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Are patients with pulmonary tuberculosis identified by active and by passive case detection different? A cross-sectional study in Pakistan.

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ABSTRACT

Objectives: Our objective was to compare the characteristics of patients with pulmonary tuberculosis (TB) identified through "extended contact screening" (ECS) with those of patients identified through routine passive case finding (PCF).
Methods: Active TB case finding by ECS was tested from 2013–2015. This was a cross-sectional study based on data collected from ECS and routine program data from Lahore, Faisalabad, and Rawalpindi districts, and Islamabad in 2015. Characteristics of patients identified through ECS and PCF were compared.
Results: Of the 12,114 patients with pulmonary TB in the study, 4604 (38%) were identified through ECS, of whom 4052 (88%) had bacteriological confirmation. Male patients comprised 56.2% (95% confidence interval [CI] 54.8–57.6) of patients with pulmonary TB identified through ECS and 49.7% (95% CI 48.6–50.8) of those identified through PCF. The proportion of bacteriologically confirmed cases was 88.0% (95% CI 87.1–88.9) in the ECS group and 50.3% (95% CI 49.2–51.4) in the PCF group. By regression analysis we found that compared with patients aged 15–44 years, children aged <15 years had higher chances of being identified through ECS (adjusted odds ratio 2.69; 95% CI 2.21–3.28). There was a higher chance of cases being detected by ECS in Faisalabad (adjusted odds ratio 2.57; 95% CI 2.01–3.29) than in Islamabad.
Conclusion: ECS identified a higher proportion of male and child patients with pulmonary TB than routine case finding; both of these groups are more often unidentified through routine TB control.

Introduction

Globally, out of the estimated 9.9 million new tuberculosis (TB) cases, approximately 4.3 million (41%) were not identified and registered during 2020. Pakistan had an estimated 0.6 million TB cases in 2020, with 272,990 (48%) reported and about 300,000 (52%) "missing," unreported, or undetected cases (World Health Organization, 2021). In most countries, the prevalence of TB is higher among men than among women (Borgdorff et al., 2000; Onozaki et al., 2015; Qadeer et al., 2016), and higher among the poor. Patients with TB who are "missed" may not seek health care, may have no symptoms or may not recognize them, or may face barriers to health care (World Health Organization, 2013a). These missing cases may remain sources of TB transmission and sustain the global TB epidemic (World Health Organization, 2015), and therefore represent an obstacle for meeting the ambitious global targets of 90% reduction in TB incidence and mortality by 2035 (World Health Organization, 2013b).

Global TB control is mainly based on "passive case finding" (PCF), in which patients with symptoms visit health facilities on their own initiative and are identified by the health system as patients with presumptive TB and followed up. In "active case finding" (ACF), the health system initiates active screening of population groups (World Health Organization, 2013a). ACF is often focused on populations with known high prevalence of undetected TB, or on marginalized and vulnerable populations with poor access to health services (World Health Organization, 2012).

The characteristics of patients identified through ACF may differ from those of patients identified through PCF. In India, ACF identified more female patients with TB (Shewade et al., 2019);

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Table 1
Basic population characteristics of Pakistan in 2015.

Characteristics	Value
Population, total (millions)	199.43
Population growth (annual %)	2.1
Surface area (sq. km) (thousands)	796
Population density (people per sq. km of land area)	258.7
Poverty headcount ratio at national poverty lines (% of population)	24.3
Income share held by lowest 20%	9
Life expectancy at birth, total (years)	67
Fertility rate, total (births per woman)	3.66
Primary school completion rate, total (% of relevant age group)	65
School enrollment, primary (% gross)	85
School enrollment, secondary (% gross)	40
School enrollment, primary and secondary (gross), gender parity index (GPI)	0.83
Urban population growth (annual %)	2.7
GDP growth (annual %)	4.7

Source: World Development Indicators database.

similar studies conducted in Eastern Nepal and Cambodia showed that ACF detected more TB cases among older adults and women (Cassels et al., 1982; Eang et al., 2012); a combination of ACF and PCF was more common in detecting TB cases among males and people aged >15 years in Vietnam (Fox et al., 2018).

The strategies of most national TB programs are based on PCF, but often include special risk groups (e.g., household contacts, patients with HIV infection) and actively try to identify them. Pakistan's National TB Control Program (NTP) tested an innovative ACF strategy, called "extended contact screening" (ECS), from 2013–2015 in four selected districts. This involved investigating community contacts in addition to the routinely investigated household contacts. All neighbors in households within a 50-m radius of the home of a smear-positive patient with TB were investigated on the basis of reported TB symptoms. This strategy increased case notification in the districts of intervention by approximately 8%, which was more than expected in relation to usual annual increases reported through routine TB control (Fatima et al., 2016). The treatment outcomes were not inferior to those of routine treatment in the NTP (Ul Haq et al., 2021). Other TB REACH projects also found increased TB case findings (Malik et al., 2020).

The question arose: were these additional cases similar to those routinely detected, or was there a higher proportion of "missing" classic risk groups? The aim of this study was to investigate if patients identified through ECS and PCF in four selected districts of Pakistan from 2013–2015 were different, and to compare their sociodemographic and clinical characteristics.

Methods

Study design

This cross-sectional study investigated the difference between ECS and routine PCF in the characteristics of detected pulmonary TB (PTB) cases, on the basis of data collected during 2015 in four selected districts in Pakistan.

Setting

According to the World Bank Annual Report 2015, Pakistan is among the world's most populous countries, with a population of nearly 200 million, 64% of which constitutes the rural population. The population characteristics are shown in Table 1.

The health system in Pakistan includes government (public) and parastatal health institutions (Pakistan Armed Forces, Sui Gas, Water & Power Development Authority, Pakistan Railways, Fauji Foundation) and the private sector. Public health care is delivered mainly through a network of primary, secondary, and tertiary-level health facilities. The primary healthcare facilities include civil dispensaries, basic health units, rural health centers, mother-child health care centers, urban health units, and urban health centers. The secondary-level healthcare facilities comprise sub-district hospitals and district hospitals. Tertiary-level health care is provided through teaching and specialized hospitals. Private health services include private-sector hospitals, teaching hospitals and universities, clinics of general practitioners, polyclinics, health facilities run by various charitable groups, informal health providers, and private laboratories. Some of these private enterprises work under the "PPM" (private-public mix) model in a national network with the NTP, and have units supported by supervision, training, and free drugs from the NTP; all TB cases must be reported quarterly to the NTP. However, most of the private sector in Pakistan is not involved with this system and is encouraged to refer patients with TB symptoms to a basic management unit (BMU) for further management, but this is often not done because of busy schedules.

TB BMUs are located at the district and sub-district levels, consisting of hospitals, rural health centers, and some basic health units. A BMU has a laboratory staff performing smear microscopy, with some also performing Xpert MTB/RIF assays, and a doctor/qualified medical staff trained to diagnose and initiate TB treatment. TB treatment involves six to eight months of treatment provided under daily direct observation by a healthcare provider, a community volunteer, or a family member. The BMU is also a facility where patients with TB return for re-examinations and confirmation of cure. The BMU maintains records in standard formats and provides periodic reports to the district coordinator, including reports on treatment outcome (World Health Organization, 2020). Sputum microscopy, Xpert MTB/RIF testing, and TB treatment services are provided free of cost.

All patients are diagnosed and treated in accordance with the national TB guidelines under direct observation (National Tuberculosis Programme, 2019).

The Pakistan NTP had a project funded by TB REACH Wave 3, intended to facilitate the detection of more TB cases (Fatima et al., 2016). From 2013–2015, ECS was implemented in four districts of Pakistan, namely Lahore, Rawalpindi, Faisalabad, and Islamabad. There were 98 BMUs for the population of 18 million. More than 80% of the population in these districts live in urban areas. The average socioeconomic status of the districts' population is higher than the national average because of better jobs and business opportunities. However, half of the population live in slums with poor socioeconomic conditions.

ECS was done as follows. Patients of all ages receiving TB treatment were identified through TB registers from BMUs. All people staying within a 50-m radius (ascertained using geographic information system [GIS]) of the households with known patients with

TB were contacted and screened for TB by trained project staff. A 50-m radius was chosen on the basis of data from the electronic TB surveillance system, which revealed the presence of many cases coming from the same family, same address, or neighboring areas, and suggested high rates of geographic clustering. The approximate number of households in this radius was deemed feasible for close community screening by the NTP. Mobile phones enabled with ArcGIS (version 10) software were used by field workers to identify households within the 50-m radius of the index case and collect data. All available people permanently residing within the 50-m radius were contacted. The participants were informed about a patient with TB in the neighborhood (50-m radius), but measures were taken to safeguard the index patient's anonymity and the confidentiality of their personal information. Any person with a productive cough for more than two weeks was defined as a patient with presumptive TB. Initially, one spot sputum sample was collected and transported to the closest BMU for diagnostic testing. The same diagnostic algorithm was used except among sputum smear microscopy–negative cases of presumptive TB, for which the Xpert MTB/RIF assay was used if available. Patients bacteriologically positive for TB were contacted by the project staff and referred to the nearest BMU for registration and treatment initiation. All patients with presumptive TB aged <15 years were referred to specialist pediatric care for diagnosis and management. People whose sputum tested negative on both microscopy and Xpert MTB/RIF were referred to the nearest BMU for follow-up according to the national guidelines. Patients identified through ECS were marked "TB REACH" in the TB register.

Study population and sampling technique

The study population were patients with PTB of all ages and sexes diagnosed and reported in the study districts. These patients were classified on the basis of case detection strategy: patients detected by routine PCF or by ECS, registered and treated at public or private facility, and engaging with the NTP in four districts of Pakistan, namely Lahore, Rawalpindi, Faisalabad, and Islamabad, between July 2013 and June 2015. The cases identified through ECS were marked as such in the TB registers at facility level. All patients were considered as identified through PCF unless referred by ECS field staff. This was confirmed by reviewing the project records. Patients with known rifampicin resistance and treated with second-line drugs were not included. Only one person from the same family was invited to participate. Patients were excluded if they already had a family member registered for TB treatment through ECS and included in the study.

For the PCF group, we selected a subset of approximately 10% of the total population identified through PCF, so that the sample was almost twice that of the ACF group. Sampling was done to ensure that the sample was representative of the PCF group with regard to sex, age, facility, and city (appended Table).

Data collection, variables, and sources

The main outcome variable was the detection method: PCF or ECS. The data were collected through a structured questionnaire by trained project staff in the community and case-based data were obtained from a centralized database, entered into Microsoft Excel (Microsoft, Redmond, WA, USA), and validated in 2015. This information was prospectively collected from routine patients with TB who consented to participate because this information was not collected routinely.

Independent variables included patient characteristics such as age, gender, district, TB category, bacteriological confirmation, marital status, education status, occupation, family income, household members, type of house, residence, people sleeping in one room, ventilation, water source for drinking, smoking, and diabetes mellitus status.

Analysis and statistics

For clinical characteristics, case-based data were entered from facility-based TB registers, whereas the research data collected through interviews were entered into Microsoft Excel and validated and analyzed using Stata (version 12.1; StataCorp LLC, College Station, TX, USA). For quality assurance, our database was compared with aggregated data from the routine quarterly reports, and disparities were manually re-checked with the original TB registers. Demographic and clinical characteristics of patients identified through ECS and PCF were compared using 95% confidence intervals (CIs). We conducted logistic regression analysis to compare determinants of case finding by ECS, adjusting for potential confounders. Unadjusted and adjusted odds ratios (ORs) were reported. *P*-values of $\leq$0.05 were considered significant.

Results

We included 12,114 patients with PTB in the study; 4604 (38%) were identified through ECS, of whom 4052 (88%) had bacteriological confirmation. Out of 74,827 patients (mean age 36 years, male = 49.6%) eligible in the routine registers in the study area and identified through PCF, we interviewed 7510 (10%) (mean age 37 years, male = 49.7%), and they represented the comparison group designated as the PCF group.

Table 2 shows the characteristics of patients in the ECS and the PCF groups. The mean age was 36 years (95% CI 35.5–36.6) in the ECS group and 37 years (95% CI 36.9–37.7) in the PCF group. The proportion of males was 56.2% (95% CI 54.8–57.6) in the ECS group and 49.7% (95% CI 48.6–49.2) in the PCF group. The proportion of bacteriologically confirmed cases was higher in the ECS than in the PCF group. Regarding education, the proportion of no schooling among patients aged <15 years was higher in the ECS than in the PCF group, and there were fewer students in the ECS than in the PCF group. Similarly, there were more unemployed patients aged <15 years in the ECS than in the PCF group. There were some differences in house type, rural-urban habitation, and location.

Table 3 shows the characteristics of patients in the ECS group, comparing those identified through household contact (HH) investigation with those identified through neighborhood screening. The mean age of patients with PTB identified through close community contact investigation was 37.0 years (95% CI 36.4–37.6), and 33.1 years (95% CI 32.1–34.2) in the HH group. The HH group had a higher proportion of patients with TB aged 15–44 years and lower proportion of patients with TB aged 45–64 years than the close community contacts group. The proportions of males and females with PTB were not significantly different.

ECS contributed to 5.8% of the total case finding, but this population was slightly different from the routine cases. Table 4 shows that, compared with patients aged 15–44 years, children aged <15 years had higher chances of being identified through ECS than PCF (adjusted OR 2.69; 95% CI 2.21–3.28). Patients in Faisalabad had higher chances of being identified through ECS than through PCF (adjusted OR 2.57; 95% CI 2.01–3.29) compared with those in Islamabad. For other factors, adjustment had little effect on the proportion of case finding by ECS.

Discussion

This study compared the characteristics of patients with PTB identified through a new method of ACF and routine program in Pakistan. There were significant differences in age, gender, laboratory confirmation of TB, occupation, and family income among the

Table 2
Characteristics of patients with tuberculosis identified through extended contact screening[a] versus passive case finding[a] in four selected districts, Pakistan, 2013–2015.

Variable	Passive case finding(N = 7510)		Extended contact screening(N = 4604)	
	n	% (95% CI)	n	% (95% CI)
Age in years				
<15	172	2.3 (2.0–2.6)	391	8.5 (7.7–9.3)
15–44	4654	62 (60.9–63.1)	2613	56.8 (55.4–58.2)
45–64	1971	26.2 (25.2–27.2)	1192	25.9 (24.6–27.2)
≥65	713	9.5 (8.8–10.2)	408	8.9 (8.1–9.7)
Gender				
Male	3731	49.7 (48.6–50.8)	2587	56.2 (54.8–57.6)
Female	3779	50.3 (49.2–51.4)	2017	43.8 (42.4–45.2)
City				
Lahore	3324	44.3 (43.2–45.4)	1994	43.3 (41.9–44.7)
Faisalabad	1983	26.4 (25.4–27.4)	1619	35.2 (33.8–36.6)
Rawalpindi	1913	25.5 (24.5–26.5)	899	19.5 (18.4–20.6)
Islamabad	290	3.9 (3.5–4.3)	92	2 (1.6–2.4)
Classification by laboratory				
Bacteriologically confirmed	3778	50.3 (49.2-51.4)	4052	88 (87.1-88.9)
Clinically diagnosed	3732	49.7 (48.6-50.8)	552	12 (11.1-12.9)
Marital status				
Married	5105	68 (66.9–69.1)	3135	68 (66.7–69.3)
Single	2405	32 (30.9–33.1)	1469	32 (30.7–33.3)
Education status				
No schooling in <15 yrs	109	1.5 (1.2–1.8)	180	4 (3.4–4.5)
No schooling in ≥15 yrs	3799	50.5 (49.5–51.7)	2222	48 (46.8–49.7)
Primary	1879	25 (24–26)	1146	25 (23.7–26.3)
Secondary	1049	14 (13.2–14.8)	648	14 (13–15)
Tertiary	376	5 (4.5–5.5)	226	5 (4.4–5.6)
Madrassah	298	4 (3.6–4.4)	182	4 (3.4–4.6)
Occupation				
Not working in <15 yrs	112	1.5 (1.2–1.8)	287	6.1 (5.6–7.0)
Not working in ≥15 yrs	2821	37.6 (36.5–38.7)	1744	37.9 (36.5–39.3)
Agriculture	693	9.2 (8.5–9.9)	406	8.8 (8–9.6)
Student	1303	17.4 (16.5–18.3)	600	13 (12–14)
Labor	1735	23.1 (22.1–24.1)	1100	24 (22.8–25.2)
Govt. service	344	4.6 (4.1–5.1)	174	3.8 (3.2–4.4)
Business	502	6.7 (6.1–7.3)	293	6.4 (5.7–7.1)
Family income				
<20,000	5828	77.6 (76.7–78.5)	3737	81.2 (80.1–82.3)
21,000–50,000	1091	14.5 (13.7–15.3)	579	12.6 (11.6–13.6)
>50,000	591	7.9 (7.3–8.5)	288	6.3 (5.6–7)
Total household members				
<5	1803	24 (23–25)	1147	25 (23.7–26.3)
>5	5707	76 (75–77)	3457	75 (73.7–76.3)
Type of house				
Kutcha	1622	21.6 (20.7–22.5)	1563	34 (32.6–35.4)
Pucca	5888	78.4 (77.5–79.3)	3041	66 (64.6–67.4)
Residence				
Urban	5653	75.3 (74.3–76.3)	3712	80.6 (79.5–81.7)
Rural	1857	24.7 (23.7–25.7)	892	19.4 (18.3–20.5)
People sleeping in one room				
Single	75	1 (0.8–1.2)	47	1 (0.7–1.3)
Double	140	2 (1.7–2.3)	92	2 (1.6–2.4)
More than 2	7295	97 (96.6–97.4)	4465	97 (96.5–97.5)
Ventilation				
Window	5820	77.5 (76.6–78.4)	3591	78 (76.8–79.2)
Ventilator	1690	22.5 (21.6–23.4)	1013	22 (20.8–23.2)
Water source for drinking				
Tube well	781	10.4 (9.7–11.1)	410	8.9 (8.1–9.7)
Borehole	3230	43 (41.9–44.1)	2027	44 (42.6–45.4)
Filter plant	879	11.7 (11–12.4)	653	14 (13–15)
Public supply	2620	34.9 (33.8–36)	1514	33 (31.6–34.4)
Smoking status				
Non-smoker	7273	96.8 (96.4–97.2)	4435	96.3 (95.8–96.8)
Smoker	237	3.2 (2.8–3.6)	169	3.7 (3.2–4.2)
DM status				
Diabetic	323	4.3 (3.8–4.8)	192	4.2 (3.6–4.8)
Non-diabetic	7187	95.7 (95.2–96.2)	4412	95.8 (95.2–96.4)

CI = confidence interval; DM = diabetes mellitus; TB = tuberculosis.
[a] Extended contact screening is close community contact screening. Passive case finding is identifying patients with TB through routine TB program.

Table 3
Characteristics of patients with tuberculosis identified through household contact screening and neighborhood screening in four selected districts, Pakistan, 2013–2015.

Variable	Community contacts (N = 3477)		Household contacts (N = 1127)	
	n	% (95% CI)	n	% (95% CI)
Age in years				
<15	283	8.1 (7.5-8.7)	108	9.6 (8.7-10.5)
15–44	1928	55.5 (54.4-56.6)	685	60.8 (59.4-62.2)
45–64	925	26.6 (25.6-27.6)	267	23.7 (22.5-24.9)
≥65	341	9.8 (9.1-10.5)	67	5.9 (5.2-6.6)
Gender				
Male	1952	57 (55.9-58.1)	635	56.3 (54.9-57.7)
Female	1525	44 (42.9-45.1)	492	43.7 (42.3-45.1)
City				
Lahore	1517	43.6 (42.5-44.7)	477	42.3 (40.9-43.7)
Faisalabad	1262	36.3 (35.2-37.4)	357	31.7 (30.4-33)
Rawalpindi	639	18.4 (17.5-19.3)	260	23 (21.8-24.2)
Islamabad	59	1.7 (1.4-2)	33	3 (2.5-3.5)
Classification by laboratory				
Bacteriologically confirmed	3058	88 (87.3-88.7)	994	88 (87.1-88.9)
Clinically diagnosed	419	12 (11.3-12.7)	133	12 (11.1-12.9)
Marital status				
Married	2350	67.6 (66.5-68.7)	785	69.7 (68.4-71)
Single	1127	32.4 (31.3-33.5)	342	30.3 (29-31.6)
Education status				
No schooling in <15 yrs	131	3.8 (3.2-4.5)	49	4.4 (3.2-5.8)
No schooling in ≥15 yrs	1680	48.3 (46.7-50)	542	48 (45.2-51)
Primary	867	25 (24-26)	279	24.8 (23.6-26)
Secondary	490	14 (13.2-14.8)	158	14 (13-15)
Tertiary	171	5 (4.5-5.5)	55	4.9 (4.3-5.5)
Madrassah	138	4 (3.6-4.4)	44	3.9 (3.3-4.5)
Occupation				
Not working in <15 yrs	226	6.5 (5.8-7.4)	61	5.4 (4.2-6.9)
Not working in ≥15 yrs	1293	37.2 (35.6-38.9)	451	40 (37.2-43)
Agriculture	308	9 (8.4-9.6)	98	8.7 (7.9-9.5)
Student	485	14 (13.2-14.8)	115	10.2 (9.3-11.1)
Labor	834	24 (23-25)	266	23.6 (22.4-24.8)
Govt. service	118	3.4 (3-3.8)	56	5 (4.4-5.6)
Business	213	6 (5.5-6.5)	80	7 (6.3-7.7)
Family income				
<20,000	2821	81 (80.1-81.9)	916	81 (79.9-82.1)
21,000–50,000	435	12.5 (11.8-13.2)	144	13 (2.5-3.5)
>50,000	221	6.5 (5.9-7.1)	67	6 (5.3-6.7)
Total household members				
<5	871	25 (24-26)	276	24.5 (23.3-25.7)
>5	2606	75 (74-76)	851	75.5 (74.3-76.7)
Type of house				
Kutcha	1168	33.6 (32.5-34.7)	395	35 (33.6-36.4)
Pucca	2309	66.4 (65.3-67.5)	732	65 (63.6-66.4)
Residence				
Urban	2755	79 (78.1-79.9)	895	79.4 (78.2-80.6)
Rural	722	21 (20.1-21.9)	232	20.6 (19.4-21.8)
People sleeping in one room				
Single	35	1 (0.8-1.2)	12	1 (0.7-1.3)
Double	69	2 (1.7-2.3)	23	2 (1.6-2.4)
More than 2	3373	97 (96.6-97.4)	1092	97 (96.5-97.5)
Ventilation				
Window	2711	78 (77.1-78.9)	880	78 (76.8-79.2)
Ventilator	766	22 (21.1-22.9)	247	22 (20.8-23.2)
Water source for drinking				
Tube well	319	9.2 (8.5-9.9)	91	8 (7.2-8.8)
Borehole	1509	43.4 (41.9-44.1)	518	46 (44.6-47.4)
Filter plant	515	14.8 (14-15.6)	138	12 (11.1-12.9)
Public supply	1134	32.6 (31.5-33.7)	380	34 (32.6-35.4)
Smoking status				
Non-smoker	3352	96.4 (96-96.8)	1083	96 (95.4-96.6)
Smoker	125	3.6 (3.2-4)	44	4 (3.4-4.6)
DM status				
Diabetic	129	3.7 (3.3-4.1)	63	5.6 (4.9-6.3)
Non-diabetic	3348	96.3 (95.9-96.7)	1064	94.4 (93.7-95.1)

CI = confidence interval; DM = diabetes mellitus; TB = tuberculosis.

Table 4
Determinants of extended contact screening among patients with pulmonary tuberculosis in four selected districts, Pakistan 2013–2015.

	OR	95% CI		aOR	95% CI	
Age in years						
<15	2.82	1.88	4.3	2.69	2.21	3.28
15–43	Ref			Ref		
45–64	0.89	0.79	1	1.03	0.95	1.12
≥65	0.47	0.39	0.56	0.97	0.86	1.1
Sex						
Female	Ref			Ref		
Male	1.7	1.54	1.88	1.3	1.21	1.4
City						
Islamabad	Ref			Ref		
Lahore	1.54	1.16	2.04	1.89	1.49	2.4
Faisalabad	2.02	1.52	2.68	2.57	2.01	3.29
Rawalpindi	1.4	1.05	1.87	1.48	1.16	1.9
Classification by laboratory						
Bacteriologically confirmed	Ref			Ref		
Clinically diagnosed	0.03	0.03	0.04	0.14	0.12	0.15
Marital status						
Married	Ref			Ref		
Single	1.11	0.97	1.26	1	0.93	1.09
Education status						
No schooling in <15 yrs	0.3	0.14	0.63	2.7	2.1	3.5
No schooling in ≥15 yrs	4.65	3.98	5.44	0.96	0.88	1.05
Primary	Ref			Ref		
Secondary	0.95	0.82	1.09	1	0.9	1.15
Tertiary	0.91	0.73	1.14	0.98	0.82	1.18
Madrassah	0.99	0.74	1.32	1	0.82	1.2
Occupation						
Not working in <15 yrs	44	21.66	90	4.1	3.3	5.2
Not working in >15 yrs	Ref			Ref		
Agriculture	0.99	0.8	1.23	0.95	0.83	1.08
Student	0.4	0.33	0.47	0.75	0.66	0.83
Labor	0.74	0.64	0.85	1.02	0.93	1.13
Govt. Service	0.51	0.4	0.65	0.82	0.68	0.99
Business	0.58	0.47	0.71	0.94	0.81	1.1
Family income						
<20,000	Ref			Ref		
21,000–50,000	0.84	0.73	0.97	0.83	0.74	0.92
>50,000	0.84	0.70	1.01	0.76	0.66	0.88
Total household members						
<5	Ref			Ref		
>5	0.68	0.61	0.77	0.95	0.87	1.04
Type of house[a]						
Kutcha	Ref			Ref		
Pucca	1.1	0.97	1.25	1.87	1.72	2.03
People sleeping in one room						
Single	Ref			Ref		
Double	1	0.60	1.7	1.05	0.67	1.64
More than 2	1.15	0.75	1.76	0.98	0.68	1.41
Water source for drinking						
Public supply	Ref			Ref		
Tube well	0.29	0.23	0.36	0.91	0.79	1.04
Borehole	0.89	0.79	1	1.08	0.99	1.18
Filter plant	0.96	0.83	1.12	1.29	1.14	1.45
Smoking						
Non-smoker	Ref			Ref		
Smoker	1.0	0.76	1.34	1.17	0.96	1.43
DM						
Non-diabetic	Ref			Ref		
Diabetic	1	0.81	1.27	0.97	0.81	1.16

Aor = adjusted odds ratio; CI = confidence interval; DM = diabetes mellitus; TB = tuberculosis.

[a] Kutcha houses are made of raw materials that are easily available such as stone, wood, mud, or straw. Pucca houses are built using materials such s iron, cement, bricks, and steel.

patients. We found no significant differences in education, marital status, number of persons in the household, number of persons sleeping in one room, ventilation, water source for drinking, smoking, and diabetes mellitus status.

In our study, the ECS group had a higher proportion of children with PTB compared with the routine PCF group. This is similar to the findings of a study on ACF conducted in Myanmar (Aye et al., 2018), and suggests that the routine program may have missed child patients, which should be addressed while scaling up this intervention. Within the ECS group, there were more patients aged 15–44 years and a lower proportion of patients aged 45-64 years identified through household-contact tracing than through neighborhood screening. Our findings are consistent with a study from Peru that screened household contacts and members of neighborhood (Becerra et al., 2005).

We observed a higher proportion of males identified through ECS than through PCF. The prevalence survey conducted in Pakistan in 2011 showed that TB prevalence among men was almost double that of women (Qadeer et al., 2016), thus we expected TB notification to also be markedly higher for men (approximately two-thirds male). The proportion of male patients identified and reported in 2015 ranged from 49% (Sindh) to 59% (Gilgit-Baltistan Province), thus it seems more men than women remain unidentified and untreated (National Tuberculosis Programme Pakistan, 2016). A study conducted in Karachi, Pakistan also showed higher TB notification rates in female than in male patients (Codlin et al., 2011). A higher prevalence of TB among men has been reported from almost all other countries in the world (Borgdorff et al., 2000), as well as from TB prevalence surveys in Asia (Onozaki et al., 2015). A systematic review and meta-analysis suggested that men may be less likely than women to seek or access care in many settings (Horton et al., 2016). From this we would expect a higher proportion of men among those missed in routine PCF but identified through ACF, which is what we observed in our study.

Of the patients identified through ECS, 88% had bacteriologically confirmed TB, compared with only 50% of those identified through routine PCF. This may be to a large extent attributed to the algorithm used for identifying patients with TB: the ECS was mostly performed using the Xpert MTB/RIF testing, resulting in most patients being confirmed bacteriologically, while a much higher proportion of routine patients with TB were clinically diagnosed and treated following standard guidelines for TB diagnosis. This is also consistent with the findings of a study from Zambia that used ACF (Kagujje et al., 2020).

There were more patients in the lowest-income category and patients living in kutcha houses in the group identified through ECS than in the group identified through PCF. Given that patients with TB identified through ECS are more often of low socioeconomic status than those identified through PCF, they have less resources to visit a clinic on their own initiative, but are likely to be identified during home visits. TB cases detected by ECS were more often from urban settings compared with the PCF group. The burden of TB disease is generally considered to be higher in urban settings than rural settings because of crowding and occupational transmission (Kapata et al., 2016). The poor peri-urban areas of developing countries, where living conditions are unsatisfactory, with overcrowding, poor hygiene, and inadequate sanitation, are usually more affected by TB (Banerjee et al., 1999; Tupasi et al., 2000b). Such living conditions of lack of access to health care and poor health-seeking behavior may promote transmission of TB (Tupasi et al., 2000a, 2000b). However, a large prevalence survey in Pakistan showed that bacteriologically positive TB was more common among rural than urban residents in Pakistan (Qadeer et al., 2016).

ACF has been widely recommended as an important strategy in addition to standard PCF for the control of TB in low- and middle-income countries with high disease burden (Reid et al., 2019). Studies conducted in different countries confirmed the obvious fact that ACF is more cost-effective in high-burden settings. A study conducted in Pakistan found that the incentive-based ACF program was more effective and less expensive than PCF (Hussain et al., 2019). Another study in Pakistan also showed that active approaches to contact investigation effectively identify additional patients with TB among household contacts at a relatively modest cost (Hussain et al., 2021). However, a study from Russia showed that ACF has low yield and high cost in low-burden settings (Bogdanova et al., 2019). Given the limited evidence on cost efficiency in high-burden and resource-limited settings, significant scale-ups of ACF should be rationally planned (Dobler, 2016; Lung et al., 2019).

This study had several strengths. There was a large sample size, enabling fairly precise estimates and using a sensitive and specific test for examining sputum. The study also had several limitations. The data were several years old, and some changes in routine PCF have occurred since then, such as the introduction of routine GeneXpert examination at many health facilities. The population of the selected study area has a somewhat higher socioeconomic status than the average in Pakistan, thus care must be taken when generalizing results. Other limitations include recall bias because participants provided responses retrospectively, after they had been registered for TB treatment. We aimed to reduce this bias by questioning and re-confirming participants' responses. Another weakness is that we used convenience sampling for the passively detected cases. This could have introduced bias because we studied mainly the cases that were easy to approach, and their characteristics may have been different from those of other cases. However, the included and excluded passively detected cases had similar distributions of age and sex, favoring a fairly unbiased selection.

In conclusion, our innovative ACF strategy identified a higher proportion of men and children with PTB than routine case finding; both of these groups are more often missed by routine TB control. ACF should be considered as an important addition to standard case finding.

Declarations of competing interest

The authors have no competing interests to declare.

CRediT authorship contribution statement

Mahboob Ul Haq: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Sven G. Hinderaker:** Conceptualization, Formal analysis, Methodology, Resources, Software, Visualization, Writing – original draft, Writing – review & editing. **Razia Fatima:** Conceptualization, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Ejaz Qadeer:** Conceptualization, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Hammad Habib:** Data curation, Methodology, Resources, Visualization, Writing – original draft, Writing – review & editing. **Kashif Hussain:** Data curation, Resources, Visualization, Writing – original draft, Writing – review & editing. **Abdul Wali Khan:** Data curation, Methodology, Resources, Supervision, Visualization, Writing – original draft, Writing – review & editing.

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Ethical approval

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.04.055.

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