Expanding Tuberculosis Case Detection by Screening Household Contacts

MERCEDES C. BECERRA, SCD[a]
ILIANA F. PACHAO-TORREBLANCA[b]
JAIME BAYONA, MD, MPH[b]
ROSA CELI, RN[c]
SONYA S. SHIN, MD[d]
JIM YONG KIM, MD, PHD[a]
PAUL E. FARMER, MD, PHD[a]
MEGAN MURRAY, MD, SCD[e]

SYNOPSIS

Objectives. Tuberculosis (TB) case detection remains low in many countries, compromising the efficacy of TB control efforts. Current global TB control policy emphasizes case finding through sputum smear microscopy for patients who self-report to primary health centers. Our objective was to assess the feasibility and yield of a simple active case finding strategy in a high incidence population in northern Lima, Peru.

Methods. We implemented this pilot strategy in one health center's catchment area. Health workers visited household contacts of new TB case subjects to identify symptomatic individuals and collect sputum for screening. Neighboring households were screened in the same manner. Secondary analyses measured risk of TB by (*1*) sputum smear status of the index case subject, (*2*) compliance with testing, and (*3*) risk factors for disease detected through active contact tracing in contrast to self-report.

Results. The TB prevalence detected through combined active and passive case finding among 1,094 household contacts was 0.91% (914 per 100,000), much higher than with passive case finding alone (0.18%; 183 per 100,000; p=0.02). Among 2,258 neighbors, the combined strategy detected a TB prevalence of 0.22% (221 per 100,000) in contrast to 0.08% (80 per 100,000) detected through passive case finding alone (p=0.25). Risk factors for being diagnosed through active case finding in contrast with self-report included age >55 years (odds ratio [OR]=5.5; 95% confidence interval [CI] 1.2, 22.8) and female gender (OR=3.9; 95% CI 0.99, 22.3).

Conclusions. Risk of active TB among symptomatic household contacts of active case subjects in this community is very high. Results suggest that contact tracing in such settings may be a powerful means of improving case detection rates for active TB disease.

[a]Department of Social Medicine, Harvard Medical School; USA/Partners In Health, Boston, MA

[b]Partners In Health, Lima, Peru

[c]Centro de Salud El Progreso, Ministry of Health, Carabayllo, Peru

[d]Division of Social Medicine and Health Inequalities, Brigham and Women's Hospital; USA/Partners In Health, Boston, MA

[e]Department of Epidemiology, Harvard School of Public Health, Boston, MA

Address correspondence to: Megan Murray, MD, ScD, Department of Epidemiology, Harvard School of Public Health, 677 Huntington Ave., Boston, MA 02115; tel. 617-432-2781; fax 617-566-7805; e-mail <mmurray@hsph.harvard.edu>.

A recent analysis of global tuberculosis (TB) case notification data estimated that only 27% of new smear positive cases that arose in 2000 were detected by the current recommended strategy (DOTS) and only 19% were successfully treated.[1] These results suggest that while good TB treatment success rates have been achieved under DOTS, low case detection rates remain an obstacle to the long-term success of TB control programs.[2,3] Current World Health Organization policy emphasizes passive case finding in contrast with the identification of cases through screening.[4] This strategy has been based on the expectation that (*1*) passive detection of individuals ill enough to seek medical care is far more cost-effective than population-based screening and (*2*) compliance will be higher in those who have identified themselves as symptomatic.[5] Nonetheless, the failure of national TB programs to detect the vast majority of new infectious cases suggests that active screening strategies should be re-evaluated in an attempt to improve case detection and, thereby, increase access to TB treatment.[6]

Contact investigation for cases of active pulmonary TB is standard practice in developed countries.[7,8] Through this process, household and other close contacts of infectious case subjects are identified and tested for TB infection and disease. Several recent studies conducted in high burden areas have shown that active case finding among household contacts yields substantially more TB cases than passive case detection.[9–11] Other groups have suggested that active case finding should be extended to high-risk communities at large, rather than only focus on households of case subjects.[12] In this study, we describe and evaluate a simple active case finding strategy in contacts of case subjects with active TB in a high incidence shantytown in Lima, Peru. This is an area characterized by poor health indicators; in the year 2000, annual public health expenditure per capita in Peru was 238 U.S. dollars (USD), average income was 130 USD, and infant mortality in Lima was 19 per 1,000 live births. Although the incidence of new TB cases was approximately 170 per 100,000 per year at the national level, rates are much higher in the densely populated shantytowns surrounding Lima; masked pockets of incidence can be as high as 340 per 100,000.[13]

We assessed active case finding in two different contact groups; the first group included individuals who were household contacts of case subjects with pulmonary TB, while the second group included residents of the case subjects' neighborhoods who may have had more causal contact with the patients. Since active case finding does not preclude self-referral, we measured the prevalence of TB detected through combined active and passive case finding in comparison with passive case finding alone in both of these groups, and we also describe the risk factors associated with failure to self-refer. The protocol for this study was approved by the Human Subjects Committee of the Harvard School of Public Health, as well as by Partners In Health in Peru and the Ministry of Health in Peru.

METHODS

Setting and study cohort

The Peruvian Ministry of Health operates four public health centers and five public health posts in the district of Carabayllo, the northernmost district of metropolitan Lima. The region is divided into catchment areas corresponding to each center or post. This study was conducted in the catchment area of one public health center, the El Progreso center, located in the northern part of the Carabayllo district. The area is characterized by shantytowns and recently occupied squatter settlements set in the desert hills of the crowded northern periphery of Lima; many of the inhabitants are recent migrants from the central rural highlands who fled the countryside during recent periods of political unrest. The catchment area comprises a population of approximately 40,000.

The Peruvian National TB Program operates through the Ministry of Health associated centers, posts, and hospitals. Like elsewhere in the country, TB control measures at the local health facility have relied primarily on passive case finding. Individuals experiencing cough of more than two weeks duration are encouraged to report to the center where they submit sputum samples for smear microscopy. Those diagnosed with TB disease initiate directly observed short-course chemotherapy regimens, which are administered at the health center or post closest to their homes. Since 1991, however, the National TB Program also has implemented a basic contact investigation protocol and has offered a six-month course of isoniazid (INH) to exposed children aged $\leq$15 years. At the time an index case subject enrolls in TB treatment, household contacts are identified and advised to report to the local health center if they experience cough of more than two weeks duration. In this study, we refer to this case finding approach as *passive case finding*.

In contrast with this approach, we implemented an *active case finding* strategy through which community health workers visited contacts in the home of the index case subject, identified symptomatic individuals, collected sputum specimens on two consecutive mornings, and transported the specimens to the regional mycobacterial laboratory for acid-fast staining and smear microscopy. Contacts who tested positive by sputum microscopy then were referred to the local health center for treatment.

Data collection

We identified two separate cohorts of contacts at risk for TB to undergo active screening. The first consisted of all household contacts of case subjects with active TB, while the second consisted of individuals dwelling in the vicinity of case subjects with active TB. Both children and adults were included. To establish these cohorts, we identified all cases of active pulmonary TB who presented to the El Progreso health center during the period from January 1, 1996, through April 21, 1997. These individuals were designated *index case subjects* and the households in which the case subjects resided were designated *index households*. For each index case subject, two nearby *neighboring households* were selected by choosing the households two doors away on the right and two doors away on the left of the index household. We avoided the households immediately adjacent to the index household because they were likely to belong to relatives of the index case subject. When the index household was the home of two index cases, we designated the households two and three doors down on either side of the index household, thereby choosing four neighboring households for that index household. In the event that a neighboring household declined participation in the study, we chose the next household, one door further away from the index household, for recruitment.

During the period from April 1997 through June 1998, two nurse-assistants and two community health workers visited index and neighboring households to conduct interviews of household members. The purpose of the visit was explained to the participants, and informed consent was obtained. The interviewers identified individuals who noted experiencing cough of at least two weeks duration and asked them to provide two early morning sputum samples (after instructing them on the appropriate manner of specimen collection). A community health worker returned on two consecutive mornings to the households of those who reported prolonged cough to collect sputum samples and transport them to the laboratory of the area referral hospital in the adjacent district of Comas.

Demographic and clinical data on the index case subjects were obtained through abstraction of health center records; these data included age, sex, education level, sputum smear grade, treatment history, and response to current treatment. Index household members and neighbors identified during household visits were interviewed during the initial visit; data collected through this survey included age, sex, education level, BCG vaccine status, and presence and duration of cough.

Microbiology

Sputum samples obtained from those with prolonged cough were examined at a regional mycobacteriology laboratory for the presence of acid fast bacilli (AFB) by smear-microscopy and culture. Sputum smears were classified as 1+ to 3+ according to a standard protocol whereby the number of detectable AFB per high power field are counted and determined to be low, medium, or high. Those who had a positive smear and/or culture were treated for pulmonary TB with standard therapy at the local health center.

Analysis

We assessed the baseline characteristics of the two cohorts by comparing the demographic characteristics of members of index households and members of nearby households using a chi-square test for dichotomous variables and a t-test comparing the means of continuous variables. The number of detected cases was standardized to a population of 100,000. We estimated the smear status-adjusted prevalence of TB among household contacts, reporting 95% confidence intervals (CIs) based on the binomial distribution. In order to identify risk factors for failure to self-report, we also examined characteristics of case subjects detected through contact tracing in contrast with case subjects detected through self-report. In addition to univariate analysis of these risk factors for failure to self-report, we used a logistic regression model to control for possible confounding. We restricted this last analysis to those variables for which we had complete data.

RESULTS

Index cases

From January 1, 1996, through April 21, 1997, we identified 208 case subjects with pulmonary TB who had self-reported to the El Progreso health center during the 15.75 month period. Given an approximate catchment population of 40,000 people, this represents approximately 398 per 100,000 (95% CI 354 per 100,000, 446 per 100,000) cases per year detected by passive surveillance. These index case subjects lived in 200 households. Of these 200 households, 192 were home to only one case subject, while eight were home to two index case subjects.

Index and neighboring households

Of the 200 index households visited, four refused to participate in the study, four were no longer occupied by the index case subject's family, and one case subject lived alone, leaving 191 index households. Within these households, 1,094 household contacts were enrolled in the study. We also identified 416 neighboring households, two for each index case subject, and enrolled 2,253 individuals living in these households. Demographic characteristics of members of index households differed little from members of neighboring households (see Table 1). We found that 188 of 2,253 (8.3%) participants in neighboring households and 107 of 1,094 (9.7%) participants in index households (not including index patients) reported having a cough of more than two weeks duration (p=0.17). Within neighboring households, children and adults were equally likely to report cough. However, within index households, 13% of those aged >15 years reported prolonged cough compared with only 4% of children (p<0.001).

Those participants who reported cough for at least two weeks duration were asked to produce two sputum samples on consecutive mornings. Table 2 shows the distribution of the number of specimens provided. Sixty-four percent of the population who reported cough provided at least one sputum sample, while only 28% of the population identified with cough provided two or more sputum samples.

Case finding

We detected eight case subjects with pulmonary TB through active case finding. Two additional case subjects, among the 1,094 household contacts, self-referred and, thus, were identified through passive case finding (see Figure). Standardized prevalence for combined active and passive detection was 914 per 100,000 in contrast with 183 per 100,000 for passive detection alone (p=0.06) Among the 2,253 neighboring household members, three cases were detected through active case finding and two further cases self-reported, thus adding to the cases identified by passive case finding. Standardized prevalence for combined active and passive case finding in this population was 221 per 100,000 compared with 89 per 100,000 for passive case finding alone. This means that 137 household contacts and 758 neighboring contacts would have needed to be screened to detect one case. The prevalence odds of TB disease among household contacts compared with neighbors was 5.5 (95% CI 1.5, 20.8; p=0.005).

Table 1. Characteristics of participants residing in index and neighboring households

	Index households		Neighboring households		
Characteristic	n	*Percent*	n	*Percent*	*p-value*
Sex					
Female	649/1,294	50.2	1,116/2,253	49.5	
Male	645/1,294	49.8	1,137/2,253	50.5	p=0.81
Mean age (years)	25.8		25.7		p=0.88
Age[a]					
<5 years	111/1,269	8.8	231/2,246	10.3	p=.10
5–15 years	273/1,269	21.7	534/2,246	23.8	
16–55 years	787/1,269	61.7	1,316/2,246	60.8	
>55 years	98/1,269	3.8	165/2,246	7.3	
Education					
< primary school[b]	141/827	17.0	211/1,473	14.3	
primary school or more	686/827	83.0	1,262/1,473	85.7	p=0.08

NOTE: Participants include 200 index case patients plus 1,094 household and 2,253 neighboring contacts.

[a]32 total observations were missing data and therefore excluded from this analysis for household and neighboring households.

[b]Individuals aged ≥15 years and have not completed primary school (181 observations were missing data and, therefore, were excluded from this analysis.)

The prevalence of TB among all those who reported cough was 7.5% (95% CI 3.3%, 14.0%) among household contacts and 1.6% (95% CI 0.3%, 4.6%) among neighbors. However, prevalence among those coughers who actually provided sputum samples was much higher; among this group, 10.0% (95% CI 4.6%, 19.4%) of household contacts and 2.7% (95% CI 0.6%, 7.6%) of neighbors were diagnosed with active TB.

We also examined predictors of failure to submit sputum samples among those who reported cough lasting at least two weeks. Except for age, no significant correlation existed between any demographic risk factor and failure to submit a sample; only 19 of 46 (41%) children aged ≤10 years who reported cough submitted at least one sputum sample, while 171 of 250 (68%) individuals aged >10 years did so (p<0.001).

When we stratified the household contacts by the sputum smear status of the index case subject, we found that contact with a case with a high bacillary load was highly correlated with disease risk (see Table 3). Further, among coughers who provided sputum samples, approximately 20% of those exposed to a 3+ smear grade index case subject were diagnosed with TB, while only approximately 5% of those exposed to a 1+ smear grade index case subject and approximately 5% of those exposed to a 2+ smear grade index case subject were diagnosed with TB (odds ratio [OR]=7; p=0.005).

Table 2. Number of sputum samples provided, by household type

Number of sputum samples	Residents of index households		Residents of neighboring households	
	n	*Percent*	n	*Percent*
0	30	28	76	40
1	41	38	65	35
2	31	29	40	21
3	5	5	7	4
Total	107	100	188	100

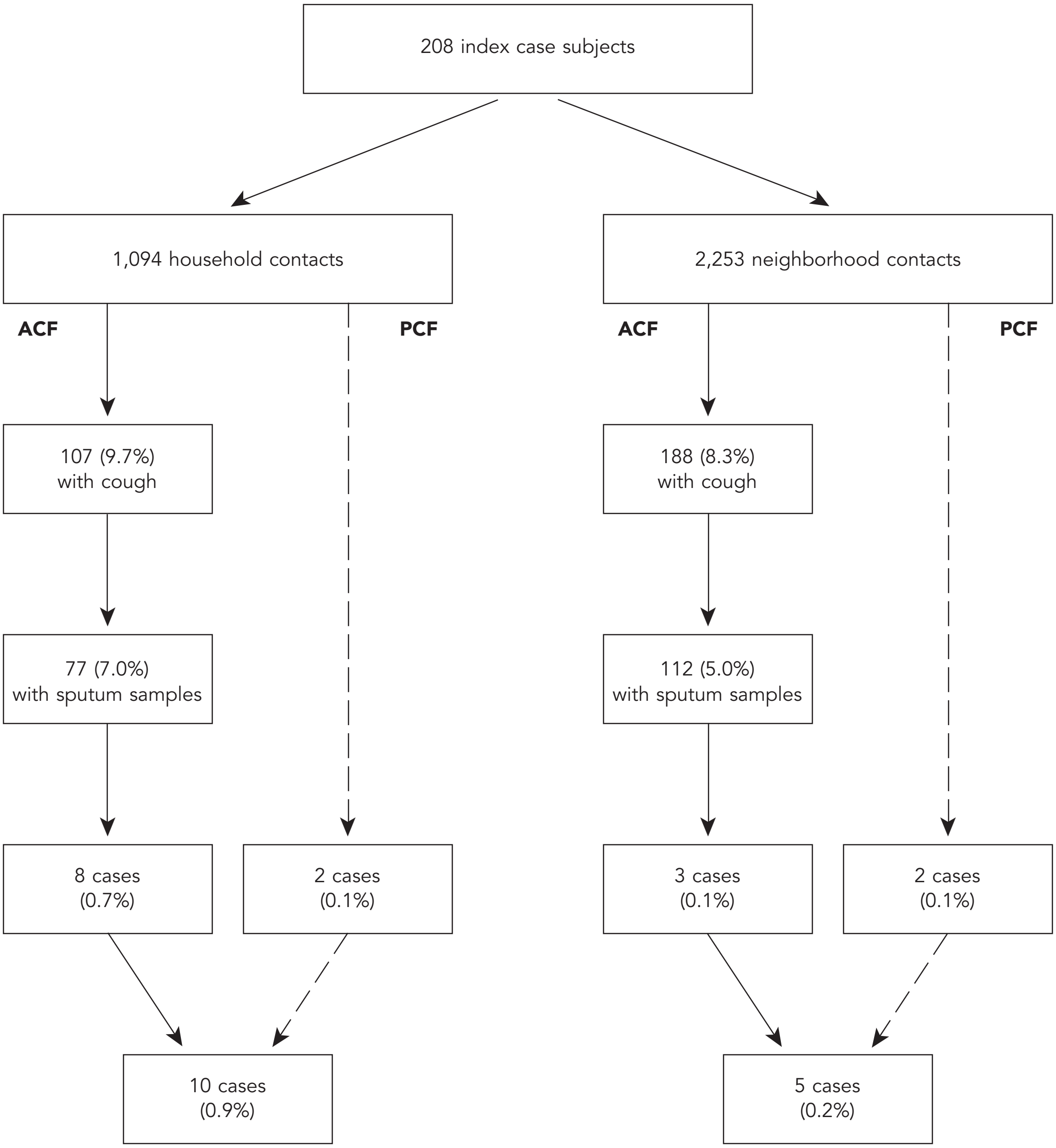
Risk factors for failure to self-refer

Case subjects detected through active case finding differed from those who self-reported in that they were more likely to be female and more likely to be aged >55 years (see Table 4). When these characteristics were entered into a logistic regression model, both were found to be strong risk factors for failure to self-report, although the confidence intervals were wide (see Table 5). No significant differences existed between the two groups by education or by duration of cough.

DISCUSSION

Poor access to effective therapy continues to present a challenge to TB control programs and suggests that the time has come to reconsider the role of active case finding. In this study, we considered the impact of active case finding among household contacts and neighbors of TB patients in a shantytown in Lima, Peru. Our results show that the detection rate among contacts who reported cough of more than two weeks duration was high both among neighbors and among household members of case subjects; also, our results show that these rates were especially high among people exposed to case subjects with high-grade sputum smears. These results suggest that, in this setting, combined active and passive case finding in household contacts may detect substantially more cases of TB than passive case finding alone.

Figure. Case finding scheme



ACF = active case finding
PCF = passive case finding

Our findings are consistent with those reported in a number of studies of screening among symptomatic household contacts in high incidence areas and are higher than those reported in studies that screened all household contacts regardless of clinical presentation.[9–12,14–18] When we further assessed the TB risk among those exposed to contacts with high-grade sputum smears, we found that 20% of the household contacts that reported cough and 23% of those who provided sputum samples had active TB. These findings are also consistent with previous data that show that people with high-grade sputum smears are highly infectious to others.[19–21] Although these data support the use of household-based contact tracing to improve case detection in high-incidence settings, especially in contacts of case subjects with high-grade sputum smears, the value of active case finding among neighbors of case subjects or in the general community is less clear. Although no significant difference existed between the prevalence of TB detected through the combined

Table 3. Prevalence of tuberculosis (TB) in household contacts by smear status of index case subject

Smear status of index case subject	Prevalence of TB in all contacts reporting cough		Prevalence of TB in contacts providing sputum samples	
	n	Percent	n	Percent
Negative	1/31	3.2	1/19	5.3
1+	1/21	4.7	1/18	5.5
2+	1/31	3.2	1/19	5.3
3+	5/24	20.8	5/21	23.8
Total	8/107		8/77	

strategy and passive case-finding only, the finding that 2.7% of neighbors who complied with testing had active TB suggests that active case finding could indeed be a useful strategy if compliance with testing could be improved.

In this study, self-reported case subjects were more likely to be male and to be aged <55 years than were case subjects detected through active case finding. These findings support the results of previous studies comparing active and passive case finding in which women with TB disease were under-notified to public health authorities when detection was based on passive case finding alone.[21–31] It is unclear whether this under-notification occurred because older women delayed seeking medical care for their symptoms or because health care providers failed to make prompt diagnoses when these individuals did seek care. Notably, older women diagnosed with TB did not report longer duration of cough than other groups in the study. Further work is needed to define the barriers to accessing appropriate health care faced by older women with TB in this community.

This study identified a number of operational problems with the simple contact tracing and testing strategies used. First, almost one-third of those who reported cough of more than two weeks duration failed to provide sputum samples for testing. Coughers from index households were somewhat more likely to provide samples, perhaps because they were more highly motivated, having lived in a household with a known case subject. Although some coughers were unable to produce sputum on demand, many others were simply not present when the community health workers visited their homes, suggesting that yield may be improved by more vigorous efforts to locate contacts for testing.

Second, as has been reported in a number of other studies of TB detection, children aged <10 years were significantly less likely to provide sputum samples than were older individuals.[32–36] Diagnosing TB in children is a notoriously difficult problem, and as noted in one recent editorial on case finding in children, "We only find what we look for."[37] Not surprisingly, the case-finding strategies employed in this study did not identify any cases of active TB among children aged <15 years despite the fact that children exposed to household contacts with TB are at much higher risk for disease than adults. It is unclear whether the absence of TB detected among children in this study is due to a true absence of disease, perhaps due to the use of INH chemoprophylaxis in this group, or a failure to detect disease even when it is present. Innovative methods of case detection among children are needed to assess the burden of undiagnosed TB in this vulnerable group.

Table 4. Univariate analysis of characteristics of cases detected by active and passive case finding

Characteristic	Case finding (N=223) Active	Passive	p-value
Sex			
Male	3	119	
Female	8	93	0.06
Mean age (years)	28.0	30.8	0.60
Age (years)			
<5	0	3	
5–15	1	18	
16–55	7	174	
>55	3	17	0.01[a]
Education			
< primary school[b]	1	24	
primary school or more	6	111	0.80
Mean duration of cough (weeks)	5.2	5.5	0.89[c]

[a]trend test

[b]Individuals aged ≥15 years and have not completed primary school (62 observations were missing data and, therefore, were excluded from this analysis.)

[c]*t*-test

Several potential limitations should be considered in interpreting the results of this pilot study. Although TB incidence in this community is high, the relatively small size of the study means that results are imprecise and CIs wide. Further, some of the case subjects that were detected through active household screening might have eventually self-referred had they not been previously detected; this may exaggerate the difference between the active and passive case finding strategies. However, we observed no difference in the duration of cough among cases found through either strategy, suggesting both groups had had active disease for similar periods. Finally, the relatively poor compliance of the coughing contacts in providing sputum samples means

Table 5. Multivariate analysis of risk factors for being diagnosed through active case detection

Risk factor	Adjusted odds ratio[a]	95% CI	p-value
Age >55 years	5.3	1.2, 22.8	0.026
Female	3.9	0.93, 23.1	0.053

[a]adjusted for sex and age only

CI = confidence interval

that the true burden of undiagnosed TB may be higher than the prevalence reported here. We conclude that targeted modifications in routine case finding approaches may improve TB case detection in high burden areas.

REFERENCES

1. Dye C, Watt CJ, Bleed D. Low access to a highly effective therapy: a challenge for international tuberculosis control. Bull World Health Organ 2002;80:437-44.
2. Xianyi C, Fengzeng Z, Hongjin D, Liya W, Lixia W, Xin D, Chin DP. The DOTS strategy in China: results and lessons after 10 years. Bull World Health Organ 2002;80:430-6.
3. Blower SM, Daley CL. Problems and solutions for the Stop TB partnership. Lancet Infect Dis 2002;2:374-6.
4. Raviglione MC, Pio A. Evolution of WHO policies for tuberculosis control, 1948–2001. Lancet 2002;359:775-80.
5. Murray CJL, Styblo K, Rouillon A. Tuberculosis. In: Jamison DT, Mosley WH, Measham AR, Bobadilla JL, editors. Disease control priorities in developing countries. New York: Oxford University Press, Inc.; 1993. p. 233-59.
6. Murray CJ, Salomon JA. Expanding the WHO tuberculosis control strategy: rethinking the role of active case-finding. Int J Tuberc Lung Dis 1998;2(9 Suppl 1):S9-15.
7. Reichler MR, Reves R, Bur S, Thompson V, Mangura BT, Ford J, et al. Evaluation of investigations conducted to detect and prevent transmission of tuberculosis. JAMA 2002;287:991-5.
8. Joint Tuberculosis Committee of the British Thoracic Society. Control and prevention of tuberculosis in the United Kingdom: code of practice 2000 [editorial]. Thorax 2000;55:887-901.
9. Kuaban C, Koulla-Shiro S, Lekama Assiene T, Hagbe P. Tuberculosis screening of patient contacts in 1993 and 1994 in Yaounde, Cameroon. Med Trop 1996;56:156-8.
10. Harries AD, Kamenya A, Subramanyam VR, Maher D, Squire SB, Wirima JJ, et al. Screening pulmonary tuberculosis suspects in Malawi: testing different strategies. Trans R Soc Trop Med Hyg 1997;91:416-9.
11. Zachariah R, Spielmann MP, Harries AD, Gomani P, Graham SM, Bakali E, Humblet P. Passive versus active tuberculosis case finding and isoniazid preventive therapy among household contacts in a rural district of Malawi. Int J Tuberc Lung Dis 2003;7:1033-9.
12. Gilpin TP, Hammond M. Active case-finding—for the whole community or for tuberculosis contacts only? S Afr Med J 1987;72:260-2.
13. Sanghavi DM, Gilman RH, Lescano-Guevara AG, Checkley W, Cabrera LZ, Cardenas V. Hyperendemic pulmonary tuberculosis in a Peruvian shantytown. Am J Epidemiol 1998;148:384-9.
14. Capewell S, Leitch AG. The value of contact procedures for tuberculosis in Edinburgh. Br J Dis Chest 1984;78:317-29.
15. Wang PD, Lin RS. Tuberculosis transmission in the family. J Infect 2000;41:249-51.
16. Noertjojo K, Tam CM, Chan SL, Tan J, Chan-Yeung M. Contact examination for tuberculosis in Hong Kong is useful. Int J Tuberc Lung Dis 2002;6:19-24.
17. Nsanzumuhire H, Aluoch JA, Karuga WK, Edwards EA, Stott H, Fox W, Sutherland, I. A third study of case-finding methods for pulmonary tuberculosis in Kenya, including the use of community leaders. Tubercle 1981;62(2):79-94.
18. Wares DF, Akhtar M, Luitel H. Is TB contact screening relevant in a developing country setting? Experiences from eastern Nepal, 1996–1998. Int J Tuberc Lung Dis 2000;4:920-4.
19. Liippo KK, Kulmala K, Tala EO. Focusing tuberculosis contact tracing by smear grading of index cases. Am Rev Respir Dis 1993;148:235-6.
20. El-Sony A, Enarson D, Khamis A, Baraka O, Bjune G. Relation of grading of sputum smears with clinical features of tuberculosis patients in routine practice in Sudan. Int J Tuberc Lung Dis 2002;6:91-7.
21. Sepkowitz KA. How contagious is tuberculosis? Clin Infect Dis 1996;23:954-62.
22. Borgdorff MW, Nagelkerke NJ, Dye C, Nunn P. Gender and tuberculosis: a comparison of prevalence surveys with notification data to explore sex differences in case detection. Int J Tuberc Lung Dis 2000;4:123-32.
23. Holmes CB, Hausler H, Nunn P. A review of sex differences in the epidemiology of tuberculosis. Int J Tuberc Lung Dis 1998;2:96-104.
24. Nsubuga P, Johnson JL, Okwera A, Mugerwa RD, Ellner JJ, Whalen CC. Gender and HIV-associated pulmonary tuberculosis: presentation and outcome at one year after beginning antituberculosis treatment in Uganda. BMC Pulm Med 2002;2:4.
25. Muula AS. Gender differences in delays to TB diagnosis. Int J Tuberc Lung Dis 2001;5:1072-4.
26. Begum V, de Colombani P, Das Gupta S, Salim AH, Hussain H, Pietroni M, et al. Tuberculosis and patient gender in Bangladesh: sex differences in diagnosis and treatment outcome. Int J Tuberc Lung Dis 2001;5(7):604-10.
27. Thorson A, Diwan VK. Gender inequalities in tuberculosis: aspects of infection, notification rates and compliance. Curr Opin Pulm Med 2001;7:165-9.
28. Needham DM, Foster SD, Tomlinson G, Godfrey-Faussett P. Socio-economic, gender and health services factors affecting diagnostic delay for tuberculosis patients in urban Zambia. Trop Med Int Health 2001;6:256-9.
29. Boeree MJ, Harries AD, Godschalk P, Demast Q, Upindi B, Mwale A, et al. Gender differences in relation to sputum submission and smear-positive pulmonary tuberculosis in Malawi. Int J Tuberc Lung Dis 2000;4:882-4.
30. Diwan VK, Thorson A. Sex, gender, and tuberculosis. Lancet 1999;353:1000-1.
31. Long NH, Johansson E, Lonnroth K, Eriksson B, Winkvist A, Diwan VK. Longer delays in tuberculosis diagnosis among women in Vietnam. Int J Tuberc Lung Dis 1999;3:388-93.
32. Maartens G, Beyers N. Tuberculosis in the tropics. Clin Chest Med 2002;23:341-50.
33. Salazar GE, Schmitz TL, Cama R, Sheen P, Franchi LM, Centeno G, et al. Pulmonary tuberculosis in children in a developing country. Pediatrics 2001;108:448-53.
34. Eamranond P, Jaramillo E. Tuberculosis in children: reassessing the need for improved diagnosis in global control strategies. Int J Tuberc Lung Dis 2001;5:594-603.
35. Beyers N, Gie RP, Schaaf HS, Van Zyl S, Talent JM, Nel ED, Donald PR. A prospective evaluation of children under the age of 5 years living in the same household as adults with recently diagnosed pulmonary tuberculosis. Int J Tuberc Lung Dis 1997;1:38-43.
36. Topley JM, Maher D, Mbewe LN. Transmission of tuberculosis to contacts of sputum positive adults in Malawi. Arch Dis Child 1996;74:140-3.
37. Beyers N. Case finding in children in contact with adults in the house with TB. Int J Tuberc Lung Dis 2003;7:1013-4.