Article:
Khanal, S, Baral, S, Shrestha, P et al. (7 more authors) (2016) Yield of intensified tuberculosis case-finding activities using Xpert® MTB/RIF among risk groups in Nepal. Public Health Action, 6 (2). pp. 136-141. ISSN 2220-8372

https://doi.org/10.5588/pha.16.0015

Title: Yield of intensified tuberculosis case finding activities using Xpert MTB/RIF among risk groups in Nepal

Authors and affiliations:

Sudeepa Khanal (1), Sushil Baral (1), Prabin Shrestha (1), Bikas Lamichanne (2), Shyam Kandel(1), Helen Elsey(3), Miranda Brouwer (4), Sonu Goel (5) Palanivel Chinnakali (6)

1-Health Research and Social Development Forum (HERD), Kathmandu, Nepal

2- National Tuberculosis Centre, Thimi, Bhaktapur, Nepal

3- Nuffield Centre for International Health and Development, Leeds Institute of Health Science, Leeds, UK

4- Independent Consultant

5- Post Graduate Institute of Medical Education and Research, Chandigarh, India

6- Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

Name and address for correspondence:

Sudeepa Khanal

Health Research and Social development Forum

Thapathali Heights

Po Box: 24133

Kathmandu, Nepal

Email: khanal.sudeepa@gmail.com

Running title: Yield of Intensified TB case finding in Nepal

Key words: Operational research, TB REACH, systematic screening, number needed to screen

Paper content:

Word count (abstract):

Word count (Narrative):

Tables/boxes: 3

Figure: 1

References:

ABSTRACT

Setting: Twenty two districts in Nepal where intensified TB case finding (ICF) activities were implemented among risk groups under TB REACH project in collaboration with National TB program from May 2013 to November 2015.

Objectives: To assess the yield (drug sensitive and drug resistant) of TB screening using an algorithm with smear microscopy followed by Xpert MTB/RIF.

Design: Descriptive study using routinely collected data.

Results: Of total 145,679 individuals screened between May 2013 and November 2015, 28,574 (19.6%) had presumptive TB; 1239 (2%) individuals were diagnosed with TB; 1195 (96%) were initiated on anti-TB treatment. The yield was highest among PLHIV (6.1%) followed by household contacts (3.5%) and urban slum dwellers (0.5%). Among other risk groups like prisoners, factory workers, refugees and diabetics, the yield was less than 0.5%. Number needed to screen (NNS) to diagnose an active TB case was 17 for PLHIV, 29 for household contacts and 197 for urban slum dwellers. Of 11,525 patients from ICF and routine program, 112 (1%) were diagnosed with MDR-TB (rifampicin resistant).

Conclusion: There was substantial yield of TB cases among risk groups like PLHIV, household contacts and urban slum dwellers and hence systematic screening should be implemented in these risk groups.

INTRODUCTION

Tuberculosis (TB) remains a global public health problem with an estimated 9.6 million new cases in 2014, of which only 6 million new cases (63%) were reported.[1] This means that 3.6 million new cases (37%) worldwide went undiagnosed or were not reported. In line with STOP

TB strategy (2006-2015)[2], the newer END TB strategy (2016-2030)[2] emphasizes early diagnosis of TB including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups to reduce the case detection gap. Further, to address the gaps in case detection, the World Health Organization (WHO) recommends intensified case finding (ICF) among selected risk groups like household contacts, people living with HIV, people in prisons and other penitentiary institutions, and geographically defined sub populations with high levels of undetected TB like urban slum dwellers.[4]

ICF has been extensively used in variety of settings and this strategy has been effective in reducing the TB prevalence, incidence and mortality. [5] With increase in the use of rapid test Xpert MTB/RIF in low and middle income countries since 2010 and its improved sensitivity in detecting TB, inclusion of the rapid test in the screening algorithm had demonstrated an improvement in case detection.[2]

In Nepal, low TB case detection among poor and marginalized groups is one of the primary strategic challenges faced by National Tuberculosis Programme (NTP). Slum dwellers, PLHIV, prisoners, refugees and congregate settings such as factories, hostels and armed service personnel barracks are identifies as high-risk groups by the NTP. [6] In 2012, of 66,000 estimated prevalent cases, only 35,438 TB cases were reported to NTP with a case notification rate (CNR) of 136/100000. There has been no substantial improvement in the overall CNR (all forms) and CNR of smear positive cases during 2010-2013.[6] Hence, to improve early case detection and overall diagnosis in risk groups, several strategies were implemented. Under the TB REACH project, a non-governmental organization 'Health Research and Social Development forum'(HERD) in collaboration with NTP, implemented ICF activities through mobile camps using Xpert MTB/RIF in

22 districts of Nepal since May 2013. These mobile camps along with two static sites with Xpert MTB/RIF diagnostic facilities focused on TB case detection among urban slum dwellers, factory workers, prisoners, refugees, monks or nuns, persons with diabetes, people living with HIV/AIDS (PLHAs) and household contacts of TB patients.

In this study, we aimed to assess the yield of these ICF strategies among different risk groups and their impact on overall CNR. Specific objectives were a) to determine the number and proportion of adults screened, diagnosed and initiated on anti-tuberculosis treatment disaggregated by risk groups b) to determine the number and proportion diagnosed with multi drug resistant tuberculosis (MDR TB) c) to assess the difference in CNR in districts before and after implementation of ICF strategies compared to difference in CNR in control districts where there was no ICF.

METHODS

Study Design: This was a descriptive study using routinely collected data under HERD's TB REACH Project and NTP.

General settings: Nepal is a landlocked country in South Asia, having an area of 147,181 km^2 and a population of 26,494,405.[9] The National Tuberculosis Centre (NTC) established in 1989 is the focal point of the National Tuberculosis Programme (NTP) in the country. It has 5 Regional Health Directorates (RHD) and 1 Regional Tuberculosis Centre (RTC) at the regional level to implement the programmes. At the district level, the District Health/Public Health Office implements the NTP activities within the districts and within each district, district hospitals and Primary Health Care Centres (PHCs), Health Post and Urban Health Clinics in the urban areas are the basic management units for diagnosis and treatment of tuberculosis patients. NTP follows WHO recommended DOTS strategy for treatment and follows passive case finding strategy for TB case detection. Patients with cough for duration more than 2 weeks (presumptive TB patients) are evaluated for TB.

In 2013/2014, a total of 37,025 TB cases were registered under NTP; 51% were pulmonary cases. TB-HIV co-infection rate is 2.5% (HIV among TB) and 11.6% (TB among HIV). As of 2013, there were 4,258 health institutions offering DOTS and 554 microscopy centres offering sputum smear microscopy services. Culture and DST services under the NTP are provided at two sites in the capital city of Kathmandu.[8]

Study sites:

Study sites included i) 22 districts where intensified case finding strategies were implemented under TB REACH program ii) 12 control districts where no intensified case finding strategies were implemented. Intervention and control districts were selected based on high proportion of urban population and/or presence of target population groups in high numbers, geographical location and case notification rates in consultation with National TB program managers.

Study population: Study population in intervention districts included risk groups such as urban slum dwellers, factory workers, prisoners, refugees, monks or nuns, people living with HIV/AIDS (PLHAs), household contacts of TB patients and diabetics) from May 2013 to Nov 2015. In control districts, all adult TB patients diagnosed through routine program were included. (July 2013 to June 2014)

Intensified case finding strategies under TB REACH programme:

Under the TB REACH programme, NTP implemented ICF strategies in 22 districts since May, 2013. In this project, two mobile Xpert MTB/RIF machines were used in mobile camps for diagnosis of TB and MDR-TB. Each mobile clinic was staffed with a laboratory assistant, a driver and a support staff. The mobile team were supported by community volunteers in urban areas and out-reach workers (ORWs) in rural areas for screening and sputum collection. The mobile camps were supervised by the project team consisting of a doctor, paramedics and a project leader trained in public health. The mobile van covered one district once in three months for 5-7 days. However, based on the need of the district (volume of risk groups), the van was mobilized for a maximum of 15 days in a district.

In addition to mobile clinics, two sites (Chitwan and Doti Hospitals) provided TB diagnostic services (static clinics) using Xpert MTB/RIF. These sites provided Xpert MTB/RIF services not only to the targeted population of the TB REACH project but also to presumptive TB patients identified in regular out-patient department (OPD). The various risk groups and different strategies used to reach them are explained in **Box-1**. Among the risk groups, any individual having cough for duration of more than 2 weeks was considered as 'presumptive TB patient' and underwent diagnostic evaluation (Algorithm in Annexure). In case of household contacts and PLHA, cough of any duration was considered as 'presumptive TB'. Those diagnosed with TB were referred to the nearest health centre for initiation of DOTS under the NTP.

Data variables and data sources:

For each risk group, aggregate numbers of people screened, presumptive TB, diagnosed with TB and initiated on anti-TB treatment were extracted from the quarterly reports of the TB REACH project for the period between July 2013 and November 2015. Aggregate number of persons

diagnosed with MDR TB were collected from the Xpert MTB/RIF register of the TB REACH project. CNR (all forms) for the study districts and control districts were extracted from NTP annual report for one year before the intervention (July 2012-June 2013) and one year after the intervention (July 2013-June 2014).

Data entry and Data analysis:

Project data was entered and aggregated using Microsoft excel. From the data obtained, frequencies and proportions of person screened, diagnosed and initiated on treatment (TB) were calculated. Yield of ICF was calculated by total number of diagnosed TB cases among each risk group divided by total risk population screened. Number needed to screen (NNS) to diagnose a TB case was calculated by taking the inverse of prevalence of active TB in that risk group. Difference in change in CNR between two time periods (2012/2013 and 2013/2014) in study and control districts was compared.

Ethics:

The study protocol was reviewed and approved by Ethics Advisory Group of The International Union Against Tuberculosis and Lung Disease, Paris, France. Permission was obtained from the Director of the NTP for using the data. Since the study used secondary data and no patient identifiable data was used, the named ethics committee waived the need for obtaining patient consent.

Results

Under ICF activities in intervention districts, a total of 145,679 individuals belonging to different risk groups were screened for TB. Of this total, 28,574 (19.6%) had symptoms suggestive of TB (presumptive TB) and 1239 individuals were diagnosed with TB; 1195 (96%) were initiated on anti-TB treatment. Number screened, diagnosed and initiated on anti-TB treatment in different risk groups is shown in **Table 1**. The yield was highest among PLHIV (6.1%) followed by household contacts (3.5%) and 0 .5% or less among other risk groups. Hence, NNS to diagnose a case of TB was 17 for PLHIV, 29 for household contacts and 197 for urban slum dwellers.

The distribution of diagnosis of TB using smear microscopy and subsequent Xpert MTB/RIF across different risk groups is shown in **Table 2**. Of 28,574 identified presumptive TB patients, sputum samples of 26,447 (93%) individuals were collected and examined for TB using smear microscopy; 523 individuals (2%) were smear positive. Of 25,924 individuals, whose sputum samples were smear negative, only samples of 9,716 (37%) individuals were subjected to Xpert MTB/RIF; 716 (7%) patients tested positive for TB. Sputum samples of 16,208 individuals (63%) were not tested for TB using Xpert MTB/RIF. Overall, of total diagnosed TB cases, 58% were diagnosed using Xpert MTB/RIF. This proportion was higher in PLHIV (77%) and household contacts (64%).

Apart from 9,716 presumptive TB patients identified during ICF, 1,809 patients were referred from routine program for the diagnosis of drug resistance TB using Xpert MTB/RIF. Of 11,525 patients, 112 (1%) were diagnosed with MDR-TB (rifampicin resistant).

The case notification rates (per 100,000 population) in the intervention districts before (July 2012-June 2103) and during (July 2013-June 2014) were 162 and 164 respectively with an increase of 2 per 100,000 population. In control districts, the CNR during the two periods were

116 and 114 with a decrease of 2 per 100,000 population indicating a change in CNR of 4 per 100,000 population in intervention districts.

Discussion

This is the first study from Nepal assessing the yield of ICF activities among adults using Xpert MTB/RIF in mobile vans. The study found that the yield was higher among PLHIV, household contacts and urban slum dwellers. More than half of TB cases under ICF were diagnosed using Xpert MTB/RIF which would have gone unidentified if Xpert MTB/RIF was not used as their microscopy results showed smear negative.

The study has the following strengths. First, this is the first study from Nepal which evaluates the yield of ICF activities among adults in several risk groups and also involved large geographical area of 22 districts. Second, the inclusion of Xpert MTB/RIF in the screening algorithm which has higher sensitivity and specificity and making it available in mobile units increased the yield. Third, the study was conducted in routine program setting in collaboration with national program which makes it easier to upscale the ICF activities to other districts.

Our study findings on high yield of screening among PLHIV and household contacts are comparable to other studies conducted in moderate prevalence countries. [9,10,11,12,13] NNS to diagnose a case of TB was 17 for PLHIV and 29 for household contacts. This is comparable with the NNS reported in a systematic review; NNS of 13 (2-120) for PLHIV and 25 (3-568) for household contacts. In our study, about two thirds of PLHIV and about half of household contacts had presumptive TB.[14] A study from Ethiopia reported that the proportion of PLHIV with presumptive TB was 39%.[15] The proportion of presumptive TB depends on many factors like the prevalence of active TB, host factors and infection control measures at health facilities.[16] The differences in the definition of presumptive TB across studies also makes it difficult to compare.

In our study, more than half of TB cases were diagnosed using Xpert MTB/RIF using the same sputum samples on which smear microscopy was done and declared as smear negative. This confirms yet again the increased sensitivity of Xpert MTB/RIF in diagnosing TB compared to conventional microscopy even in field settings. Among presumptive TB patients who were smear negative, more than half of them did not get tested with Xpert MTB/RIF reasons being poor quality of sputum samples collected by volunteers without proper instructions to the patients, poor understanding of the patients despite instructions on sputum production, inability to operate Xpert MTB/RIF machine to conduct test due to power failure, problems related to transportation of sputum samples from microscopy centres to static or mobile Xpert MTB/RIF units and issues related to calibration of Xpert MTB/RIF machines leading non-availability for testing for short time periods.

Though the ICF activities showed a substantial yield among few risk groups like PLHIV, household contacts and urban slums, there was only a small increase in the overall CNR in the intervention districts. The total yield (absolute number of TB cases detected) is driven by both the size of the risk group in the general population and the prevalence of TB within that risk group. Often, the groups at the highest risk of TB like PLHIV and household contacts are also the smallest, and groups with only a moderately elevated risk like urban slum dwellers and diabetes patients can be very large. Hence, the success of ICF activities depends on many factors including the proportion of undiagnosed cases in the risk groups, size and coverage of the risk groups, algorithm used in screening.

In the current study, data for CNR for all the districts was available for only one year period and there were delays in implementation of the ICF in selected districts which might have decreased the impact. Previous studies have shown the usefulness of the ICF and its role in reduction of TB incidence, prevalence and mortality in different settings.[4] The impact of ICF activities in several districts on improving childhood TB case notification rates have been documented recently in Nepal.[17] However, ZAMSTAR, a community-randomised trial done in Zambia and the Western Cape province of South Africa showed neither of the intervention (community-level enhanced tuberculosis case-finding (ECF) and household level tuberculosis-HIV care) led to a statistically significant reduction in tuberculosis burden in the community. It

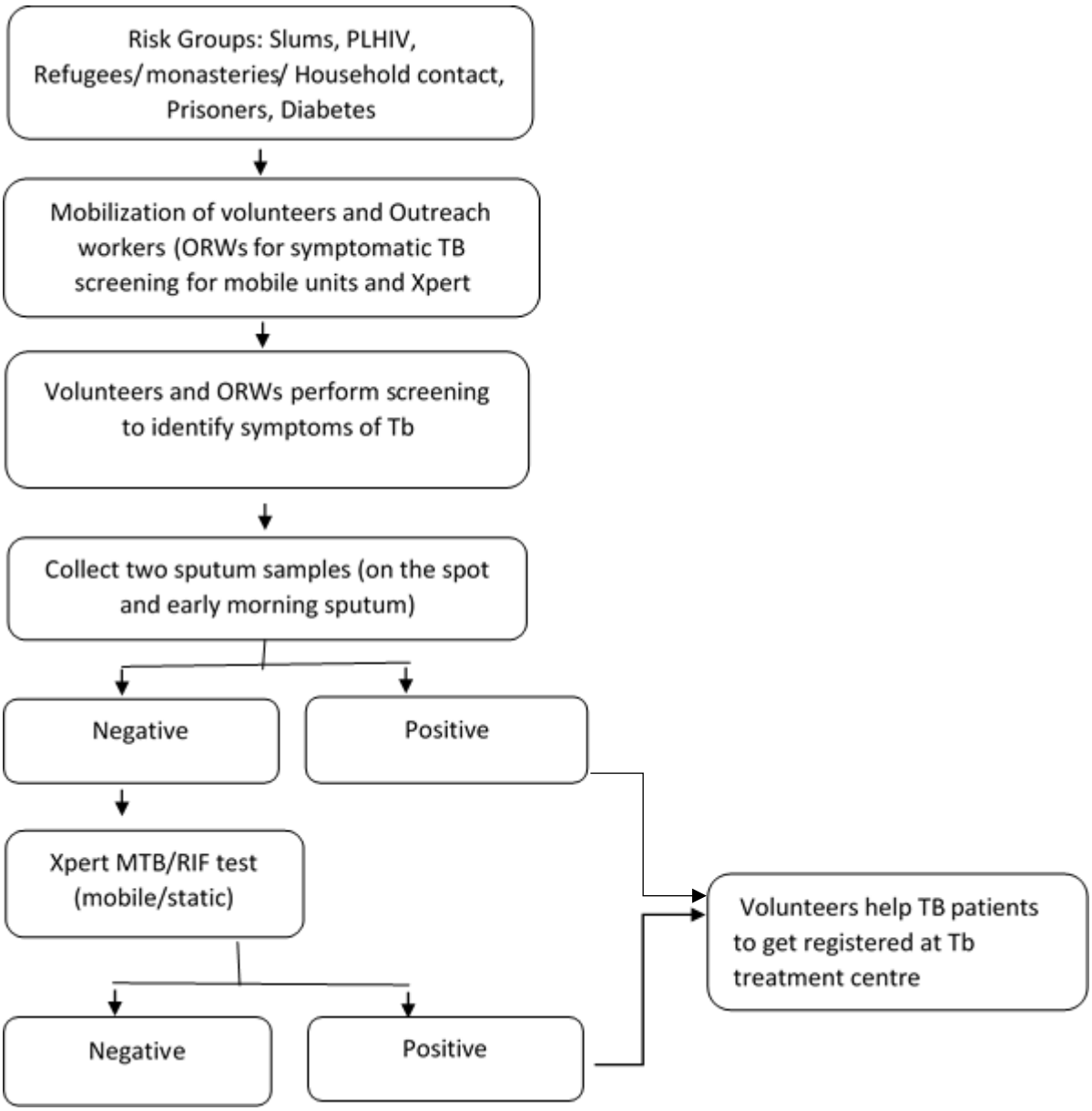
is important to note that the trial involved only enhanced case finding, not systematic screening (active screening) as done in the present study.[18]

There were limitations. More than half of presumptive TB patients who were smear negative did not get tested with Xpert? and this would have underestimated the yield. Since community volunteers were involved in identification of presumptive TB in risk groups, errors would have happened in asking for the symptoms leading to decreased yield. We did not assess the coverage of each risk group as valid estimates were not available at district level for all risk groups. Since large manpower and material resources were involved in these ICF activities, cost-effectiveness study would have helped to assess the usefulness of these interventions.

The study has several policy implications. First, considering the yield among PLHIV and household contacts, in a resource limited setting, ICF activities should be targeted to PLHIV and household contacts for better utilization of resources. Strengthening the existing strategies including ICF in these groups will enhance early case detection and reduce disease complications and mortality in this group. Second, though the yield is moderate among urban slums, systematic screening should be initiated considering the large population size and poor health seeking behaviour of urban slum dwellers. This will help in improved case detection, reduce delays in treatment initiation and also early detection and management of drug resistance TB.

In conclusion, there was substantial yield of TB cases in different risk groups using ICF strategies. Though there was no significant increase in overall case notification in the short term, considering the benefits of early case detection, systematic screening can be implemented for selected high risk groups like PLHIV, household contacts and urban slum dwellers.

Figure: Algorithm of intensified tuberculosis case finding strategies used for different risks groups for screening and testing in Nepal, 2013-2015



*[1] PLHIV refers to People Living with Human Immunodeficiency Virus

*[2] For PLHIVs, their sputum samples were tested both using a microscope and Xpert MTB/RIF machine simultaneously

*Patient suspected of TB means someone with a productive cough of more than 2 weeks duration and/or other symptoms of TB (e.g. fever, night sweats, loss of weight, chest pain, hemoptysis, and clinical signs of EPTB such as swollen glands)

Box 1: Intensified TB case finding strategies for various risk groups under HERD's TB REACH project in 22 districts of Nepal from May 2013-Nov 2015

Risk Groups	**Strategies***
Urban Slum Population	Mapping of slum areas. Microscopic camps conducted using mobile van with microscope and Xpert MTB/RIF. Mass screening was done by Volunteers/Outreach Workers (ORW). Identified presumptive TB patients were brought to mobile clinics and evaluated for TB following the NTP algorithm. Samples of those presumptive TB patients not visiting mobile clinics were collected by volunteers/ORWs during home visits and submitted in the mobile clinic or transported to the static laboratory. Besides, the awareness about mobile clinics were conducted by the volunteers/ORWs. Door to door screening for cough> 2 weeks by mobilization of volunteers/ORWs. Sputum of presumptive TB patients were collected from the households by Volunteers/ORWs during their home visits and their sputum transported to static laboratory.
People Living with HIV/AIDS	Communication links were established with all VCT/ART centres and PLHIV networks. Volunteers/ORWs screened existing PLHIV for TB, collected their sputum and transported it to mobile clinic or static clinic for TB diagnosis.
Household contacts of smear positive TB patients	Coordination was established with DOTS centres to identify existing index cases. Household contact of the index cases were identified, contacted and called for screening. Volunteers/ORWs screened the contacts for TB, collected their sputum and transported it to mobile clinic or static clinic for TB diagnosis. Definition of a household contact: A household contact is considered as all those living within the same house. Any individual who have stayed for overnight or longer in the household of an index case, were also considered as a household and called for screening.
People in Institutional settings (Factories, prisons, monasteries, refugee camps)	Institutional setting were identified and coordination done. Mobile camps were conducted at each of these institutions and those with >2 weeks of cough, their sputum was sent to mobile clinic or static clinic for diagnostic evaluation using the NTP algorithm.
Diabetics (Kathmandu district only)	Nursing staffs of the clinic were oriented on screening and sputum collection. Volunteers and mobile team visited the diabetes clinic to identify presumptive TB patients and followed NTP algorithm for diagnosis.

*In addition to mobile camps, the diagnosis was also carried out at static clinics in Kathmandu valley where Xpert MTB/RIF is available under the project.

Table 1. Yield and number needed to screen under intensified TB case finding activities among risk groups in twenty two districts of Nepal, 2013-2015.

Risk groups	Population screened (a)	Presumptive TB n(%) (b)	Number diagnosed with TB n(%) (c*)	Initiated on treatment n (%)	Yield (%) d=(c/a)	NNS (1/d)*100
Total	**145679**	**28574 (20)**	**1239 (4.3)**	**1195 (96.4)**	**0.8**	**118**
Slum dwellers	103027	10667 (10)	523 (5)	503 (96.1)	0.5	197
PLHIV	2149	1662 (77)	130 (8)	122 (93.8)	6.1	17
Household contacts	14547	7619 (52)	503 (7)	491 (97.6)	3.5	29
Prisoners	5490	2649 (48)	21 (0.7)	21 (100)	0.4	261
Factory Workers	12023	3457 (29)	36 (1)	32 (88.8)	0.3	334
Refugees/Monasteries	7424	2305 (31)	24 (1)	24 (100)	0.3	309
Diabetics	1019	215 (21)	2 (0.9)	2 (100)	0.2	510

TB-tuberculosis, NNS-number needed to screen to diagnose a case of TB

* diagnosed either by smear microscopy or by Xpert MTB/RIF

Table 2: Diagnosis of tuberculosis under intensified case finding activities stratified by smear microscopy and Xpert MTB/RIF in twenty two districts of Nepal, 2013-2015

Risk groups	Smear microscopy		Xpert MTB/RIF		Total Positive n	Proportion diagnosed by Xpert MTB/RIF (%)
	Tested n	Positive n (%)	Tested n	Positive n (%)		
Total	**26447**	**523 (1.9)**	**9716**	**716 (7.4)**	**1239**	**58**
Slum dwellers	9519	287 (3.0)	2974	236 (7.9)	523	45
PLHIV	1473	30 (2.0)	980	100 (10.2)	130	77
Household contacts	7122	181 (2.5)	2599	322 (12.4)	503	64
Prisoners	2628	9 (0.3)	546	12 (2.2)	21	57
Factory Workers	3385	11 (0.3)	1232	25 (2.0)	36	69
Refugees/Monasteries	2182	3 (0.1)	1319	21 (1.6)	24	88
Diabetics	138	2 (1.4)	66	0 (0.0)	2	0

TB-tuberculosis, PLHIV-people living with HIV

Acknowledgement

This research was conducted through the Structured Operational Research and Training Initiative (SORT IT), a global partnership led by the Special Programme for Research and Training in Tropical Diseases at the World Health Organization (WHO/TDR). The model is based on a course developed jointly by the International Union Against Tuberculosis and Lung Disease (The Union) and Medécins sans Frontières. The specific SORT IT programme which resulted in this publication was jointly developed and implemented by: The Union South-East Asia Regional Office, New Delhi, India; the Centre for Operational Research, The Union, Paris, France; the Operational Research Unit (LUXOR), Médecins Sans Frontières, Brussels Operational Center, Luxembourg; School of Public Health, Post Graduate Institute of Medical Education and Research, Chandigarh, India; and the Department of Preventive and Social Medicine, Jawaharlal Institute of Postgraduate Medical Education & Research, Puducherry, India.

We would like to express our deepest appreciation to all those who supported us to successfully complete this study. The data has been taken from the study "Using Gene Xpert MTB/RIF to Reach the Unreached: Mobile Diagnostic Case Finding in Nepal" a TB REACH project delivered by HERD in collaboration with the National Tuberculosis Control Programme. The implementation of the study was funded by Stop TB partnership, World Health Organization. We would also like to acknowledge the support of the respective District Health Officers, volunteers and districts staffs involved for their support throughout the implementation of the study.

FUNDING

The programme was funded by the Department for International Development (DFID), UK. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

The funding for the programme implementation "Using Xpert to Reach the Unreached: Mobile Diagnostics Case Finding in Nepal" was from the World ealth Orgabisation

CONFLICT OF INTEREST: No conflict of interest

References

1. World Health Organization. Global Tuberculosis Report 2015. WHO, Geneva, Switzerland.
2. World Health Organization. The Stop TB Strategy. 2006. WHO, Geneva, Switzerland.
3. World Health Organization. The End TB Strategy. 2015. WHO, Geneva, Switzerland
4. World Health Organization. Improving early case detection of active Tb through systematic screening. 2013 WHO, Geneva, Switzerland. WHO/HTM/TB/2013.04.
5. Saraceni V, King BS, Arduini D, et al. Ruling out tuberculosis to start preventive therapy in HIV co-infected patients as an opportunity to find TB. The International Journal of Tuberculosis and Lung Diseases. 2008; 12(11 (Suppl 2)):S56.
6. National Tuberculosis Programme, Annual Report FY 2069/70 (2012/2013). National Tuberculosis Centre, Ministry of Health and Population, Government of Nepal
7. National Tuberculosis Programme, Annual Report FY 2070/71 (2013/2014). National Tuberculosis Centre, Ministry of Health and Population, Government of Nepal
8. World Health Organization, World Health Statistics 2014. WHO, Geneva, Switzerland

9. Nsanzumuhire H, Aluoch JA, Karuga WK, et al. A third study of case-finding methods for pulmonary tuberculosis in kenya, including the use of community leaders. Tubercle. 1981;62(2):79–94.
10. Jackson-Sillah D, Hill PC, Fox A, et al. Screening for tuberculosis among 2381 household contacts of sputum-smear-positive cases in The Gambia. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2007;101(6):594–601.
11. Zachariah R, Spielmann MP, Harries AD, et al. Passive versus active tuberculosis case finding and isoniazid preventive therapy among household contacts in a rural district of Malawi. The International Journal of Tuberculosis and Lung Disease. 2003;7(11):1033–9.
12. Mangi R, Pfau R, Ahmad S, et al. Incidence of child tuberculosis among household contacts of all types of TB patients: a 4-year study. The International Journal of Tuberculosis and Lung Disease. 2010;14(11 (Suppl 2)):S58.
13. de Jong BC, Hill PC, Aiken A, et al. Progression to active tuberculosis, but not transmission, varies by Mycobacterium tuberculosis lineage in The Gambia. The Journal of infectious diseases. 2008;198(7):1037–43.
14. Shapiro A, Chakravorty R, Golub J, Akande T, Lönnroth K (2013) A systematic review of the number needed to screen to detect a case of active tuberculosis in different risk groups. Geneva: World Health Organization. Available: http://www.who.int/tb/Review3NNS_case_active_TB_riskgroups.pdf Accessed 2013
15. Adelman MW, Tsegaye M, Kempker RR, Alebachew T, Haile K et.al. Intensified tuberculosis case finding among HIV-infected persons using a WHO symptom screen and Xpert MTB/RIF. The International Journal of Tuberculosis and Lung Diseases. 2015. Int J Tuberc Lung Dis. 2015 Oct;19(10):1197-203. doi: 10.5588/ijtld.15.0230.
16. World Health Organization. Systematic screening for active tuberculosis: An operational guideline. 2015. Geneva, Switzerland
17. B. Joshi, P. Chinnakali, A. Shrestha, M. Das, et.al.Impact of intensified case finding strategies on childhood TB case registration in Nepal.2015. Public Health Action. 2015 Jun 21; 5(2): 93–98.

18. Ayles, H., Muyoyeta, M., Du Toit, E. et al. 2013. Effect of household and community interventions on the burden of tuberculosis in southern Africa: the ZAMSTAR community-randomised trial. Lancet, 382(9899), 1183–94.