST	Sm	Cx	CXR	Results
																		sputum specimens, 127 (9.1%) Cx+; 47 (4%) were Sm+; prevalence of ac
73	Demissie	2002 Ethiopia	12 149 people >14 years in 2440 households		x								x		x			173 (1.4%) were symptomatic, of which 23 (189/100 000) were Sm+; only 2 patients were receiving TB treatment when detected through survey.
74	Sanchez-Perez	2002 Mexico	~4000 hospitalized patients; 6140 residents in 32 communities; 2203 patients from 7 primary care centers.			x		x					x		x	x		Hospital: 44 of 209 coughers had TB (21 053/100 000); primary care centers: 17 of 153 coughers had TB (11 111/100 000); community: 17 of 228 had TB (7456/100 000); denominators were likely biased towards sicker patients.
75	Aluoch	1985 Kenya	87 845 new out-patients attending 4 district hospitals					x					x		x	x	x	2299 (2.6%) were TB suspects; 109 (4741/100 000) Cx+, 82 (3567/100 000) Sm+.
76	Armstrong	1921 USA	16 000 residents of Framingham, MA			x							x					1% had active TB.
77	Grzybowski	1987 British Columbia	1271 persons in a socially and economically depressed inner-city area of Vancouver, BC						x					x	x	x	x	Of 1271 volunteers, 8 (0.7%) cases of active TB were diagnosed; 6 had an X-ray suggestive of TB, 3 were initially SM+ and 6 were Cx+ on their initial sputum examination, while the other 2 were Sm+ and Cx+ on their second sputum specimen.
78	Aluoch	1987 Kenya	342 contacts identified by mothers attending maternity and child welfare clinics					x		x					x	x	x	Of 342 suspects, 261 were identified by the mothers, 81 others came on their own initiative. Of 238 examined bacteriologically, 6 (2.5%) were Sm+/Cx+, and 2 (0.8%) Sm−/Cx+.
80	Harper	1996 Nepal	4009 persons with symptoms were evaluated in mountainous region of Nepal				x		x				x		x			71 (1.8%) were Sm+. Of all the TB diagnosed in these regions during the time period, 5.7% were identified through the camps.
81	Schuurman	1996 Thailand	20 730 people in 40 villages of Khon Kaen Province, North-East Thailand		x	x	x		x				x		x			In the rapid village survey (RVS), 7 (627/100 000) new Sm+ cases were identified (14 overall); only 1 more was identified with the total village survey (TVS).
82	Alvi	1998 Pakistan	1077 inhabitants in Shimshai valley			x	x						x		x		x	An RVS determined that 231 (21%) people be examined. Of 109 with sputum specimens, 6 were Sm+ for a population prevalence of 557/100 000.
83	Becx-Bleumink	2001 Indonesia	362 700 in 224 villages in central Sulawesi						x				x		x			Case notification rates increased in intervention villages from 51 to 166/100 000 over a 3-year period, compared to an increase from 62 to 70/100 000 in control communities.
84	Jaramillo	2001 Colombia	Cali, Colombia						x						x			Media campaign increased the number of smears processed by 64% and number of new cases of PTB discovered by 53% compared with previous time period.

sputum specimens, 127 (9.1%) Cx+; 47 (4%) were Sm+; prevalence of ac

Ref #	Author	Year and country	Sample surveyed	Case detection method†									Case detection tool‡					Results
				Mass CXR	H-H (home)	H-H (refer)	Temp site	Hosp/ clinic§	Publ/ educ	CI	Reg/ FU	PCF	Sym sur	TST	Sm	Cx	CXR	
88	Desormeaux	1996 Haiti	10 611 residents of Cité Soleil, Haiti					V	x				x	x	x	x	x	10 611 adults screened, representing 10% of adult population; 94 (603/100 000) of HIV-infected had TB. In total, 242 (2281/100 000) patients were diagnosed with TB.
89	Espinal	1995 Dominican Republic	200 HIV+ clients and 200 age- and sex-matched HIV− clients at HIV clinic					V					x	x	x		x	29 HIV+ clients had TB and 10 HIV− clients had TB; (aOR = 3.3, 95%CI = 1.3–8.7); 85% of patients diagnosed with TB had ≥1 symptom readily attainable through brief screening interview.
90	Burgess	2001 Haiti	1327 adults at HIV VCT center in Haiti					V					x		x	x	x	263 (20%) reported cough; 241 were evaluated; 76 (32%) diagnosed with PTB; 42 Cx+; 28 (12%) Sm +.
91	Aisu	1995 Uganda	1524 HIV-infected patients being screened for enrollment into a preventive therapy study at HIV clinic					V					x		x		x	Overall, 85 (5.6%) of 1524 patients were diagnosed with active TB.
92	Schneider	1996 USA	1065 HIV+ patients from 6 HIV clinics throughout the US					V						x	x	x	x	Of 114 patients with abnormal X-rays, 13 (11%) new pulmonary diagnoses were made, 1 was TB (877/100 000); of 951 patients receiving normal X-rays, 2 were diagnosed with TB within 2 months (210/100 000).
93	Ho	1999 Hong Kong	191 HIV-infected patients at an HIV clinic					C							x	x	x	Among 191 patients, 311 routine CXRs were taken with a total follow-up of 792 person years; only 1 of 22 abnormal X-rays led to a PTB diagnosis.
94	Kvale	1994 USA	1171 HIV+ at 6 HIV centers					C							x	x		Only 1 (0.04%) TB case was detected among asymptomatic, HIV-infected individuals.
95	WHO	2003 South Africa, Malawi, Zambia	HIV-infected at HIV VCT centers: South Africa: 3463; Malawi: 2217; Zambia: 1453					V					x		x	x		In South Africa, among 3463 screened patients, 8.4% were diagnosed with TB. In Zambia, among 1453 patients, 6% were diagnosed with TB. In Malawi, prevalence of 0.7%.
96	Pronyk	2001 South Africa	10 542 households in rural area of South Africa		x								x		x	x		Of 38 251 residents, 366 (1%) were confirmed chronic coughers and 6 (1.6%) were positive on smear and/or culture. Prevalence of 16/100 000 cases of Sm+ PTB.
97	Kimerling	2002 Cambodia	441 home-based HIV patients		x										x	x		40 (9%) new patients identified compared to 14 detected prior to this screening using PCF.
98	Nachega	2003 South Africa	438 HIV-infected women and their partners in an HIV transmission prevention program in Soweto, South Africa					C						x	x	x	x	Of 483 HIV-infected women, 318 (73%) returned for a reading; 157 (49%) were TST+. Of 120 patients who were further examined, 13 (11%) were found to have active TB.
100	Styblo	1984 Netherlands	15 000 patients with inactive TB or fibrotic lesions	x											x	x	x	Check-up group: 42 TB cases: 36 Cx+; 4 Sm+; discharge group: 27 TB cases: 27 Cx+; 10 Sm+.

Ref #	Author	Year and country	Sample surveyed	Case detection method[†]									Case detection tool[‡]					Results
				Mass CXR	H-H (home)	H-H (refer)	Temp site	Hosp/ clinic[§]	Publ/ educ	CI	Reg/ FU	PCF	Sym sur	TST	Sm	Cx	CXR	
102	Mohammed	2004 South Africa	129 patients with advanced HIV disease					C					x	x	x	x		11 of 129 patients (8.5%) had active disease.
103	Mosimaneotsile	2003 Botswana	560 HIV-infected patients					C					x		x			96% of 560 HIV-infected patients who had a CXR were normal. Only 1 patient was found to have active disease.
107	Kimerling	1999 USA	127 homeless people from 2 shelters in Birmingham, AL					H					x		x			Only 7% reported symptoms; 4 (3%) of 127 were Cx+; 1 (0.8%) Sm+.
108	Barry	1986 USA	586 homeless living shelters in Boston, MA					H					x	x	x	x	x	Of 586 in the program, 465 had a CXR taken: 24 were suspicious for TB, only 3 diagnosed with TB (645/100 000). Sputum specimens from 217 revealed 1 Sm+ that was ruled out and 2 Cx+.
110	Lau	1997 Australia	3555 homeless men in 5 major hostels in eastern Sydney					H							x	x	x	506 (14%) with abnormal CXR; 2 active TB cases; 7 cases found among population from non-screening exams.
111	Goldgrub	2002 Brazil	2181 clients at 17 homeless shelters					H					x		x			346 identified as respiratory symptomatics; 334 sputum smears examined; 3 with active TB (867/100 000).
112	Solsona	2001 Spain	447 homeless individuals and 48 individuals in 2 long-term shelters					H						x	x	x	x	75% of homeless study participants were infected and 1% had active TB. No statistically significant difference was found between homeless and residents of long-term shelters.
113	Galesi	2001 Brazil	2.4 million people interviewed					M					x		x			81 797 people were identified with prolonged cough, among whom 46 377 smear exams were conducted and 591 Sm+ cases detected (723/100 000).
117	Friedman	1987 USA	2641 alcoholic and drug abusing welfare clients					A					x	x			x	Of 970 clients meeting alcoholic and/or drug abuse criteria, 9 (0.5%) TB cases were diagnosed.
118	Manalo	1990 Philippines	55 000 residents of Villa Sabina district				Church						x		x	x		1990 coughers identified, of whom 207 (10.4%) were Sm+.
119	Garcia-Garcia	2000 Mexico	1424 persons with chronic cough in community					M		x		x	x		x	x		124 (44/100 000) had microbiologically confirmed TB. This study recruited 86% of cases notified during 8-month period; 38 of 95 (40%) TB cases with DNA fingerprints were in clusters.
120	Chaucer	1955 USA	1001 inmates at the Hartford County Jail in Connecticut					J									x	29 prisoners discovered to have active TB (2897/100 000).
121	White	2001 USA	5359 (1994) and 9331 (1998) San Francisco City and County Jail inmates					J					x	x			x	Prevalence was 78.5/100 000 inmates in 1994 and 72.1/100 000 in 1998. In 1998, 33% of active TB cases found through jail screening.

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122	Sretrirutchai	2002 Thailand	4751 inmates in 4 provincial prisons					P					x		x	x	x	304 of 4751 inmates had symptoms ≥2 weeks. 49 had CXR indicative of TB; 27 were Sm+ (568/100 000).
123	Martin	1994 Spain	729 inmates in a Barcelona prison					P						x	x	x	x	Among 702 prisoners studied, 19 diagnosed with active TB (2707/100 000); 6 Sm+ (855/100 000).
124	Puisis	1996 USA	126 608 inmates at Cook County Jail in Chicago					J					x		x	x	x	388 (0.3%) CXRs were suspicious; 67 cases of TB detected (4089/100 000); 35 diagnosed in the jail; 32 were diagnosed prior to jail stay.
125	Saunders	2001 USA	1639 inmates entering a San Diego detention facility					P					x	x			x	64 symptomatics (4%) were isolated; 16 began TB treatment; 7 diagnosed with TB (427/100 000).
126	Nyangulu	1997 Malawi	1315 prisoners at the Zomba Central Prison					P					x		x		x	914 of 1315 prisoners were screened. 33 previously undiagnosed cases of TB detected.

*We have sometimes used per cent (%) in this table for rates and ratios, such as incidence and prevalence, to save space. In the field of TB, these and similar measures of risk are usually expressed as per 100 000. Note that 2%, which seems low, is equal to 2000/100 000, a high risk. To avoid potential misunderstanding of risk, we have used per 100 000 in the text where space is not at such a premium.

†Mass CXR = mass radiography; H-H (home) = house-to-house ACF with diagnostic test conducted at home; H-H (refer) = house-to-house ACF with patient referral to a diagnostic facility; Temp site = patients referred to a temporary diagnostic facility; Hosp/clinic = patients screened at a hospital or clinic; Publ/educ =mass media campaign and/or TB education; CI = contact investigations; Reg/FU = tuberculosis registry follow-up; PCF = passive case finding.

‡Sym sur = symptom survey; TST = tuberculin skin test; Sm = smear microscopy for AFB; Cx = culture for *Mycobacterium tuberculosis*; CXR = chest radiograph.

§V = HIV VCT; C = HIV clinic; H = homeless; M = many sites; A = alcohol/drug clinic; J = jail; P = prison.

**Roux S, Fielding K, Grant A D, et al. Annual vs. 6 monthly radiological screening for the active case-finding of TB: a randomized controlled trial. Presentation at the 34th IUATLD World Conference on Lung Health. Paris, France: 2003.

NYC = New York City; TB = tuberculosis; PTB = pulmonary TB; py = person-years; AFB = acid-fast bacilli; + = positive; ACF = active case finding; −= negative; HIV = human immunodeficiency virus; VCT = voluntary counseling and testing center; aOR = adjusted odds ratio.